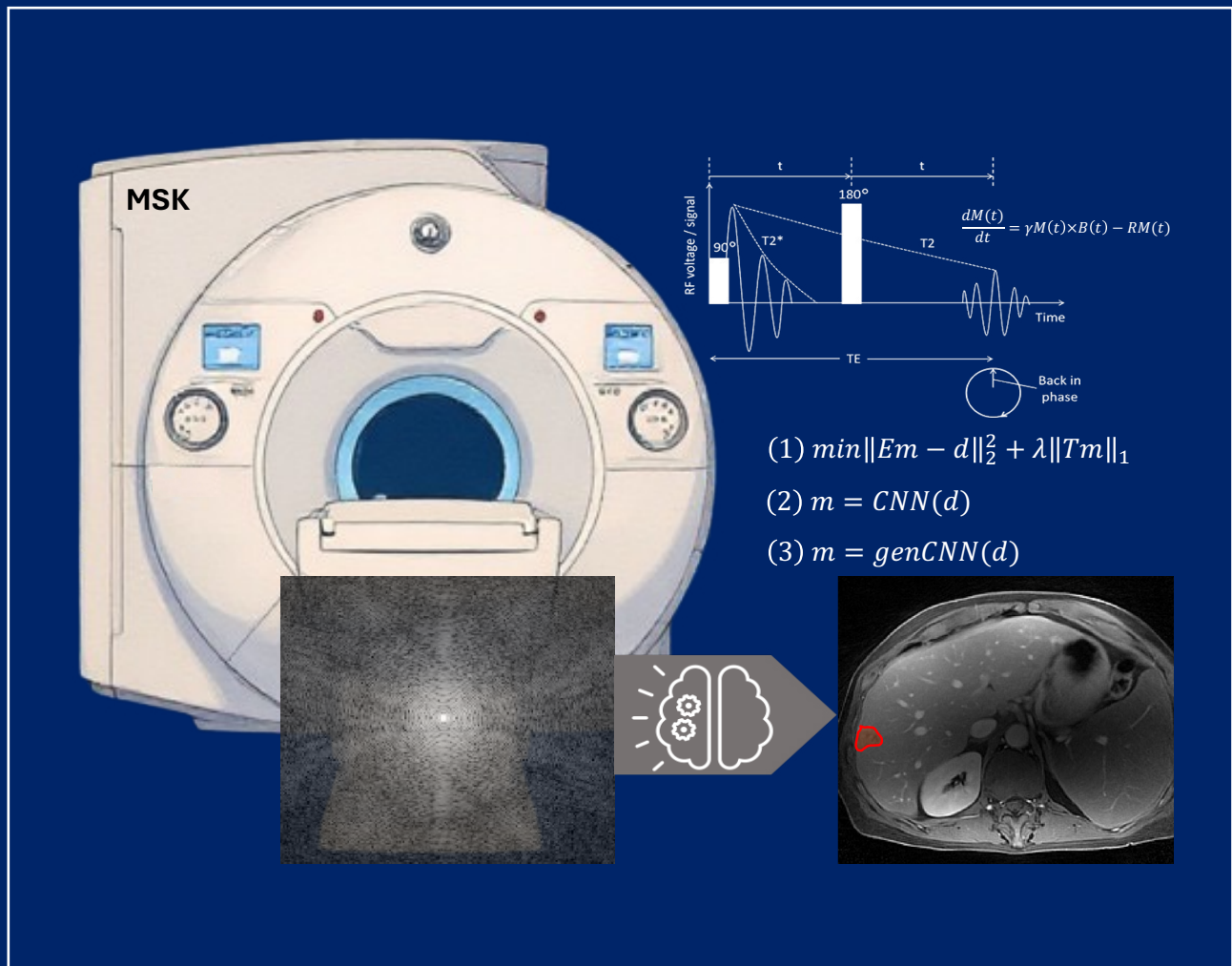


DEPARTMENT OF MEDICAL PHYSICS

Research and Development Report 2026



Memorial Sloan Kettering
Cancer Center



Cover: The cover figure illustrates the power of digital representations of medical equipment to go beyond hardware capabilities. For example, the digital representation of an MRI scanner using MR physics equations, simulations and AI can be employed to produce high-quality images.

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The Department of Medical Physics

More Information:



The Department of Medical Physics is a world leader in developing and applying advanced radiation therapy methodologies, biomedical engineering tools, and imaging techniques for cancer diagnosis, therapy guidance, and treatment response evaluation. The more than 300 faculty, fellows, and staff work together to ensure the highest quality and safety across a broad range of technologies used at MSK, and to develop new tools for cancer care from the latest advancements in physics, engineering and computer science.

Vision

- To advance, promote, and translate the latest concepts in science and technology that ensure MSK's continued leadership in cancer care

Mission

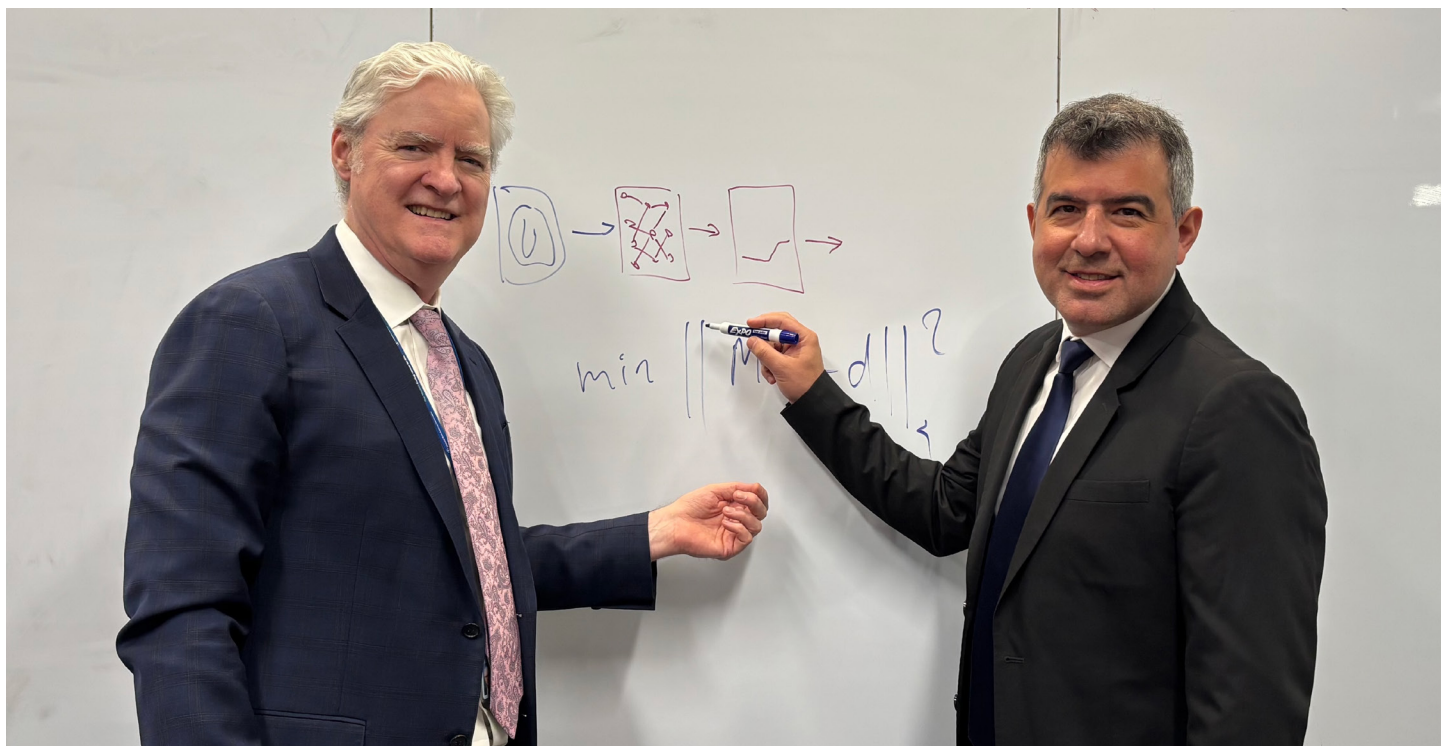
- Quality assurance of medical equipment (imaging, radiation therapy, surgery, telemetry, etc.) used at MSK – currently more than 50,000 medical instruments
- Ensure safety and regulatory compliance of imaging and therapy devices
- Implement new technologies into clinical practice
- To support excellence in patient care, innovative research, and training of future professionals in alignment with MSK's mission

A unique model for collaborative research

The departmental structure provides a critical mass of expertise that allows synergy across different activities performed at MSK. As an example, the Imaging and Radiation Sciences (IMRAS) program provides a unique model for collaborative research, where physicists and engineers develop and apply new technology according to realistic needs provided by clinicians. New technologies on imaging, radiation therapy, image analysis, biomedical engineering and informatics from Medical Physics are being pushed to Radiology, Radiation Oncology, Pathology, Surgery, Neurology, Medicine, and other departments.

Leader in AI innovation for cancer care

Over the last few years, the department has developed impactful AI techniques for improved cancer care using our rich, diverse patient data, including accelerated and motion-tolerant MRI scans, real-time tumor tracking to guide radiotherapy, cell-level quantitative pathology, image auto-segmentation, longitudinal treatment response evaluation, and large language models to assist clinicians. Development goes beyond applying standard AI technology to patient data; the approach is to develop new methods to tailor existing AI technology to clinical problems using models built upon advanced physics and engineering principles.

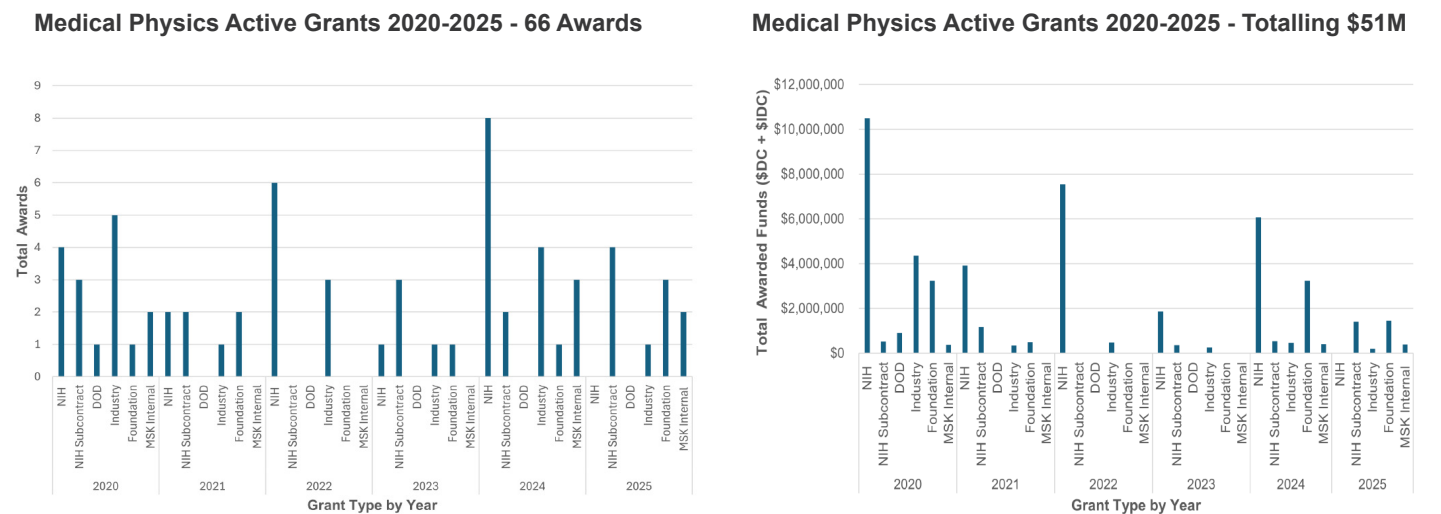


Dr. Joseph Deasy (Chair, Medical Physics) and Dr. Ricardo Otazo (Vice-Chair for Research, Medical Physics)

Research Grants

One of the main priorities of the Department of Medical Physics is the obtention of extramural funding to support our research and development program. Researchers have been successful in obtaining extramural grants from the National Institutes of Health (NIH), Department of Defense (DOD), industry, and foundations. Despite a competitive funding landscape, the high quality of innovation produced in the department has increased our NIH funding portfolio over the years. Industrial funding is obtained from medical imaging companies, such as General Electric and Philips, and radiotherapy companies, such as Varian and Elekta. These companies also participate in academic-industrial partnership grants sponsored by the NIH.

There are currently 66 active awards totaling 51 million dollars received in the period 2020-2025.



Total number of awards for the year when the notice of award was received and funding source (NIH, DOD, industry, foundation, MSK). Total award amount for the year the notice of award was received and funding source (NIH, DOD, industry, foundation, MSK).

Grant Writing and Submission Support: The department has a team of dedicated grant writer/editors who support investigators throughout the writing and submission process. The team develops and executes an annual training webinar in collaboration with the offices of Research and Technology Management (Research Development and Outreach, Grants & Contracts, and Research Finance) for new investigators and performs a complete review of the grant application to be submitted, providing copyedits and recommendations related to compliance with sponsor policies.

Research Committee: In 2023, a research committee was established to provide guidance and feedback on grant applications, particularly for early-stage investigators. The committee also proposes strategic directions for research projects and grant proposals that are aligned with departmental and hospital goals.



Jim Keller
Senior Editor and Grant Writer



Kylie Chester
Assistant Editor and Grant Writer



Laura Cerviño



Amita Dave



Joseph Deasy



John Humm



Jean Moran



Ricardo Otazo

Standing members of the Medical Physics Research Committee. Additional ad hoc members are added according to the expertise required to review a particular grant application.

Research Retreats

The Department of Medical Physics organizes regular retreats to facilitate interactions among different departmental and interdepartmental groups, including Radiology, Radiation Oncology, and Medicine. The retreats are organized to stimulate multi-disciplinary interactions between clinicians, physicists, and engineers in pre-defined areas of topical interest that focus on clinical problem solving in each disease site or address how to optimize the use of a new technology.

2022 Medical Physics Research Retreat

The 2022 Research Retreat was held at the NY Academy of Medicine on Saturday, May 21, 2022. The main topics were:

- Advances in Computational Treatment Planning & Segmentation
- Advances in Imaging
- Radiation Therapy Workflow and Automation
- MRI-guided Radiotherapy
- Predictive and Adaptive Radiotherapy
- Targeted Radionuclide Therapy
- Head & Neck Imaging and Therapy
- Lung Imaging and Therapy



2022 Medical Physics Research Retreat, Central Park

2024 Joint Medical Physics and Radiology Research Retreat

On Wednesday, May 29, 2024, the first joint research retreat between Medical Physics and Radiology took place at the Breast and Imaging Center (BAIC). The retreat content focused on imaging research and included the following topics:

- AI – From Image Acquisition to Image Analysis, including a panel discussion on clinical priorities for AI moderated by the Chair of Radiology, Dr. Lawrence Schwartz
- New imaging technology: total-body PET, MR fingerprinting, photon-counting CT and a demo session on virtual reality
- Combined Technology: theranostics, PET-MR, MRI-Linac and imaging-guided 3D printing



Drs. Ricardo Otazo (Vice-Chair for Research, Medical Physics), Joseph Deasy (Chair, Medical Physics), Lawrence Schwartz (Chair, Radiology) and Jason Lewis (Vice-Chair for Research, Radiology) at the 2024 Joint Medical Physics and Radiology Research Retreat

2025 Medical Physics Retreat focused on Radiation Oncology

The 2025 retreat was held on April 24, 2025 focusing on radiation therapy. The main topics were:

- Innovative Pilots for AI Auto-Segmentation
- Offline and Online Adaptive Therapy
- Digital Twins and Adaptive Therapy
- Planning Workflow Considerations and Automation Opportunities
- Reirradiation – Volumetric Assessment



2025 Medical Physics Research Retreat, Zuckerman Auditorium, MS

2026 Medical Physics Research Retreat focused on Imaging

The 2026 Research Retreat was held at the NY Academy of Medicine on Sunday, May 3, 2026, including the following main topics:

- AI-powered MRI: generative reconstruction, Movienet
- Molecular imaging: theranostics, total-body PET
- New developments: ultrasound imaging, oxygen-enhanced MRI
- Image analysis: AI, optimal mass transport



2026 Medical Physics Research Retreat, NY Academy of Medicine

Special Awards

Each year, the Department of Medical Physics is proud to recognize individuals for their contributions to the Department in the areas listed below.

Research Award of Excellence

Presented to eligible faculty who have demonstrated excellence in research through grant submission, publications, prizes & honors, clinical protocols, and patents.

2026: Antonio Damato, PhD, Jung Hun Oh, PhD
2025: Masoud Zarepisheh, PhD
2024: C. Ross Schmidtlein, PhD
2023: Harini Veeraraghavan, PhD
2022: Ellen Yorke, PhD
2021: Jung Hun Oh, PhD
2020: Harini Veeraraghavan, PhD
2019: Wei Lu, PhD
2018: Jung Hun Oh, PhD, C. Ross Schmidtlein, PhD
2017: Larry Dauer, PhD, Kyung Peck, PhD
2016: Guang Li, PhD
2015 (inaugural): Amita Shukla-Dave, PhD

Junior Faculty Research Award

Presented to junior faculty (Assistant level) who have demonstrated excellence in research through grant submission, publications, prizes & honors, clinical protocols, and patents.

2026: Tonghe Wang, PhD
2025: Saad Nadeem, PhD, Mark Burgess, PhD
2024: Maria Thor, PhD
2023: Gary Lim, PhD
2022 (inaugural): Saad Nadeem, PhD

Distinguished Teaching Award

Nominated by the Residents and Fellows and presented to the individual(s) who have demonstrated excellence through their enthusiasm, proactivity, and constructive feedback.

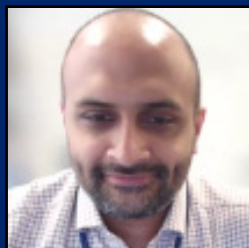
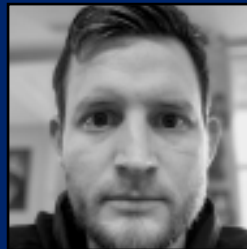
2026: Steven Blum, M.S., Yunjie Yang, PhD
2025: Brian Serencsits, M.H.P.
2024: Brian Leong, Brad Beattie, PhD
2023: James Mechalakos, PhD, Ross Schmidtlein, PhD, Matthew Williamson, M.P.H.
2022: Laura Happersett, M.S., Wendy Harris, PhD, Adam Kesner, PhD
2021: Bae Chu, M.P.H., Niraj Shah, M.S.
2020: Daniel Chiappetta, M.S., Katherine Chapman Ohri, PhD
2019: Ellen Yorke, PhD
2018: Gil'ad Cohen, M.S.
2017: Sean Berry, PhD, Brian Quinn, M.S.
2016: Pat Zanzonico, PhD
2015 (inaugural): Marco Zaider, PhD

Clinical Service Award

Presented to the individual(s) who have demonstrated excellence with a significant clinical contribution.

2026: Finn Augensen, M.S.
2025: Toni Roth, Shi Liu, PhD, Dinesh Kumar Mynampati
2024: Qiyong Fan, PhD
2023: Laszlo Voros, M.S., Samuel Hellman, PhD
2022: Alison Kelly, LL.D.
2021: Neelam Tyagi, PhD, Sharif Elguindi, M.S.
2020: Cesar Della Bianca, PhD
2019: Linda Hong, PhD, Masoud Zarepisheh, PhD, Ying Zhou, M.Sc.
2018: Usman Mahmood, M.S.
2017: Neelam Tyagi, PhD
2016: Bae Chu, M.P.H., Åse Ballangrud-Popovic, PhD, Christopher Horan, B.S.
2015 (inaugural): Sean Berry, PhD, Seng Boh Lim, M.S.

Biomedical Engineering



Biomedical Engineering

Biomedical Engineering, through its multiple sections, represents a breadth of capabilities and specialties that support clinical operations, research, and development for MSK. Biomedical Engineering is broadly divided into two areas: (1) Clinical Support and, (2) Development with frequent, overlap between the two. Clinical Support focuses on maintaining the operation and compliance of the multitude of medical devices throughout MSK. Sections, such as Medical Electronics, focus on specific subsets of medical devices, e.g., linear accelerators whereas the Clinical Engineering section is broader and is responsible for thousands of medical devices. As these groups work closely with their clinical counterparts, they are heavily involved in the development and evolutions of their respective areas. Developmental sections, such as Biomedical Systems and Mechanical Engineering, are more focused on new technology and systems developments and deployments. Projects range from medical device development for clinical practice and clinical trials to simulation development, where training, practice, and testing are advanced in a realistic hospital environment. Representative areas of development include:

Simulation Lab – AR/VR:

The Simulation Lab provides the department and institution with a clinical environment suitable for training, testing, and evaluating equipment and processes in real-world settings with real-world scenarios. The Sim Lab integrates the latest medical AR/VR visualization technologies, providing MSK with a test and evaluation environment for development and evaluation.

Medical Device Development:

Biomedical Engineering works with clinician partners to develop novel medical devices designed to enhance the care of our patients. From nursing to surgery, we work with clinicians to provide direct engineering and technical management expertise to bring ideas from concept to the clinic.

Clinical Process Improvement:

Working alongside clinicians, we develop solutions to existing clinical challenges, often using our combined knowledge of the clinical need directly with engineering principles. These solutions routinely and directly impact the care our patients receive.

Patient-Specific Solutions:

Using 3D scanning, printing, manufacturing, and visualization technologies, patient-specific solutions are implemented to directly tailor the care that individuals receive. From immobilization devices to cutting guides and 3D models, Biomedical Engineering is central to developing the technologies and techniques needed to provide our patients with individualized care.

Breath-Hold Sensor for MR-Linear Accelerator

Neelam Tyagi¹, Victoria Yu¹, Ryan Abuasi², Michael Crouch¹, Samuel Hellman³, and Paul Booth¹

¹Department of Medical Physics, ²Health Systems Operations, and ³Formerly Department of Medical Physics

Motivation: MR-Linear accelerator (MR-Linac) treatment of disease in the chest requires the patient to match the volume of inhalation determined in the treatment planning process and maintain that volume for the duration of a breath-hold during treatment in order for the electron beam to achieve the appropriate depth of penetration. Additionally, the physicist performing the therapy must be able to determine when the patient releases the breath-hold in order to turn off the Linac beam to prevent damage to healthy tissues.

Methods: A manometer is attached to a bellows which is fixed on a belt to the patient's chest prior to positioning on the treatment couch. Patient inhalation while wearing the bellows will cause compression, generating pressure within an MR-safe tube. A manometer attached to the tubing will be capable of measuring the pressure generated, which can then be used to determine appropriate breath depth for treatment. The manometer will then be displayed for both the patient (as seen in Fig. 1) and the physicist in order to show the predicted threshold for achieving appropriate beam penetration, and when that volume has been lost, to signal the physicist to turn off the electron beam.

Results: Preliminary testing has shown that the bellows is capable of displaying pressure change with inspiration over the distance required to ensure the manometer is out of the magnetic field generated by the MR-Linac. Next steps on the project include transferring from an analog to a digital manometer with a live feed that can be displayed on the screens of both the control room, and zone 4, and mounting the digital manometer in place once validated.

Scientific Significance: Effective measurement of chest volume for MR-Linac planning and treatment.

Potential Clinical Impact: Improved patient breath-hold compliance and applicability of the treatment technique through easier interpretation of feedback.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

References:

Botticella, A., Levy, A., Auzac, G., Chabert, I., Berthold, C., Le Pechoux, C. (2021). Tumour motion management in lung cancer: A narrative review. *Translational Lung Cancer Research*. 10(4). doi: 10.21037/tlcr-20-856

Cervino, L., Gupta, S., Rose, M. A., Yashar, C. M. (2009). Using surface imaging and visual coaching to improve the reproducibility and stability of deep-inspiration breath hold for left-breast-cancer radiotherapy. *Physics in Medicine & Biology*. 54(22). doi: 10.1088/0031-9155/54/22/007

Godley, A. Zheng, D., Rong, Y. (2019). MR-linac is the best modality for lung SBRT. *Journal of Applied Clinical Medical Physics*. 20(6). doi: 10.1002/acm2.1215

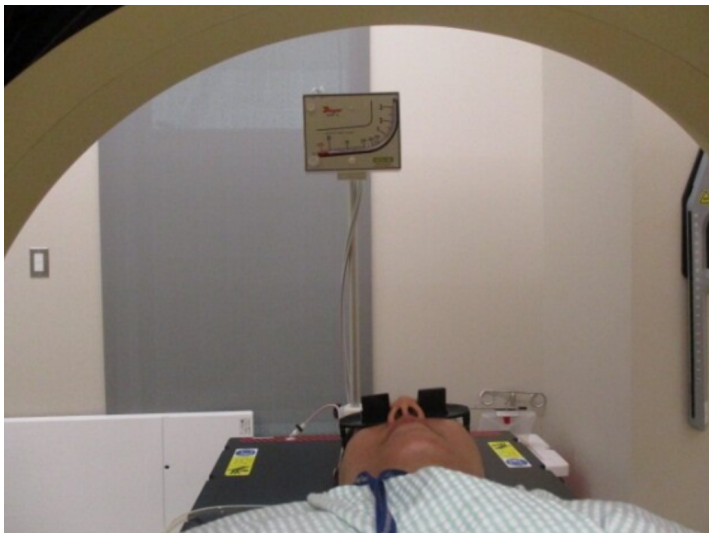


Fig. 1: Proof of concept using direct manometry.

Three-Dimensional Volumetric Rendering on Augmented Reality Headsets for Ovarian Cancer Cytoreduction Planning: A MSK Team Ovary Study

Ryan M. Kahn², Kimberly Murphy², Tulsi Patel¹, Effi Yeoshou², Emily Tian², Lindsey Finch², Qin Zhou², Alexia Iasonos², Paul Booth¹, Joshua N. Honeyman², Javin Schefflein³, Michael Crouch¹, Sameer Kaza¹, Vance Broach², Ginger J. Gardner², Kara Long Roche², Yukio Sonoda², Nadeem R. Abu-Rustum², and Dennis S. Chi²

¹Department of Medical Physics, ²Surgery, and ³Radiology

Motivation: To conduct a comparative study evaluating disease extent and location across various anatomical sites, both pre-operatively and intra-operatively.

Methods: Nineteen patients were evaluated for this study. A clinical fellow assessed patient imaging prior to surgery to predict which areas of each patient's anatomy had disease present, as seen in Fig.1 and Fig. 2. These assessments were recorded in a survey, and pathology records were reviewed post-operatively to confirm the predicted outcomes. The study involved use of a Medivis unit (Medivis, New York, NY, USA) with a HoloLens headset (Microsoft, Redmond, WA, USA), and the imaging was uploaded to the unit for the clinical fellow's use.

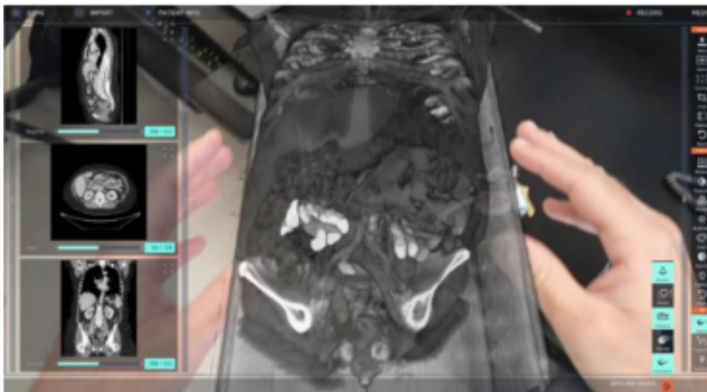


Fig. 1: The view of a patient being evaluated in the HoloLens headset (Microsoft, Redmond, WA, USA).

Results: Of the 19 patients, 15 met the inclusion criteria. Using pathology results as the gold standard, the augmented reality (AR) headset accurately supported the clinical fellow's disease predictions. Accuracy across different anatomical sites ranged from 80%-100%. Further research is needed to evaluate how the application of this technology impacts patient outcomes.

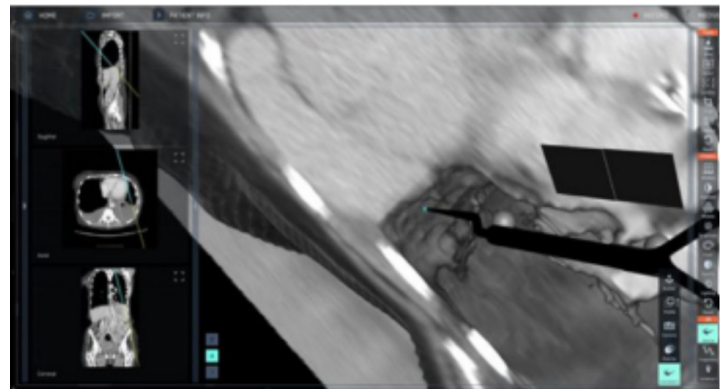


Fig. 2: Clinician reviewing patient imaging with a trajectory pen.

Potential Clinical Impact: This application of mixed reality has the potential to improve surgical planning and enhance the clinical fellowship program offered by Memorial Sloan Kettering Cancer Center.

Acknowledgments:

- Medivis
- MSK Cancer Center Support Grant (P30 CA008748)

References:

Kahn, Ryan M. et al. Three-dimensional volumetric rendering on augmented reality headsets for ovarian cancer cytoreduction planning: A Memorial Sloan Kettering Cancer Center Team Ovary study. *Gynecologic Oncology*, Volume 196, 107 – 112.

Surgical Drain Strip (SDS) Buddy – Medical Device Design to Improve Management of Jackson-Pratt Surgical Drains

Eleni Kalandranis¹, Amy Setesak¹, and Paul Booth²

¹Department of Nursing and ²Department of Medical Physics

Motivation: For patients requiring a drainage tube, periodically evacuating the tube is a clinical requirement that often requires two people to complete. Even when a patient can perform the operation independently, it is often difficult to safely and effectively do so. The SDS Buddy is intended to allow single-handed operation of the tube drainage operation by the patients themselves.

Methods: The SDS Buddy is a nurse-invented medical device designed to streamline and improve the management of Jackson-Pratt (JP) surgical drains. It is intended to make the stripping process safer, easier, and more accessible for both healthcare providers and patients. The device allows one-handed, independent operation, helping to reduce infection risk, enhance drain patency, and empower patient self-care in home and clinical settings. It is designed to deliver a cost-effective, reusable, and user-friendly device for JP drains, which enhances patient safety by simplifying and improving the stripping process — ultimately promoting better surgical outcomes, reducing pain and infection, and supporting effective wound healing. Our solution (Fig. 1) empowers patients to confidently manage their drain care independently at home, helping to shorten hospital stays, and reduce the risk of complications and re-hospitalization.

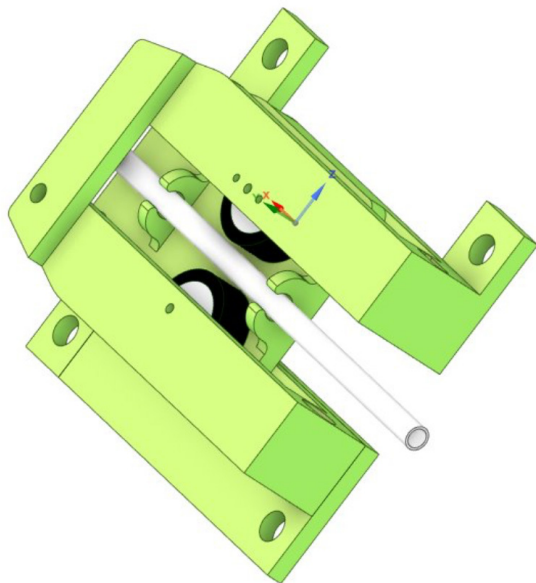


Fig. 1: Computer-aided design concept of a roller mechanism to “pinch” the Jackson-Pratt (JP) drain, maneuver it down the tubing, and provide clearance of the drain.

Results: We have initiated the development plan by evaluating several conceptual ideas and prototyping a motorized proof-of-concept drain stripper that validates the concept (Fig. 2). Upon performing this validation, we have initiated formal engineering development and are in the initial stages of creating a workable prototype suitable for clinical testing. We have partnered with a medical device engineering company, MPR Associates, specializing in bringing medical device concepts through the development process to the clinic. Currently, the Memorial Sloan Kettering Cancer Center team is responsible for clinical requirement specifications (Department of Nursing, Department of Surgery), engineering (Biomedical Engineering [under the Department of Medical Physics]), engineering management (Biomedical Engineering), and testing requirements (entire team). Our external partner, MPR Associates, is performing engineering, first-in-human development, hazards analysis, and manufacturing for development and delivery of a first-inhuman prototype suitable for a clinical trial. We expect the initial phase of this work to be completed in Q4 2025 (fourth quarter of 2025), with subsequent development phases delivering a working prototype in Q2 2026.

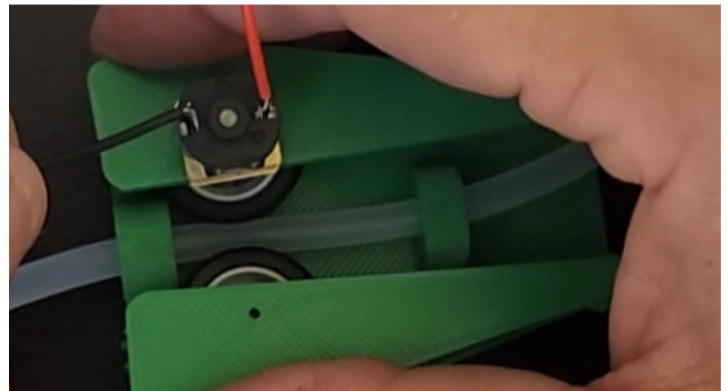


Fig. 2: Proof-of-concept of a motorized drain stripper. Motorized roller wheels drive the unit down the tubing.

Potential Clinical Impact: We aim to revolutionize surgical drain management by minimizing physical strain and injury among clinical staff, bridging care gaps caused by limited in-home support and insurance limitations, and fostering greater patient autonomy, along with improved quality of care across a variety of healthcare settings.

Acknowledgments:

We thank our supporting development partners, including Dr. Evan Matros, Attending Physician of the Plastic Surgery Department, Tracy Gosselin, Senior Vice President & Chief Nursing Executive of Nursing Department Executive Leadership, Margaret Barton-Burke, Director of the Office of Nursing Research, and Keri Wagner, Director of the Innovation Taskforce. This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

Novel Ophthalmic Prosthesis

David Abramson¹ and Paul Booth²

¹Ophthalmic Oncology Surgery and ²Department of Medical Physics

Motivation: There is a need to develop an ophthalmic prosthesis that more accurately represents the look, movement, and illumination response of the natural eye than the current standard prosthesis.

Methods: Each year, approximately 35,000 people in the U.S. and Europe undergo eye removal due to injury, disease (including cancer), or congenital anomalies. For these individuals, the resulting disfigurement remains a lifelong burden, despite the current state-of-the-art techniques used to minimize the physical effects of the corrective measures. The burden is significantly greater for individuals who have had this corrective procedure in their formative years, with lifelong social and psychological issues being common. To address limitations in existing eye prostheses, we are developing a new type of prosthesis which more accurately simulates healthy eye movement and exhibits a “normal” pupillary response to light for patients who have had an eye removed. Our concept involves embedding an image of an eye on a screen and enabling the image to move, eliminating the need for physical movement of the prosthesis itself (Fig. 1)



Fig. 1: Conceptual electronic ophthalmic prosthesis.

Results: In order to determine the correct location of the eye image, we need to identify where the eye pair is looking. One passive method identified to achieve this is measuring the movement of the post-enucleated conjunctiva. We have validated the measurement technology using a dedicated camera to image the conjunctiva and identify surface structures. Furthermore, we have written code in MATLAB to identify interframe movement of the venous structures in the conjunctiva that correspond to eye movement. In accordance with an institutional review board (IRB) protocol currently in process, we will create a patient-specific test prosthesis (Fig. 2), which is a three-dimensional printed geometric copy of a patient's existing prosthetic. Each test prosthesis will include an embedded imaging sensor, illumination source (LED), and associated control electronics. Control wires will extend from the prosthesis and connect to a computer for data collection. Images will be captured and processed (Fig. 3). The clinician will insert the test prosthesis into the ocular cavity and maintain its position manually. The participant will follow a moving target on a mobile screen, held by a research assistant, while their healthy eye movements are recorded for gaze comparison analysis.

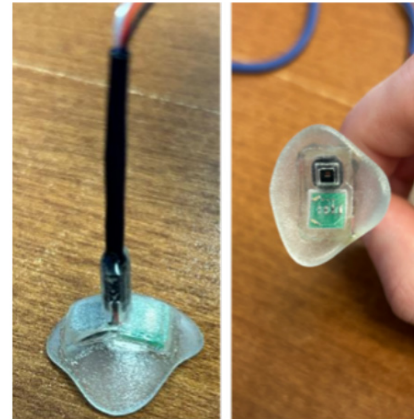


Fig. 2: Micro-camera and housing integrated into a custom prosthesis for conjunctiva motion testing and analysis.

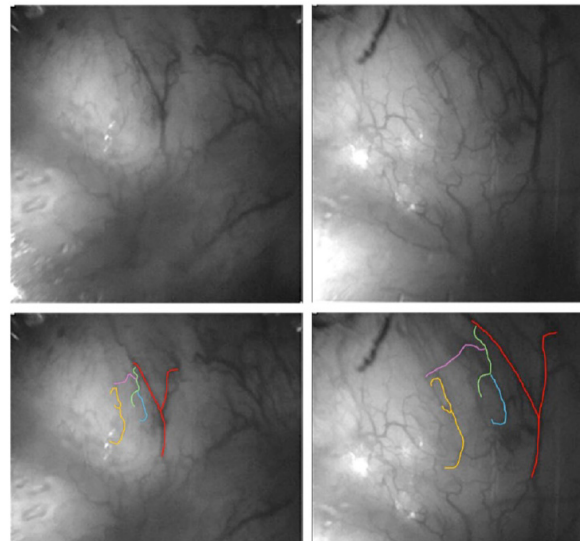


Fig. 3: Conjunctiva imaging and analysis.

Potential Clinical Impact: Our concept is to create a prosthesis, which will display an eye image that moves easily in consort with the fellow eye and precisely matches iris color, vasculature, and lifelike responses to light via a microprocessor-controlled display. This prosthetic will allow users to lead a better quality of life in through their day-to-day activities by mimicking normal movement of an eye. The system comprises a fully encapsulated prosthesis, housing power, sensors, electronics, and display technologies to provide a realistic facsimile of the patient's original eye, along with an implanted emitter that directs the prosthesis where to place the eye image, as if it were “looking” in the correct direction.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748) and The Fund for Ophthalmic Knowledge, Inc.

References:

Patent Issued: Ocular Prosthesis with Display Device Feb 18, 2021 Pub. No. US 2021/0045865 Inventors: David Abramson, George C. Bohle, III, Paul Frisch, Brian P. Marr, Paul Booth, Philip C. Black, Alan B. Katze, James G. Moore

Peel-away Nasal Trumpet for Fiberoptic Tracheal Intubation: Buckle Resistance and Geometry of 3D-printed Prototypes with High Performance in Airway Manikin Simulations

Andre Deosaran^{1,2}, Jessica Winakor³, Justin D. Kuligowski⁴, Gregory W. Fischer¹, Samuel Hellman⁴, and Takeshi Irie³
¹Department of Anesthesiology and Critical Care Medicine, ²Department of Medical Physics, ³Formerly of the Department of Anesthesiology, and ⁴Formerly of the Department of Medical Physics

Motivation: There is a need for a peel-away nasal trumpet (PANT), introduced here, that can be reliably detached at will from fiberoptic bronchoscopes during tracheal intubation, with buckling thresholds which exceed those of traditionally slit nasal trumpets.

Methods: Difficult airway management is a rare but high-stakes scenario encountered in perioperative and other acute care settings. The 2022 update to the American Society of Anesthesiologists difficult airway algorithm continued to recommend awake tracheal intubation for anticipated difficult airways, and awake fiberoptic intubation is considered the gold-standard approach in this context.¹ Awake fiberoptic intubation is a skill which is both difficult to learn and to maintain,^{2,3} and slit nasal trumpets can facilitate nasal awake fiberoptic intubation.⁴⁻⁷ In this approach, a nasal trumpet is slit longitudinally before insertion, allowing trumpet decatenation from the fiberoptic bronchoscope prior to railroading the tracheal tube into the trachea (shown in Fig. 1). However, this method remains underrepresented in the literature. Anecdotally, one author (Takeshi Irie) observed that slit trumpets can buckle under longitudinal compression during insertion, making deployment occasionally challenging, and, to our knowledge, this problem had remained unsolved. Our primary aim in this study was to prototype peel-away nasal trumpets (PANTs) that could be faithfully peeled at will from fiberoptic bronchoscopes during intubation, implemented with buckling thresholds exceeding those of slit nasal trumpets. We focused on designs featuring bilateral tear guide grooves extending longitudinally along endoluminal surfaces and hypothesized that groove geometry variations may impact peeling fidelity. Here, we present mechanical characterizations of nasal trumpet variants through Instron testing, and the results of airway mannequin simulations of PANT-assisted intubations.

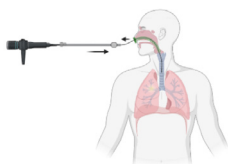


Fig. 1: Cartoon workflow depicting a peel-away nasal trumpet (PANT)-assisted nasal fiberoptic intubation. First, a PANT is inserted, next, the bronchoscope is advanced through the PANT into position, then the PANT is withdrawn and decatenated, and finally, the tracheal tube is advanced.

Results: Functional 3D-printed, biomedical-grade preclinical prototype PANTs were manufactured. PANTs were successfully peeled in airway mannequin simulations, and variations in defect geometries were compared for peeling success rates, with trapezium-grooved PANTs showing the best performance (16 of 16 successful tears) (Fig. 2). PANT compressibility more closely approximated that of commercial nasal trumpets than that of polyvinylchloride tracheal tubes, and should be acceptable for nasal insertion (Fig. 3). With additional testing, clinical validation of PANTs may ultimately secure avenues for trumpet-facilitated fiberoptic intubation without liabilities incurred through post-market device modifications.



Fig. 2: Preclinical prototype in a mannequin simulation of peel-away nasal trumpet (PANT)-assisted nasal fiberoptic intubation.

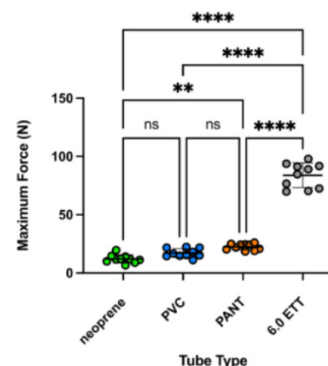


Fig. 3: Buckle tests of peel-away nasal trumpets (PANTs) compared with commercial nasal trumpets and polyvinyl chloride tracheal tubes, confirming that the PANT stiffness is approximately equal to existing commercial nasal trumpets.

Scientific Significance: Advantages of the groove geometries may extend to other materials and other peel-away device designs.

Potential Clinical Impact: Three-dimensional-printed PANTs can be point-of-care manufactured in hospitals, with clinical-grade printing capabilities within 30 hours and at a relatively low cost.

Acknowledgments:

- Mechanical design and technical assistance were provided by the Mechanical Engineering and Instrumentation group.
- Helpful discussions were contributed by Daniel A. Heller and Michael G. Kharas.
- Departmental support was provided by Gregory W. Fischer.
- Mannequin access was facilitated by Michael Crouch and Michelle Rausen.
- This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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1. Apfelbaum JL, Hagberg CA, Connis RT, et al. 2022 American Society of Anesthesiologists Practice Guidelines for Management of the Difficult Airway. *Anesthesiology* 2022; 136: 31-81
2. Heidegger T, Asai T. Fiberoptic intubation: a commitment to an indispensable technique. *Br J Anaesth* 2023; 131: 793-6
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Remote Surgical Consultation Utilizing 3D Screen-Mirroring Glasses

Michael Crouch¹, Tulsi Patel¹, Samer Michael², Javin Schefflein³, and Paul Booth¹

¹Department of Medical Physics, ²Department of Pediatric Surgery, and ³Department of Radiology

Motivation: To assess the feasibility of utilizing three-dimensional (3D) screen-mirroring glasses to perform a remote intraoperative physician consultation.

Methods: Eight 3D-printed cubes of varying sizes (5 mm x 2, 10 mm x 2, 15 mm x 2, and 20 mm x 2) and colors were arranged on a Mayo stand (McKesson, Irving, TX). A pediatric surgeon, with no prior knowledge of the locations, colors, sizes, or any other details regarding the placement of the cubes, was located in a nearby room, unable to physically see the working area. A Microsoft Teams video call was made from an iPhone 15 (Apple Inc., Cupertino, CA) to the consulting physician. The consulting physician connected the Viture XR Pro glasses (San Francisco, CA) (Fig. 1) to the iPhone 15 Pro receiving the call. The surgeon was then asked to identify the cubes to determine the minimum feasible size of identifiable features through the glasses. Next, five 3D-printed blocks were deployed on the abdomen of an Echo Healthcare Lifecast Body Simulation manikin (Echo Healthcare, Golden, CO). The blocks each had a 20 mm x 20 mm base, but the height varied by 2 mm each (20 mm, 22 mm, 24 mm, 26 mm, and 28 mm) (Fig. 2). The blocks each had a random single-digit reference number assigned to each end with no repetition. The consulting physician was then asked to arrange the blocks from shortest to tallest.



Fig. 1: Viture XR Pro screen-mirroring glasses (San Francisco, CA).

Results: The consulting physician was able to identify all cubes in the first test, indicating a reasonable minimum identifiable size of 5 mm. Furthermore, in less than ten seconds, the physician was able to arrange the blocks in the correct order by height without making any mistakes, despite the color similarities and minute variations in height. These results indicate that performing a remote surgical consultation utilizing 3D screen-mirroring glasses through a Microsoft Teams video call could be feasible.

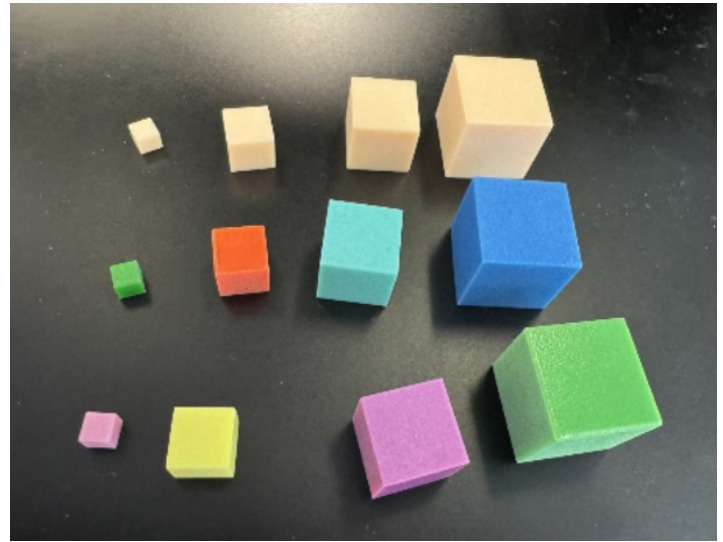


Fig. 2: Three-dimensional (3D)-printed cubes.

Scientific Significance: These findings represent a step toward validating a metric for assessing the quality of remote consultation and serve as the first step in conducting a randomized controlled trial on the effectiveness of remote consultation, addressing two major gaps in the literature.

Potential Clinical Impact: By validating the model for remote surgical consultation utilizing these glasses, we hope to provide a mechanism for remote mentoring and expert consultation, which can improve patient outcomes and increase safety in situations where a specialty surgeon or a more experienced consulting surgeon may not be readily available in-person.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Robotic Uterine Manipulator

Richard Barakat¹, and Paul Booth²

¹Gynecologic Surgery, and ²Department of Medical Physics

Motivation: Over 700,000 hysterectomies are performed annually in the United States and over 3.5 million globally. Uterine manipulation is a critical component of a successful, minimally invasive hysterectomy, the second most common surgical procedure women undergo in the United States. In current standards of practice, a surgical assistant takes positional instructions from the operating surgeon to manipulate the anatomy using hand-held tools. This workflow is challenging for both the surgeon and assistant, as it can place significant physical demands on the assistant and may not achieve the exact anatomical positioning the surgeon requires.

Methods: Uterine manipulation is a critical component of a successful, minimally invasive (laparoscopic or robotic) hysterectomy. In performing minimally invasive hysterectomies, the operating surgeon must position the uterus precisely, according to the specific requirements of the case, throughout the procedure. The current standard of practice is for a surgical assistant (resident, fellow, physician assistant, etc.), to follow detailed positional instructions from the operating surgeon, to manipulate and stabilize the anatomy using hand-held tools. Over the course of the surgery, this presents a number of challenges for the surgeon – from communication issues to the physical demands and fatigue of the assistant, who often must maneuver around other surgical equipment used in the surgery while attempting to maintain accurate positional stability of the uterus for hours at a time.

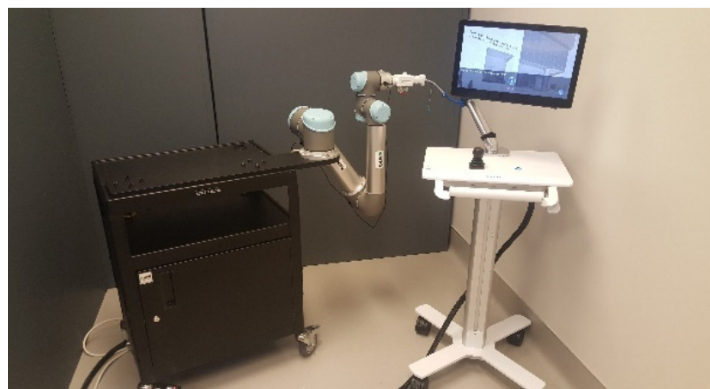


Fig. 1: Robotic Uterine Manipulator system – comprised of a robotic arm and a surgical control console.

The Robotic Uterine Manipulator (Fig. 1) is a telemanipulated device which solves such clinical needs by providing direct anatomic control to the surgeon. This eliminates the need for a surgical assistant to occupy the largely routine and physically demanding position required for uterine manipulation, while enabling the operating surgeon to work more precisely. It is intended to assist in positioning anatomy in both robotic and traditional laparoscopic hysterectomy procedures. The enhanced control offered by the system enables the operating surgeon to have total control over instruments and patient anatomy, allowing more precise adjustments of the instruments and anatomy to the exact desired positions, thereby yielding superior surgical results. Combined with the superior stability and drift characteristics inherent to our design, the surgeon can maintain critical anatomical positioning for prolonged periods.

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Fig. 2: Uterine Manipulator System in the room alongside the Da Vinci Surgical Robot (Intuitive Surgical, Sunnyvale, CA).

Results: A Barakat Automated Uterine Manipulator Clinical Trial resulted in 18 successfully completed hysterectomy surgeries (Fig. 2). Surgeon feedback was overwhelmingly positive, validating both the concept and the enhanced surgeon controls. Improvements in stability and drift were measured and quantified through video analysis and compared to manual manipulation (Fig. 3). The device has been successfully patented and licensed to a startup to further develop and market the technology.

Clinical Impact: Surgeons had more direct control over the positioning of the anatomy without the need for an assistant. That assistant is now able to perform other clinical duties during the surgery. The anatomy also was stabilized more effectively as there was no anatomical drift once positioned.

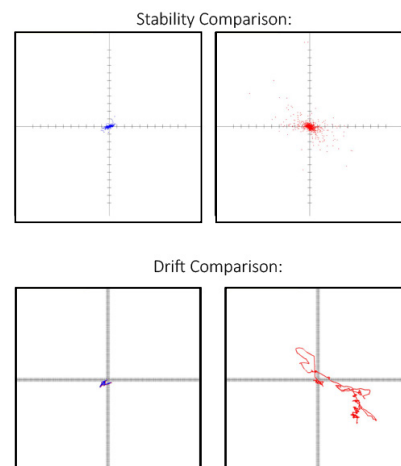


Fig. 3: Stability and drift graphs, comparing manual uterus manipulation with robotic uterus manipulation. Tick marks in x and y axis represent pixels in the images from which movement analysis was based.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

References:

Patent Issued: Robotic Surgical Manipulation Systems and Methods Dec. 24, 2024. Pub. No. US 12,171,515 B2
Inventors: Richard Barakat, Paul Booth, Charles Kim, Kelsey Ann Tacca, Jordan Anthony Rivera, Samuel Thomas Pratt.

Three-dimensional Visualization of Clinical Spaces

Sameer Kaza¹, Joshua Honeyman², Javin Schefflein³, Paul Booth¹, and Ricardo Otazo¹

¹Department of Medical Physics, ²Pediatric Surgery, and ³Radiology

Motivation: The advancement in image and spatial capturing technology has allowed the creation of more immersive environments when viewed in virtual reality (VR). The aim of this project is to investigate the different 3D capturing techniques to create an immersive clinical environment for patients to visualize before they are treated.

Methods: For this project, we used different image and spatial capturing techniques (Fig. 1) of various clinical environments to create an immersive environment. We used a Kandao Obsidian Pro (Kandao Technology Co., Shenzhen, China) camera, which has six lenses to capture images, along with the Kandao Studio software, which stitches the images/videos together to create a 360° scene that can be visualized on VR glasses such as Meta Quest 3 (Meta Platforms, Menlo Park, CA) and Apple Vision Pro (Apple Inc., Cupertino, CA). We also used light detection and ranging (LiDAR) scans using the Apple iPhone 13 Pro and 15 Pro to generate point cloud data of the SimLab, which was processed using 3D scanning software Scaniverse (Fig. 4) and Polycam (San Francisco, CA). The point cloud data was then converted to a 3D model using Blender version 4.5.1. The 3D model was imported into Unity version 5.0 to create a game environment where participants can navigate through the SimLab space. We are also exploring the technique of photorealistic capture based on Gaussian splatting using Postshot software to create 3D environments. The 3D environments are then loaded into Unreal Engine version 5.5 to create a gamified environment through which users can walk through a clinical space. The clinical spaces being targeted include the Pediatric Procedure Room, Operating Room Suite, Magnetic Resonance Imaging (MRI) Room and Computed Tomography (CT) Room. We have created a VR 360° image of the Pediatric Procedure Room (Fig. 2), entrance to the MRI room (Fig. 3) and the SimLab. These images were uploaded to the MetaQuest to simulate a demo experience for the surgical team to present. LiDAR scans were obtained for the Pediatric Procedure Room and SimLab. For Gaussian splatting implementation, images of the Pediatric Procedure Room were obtained.

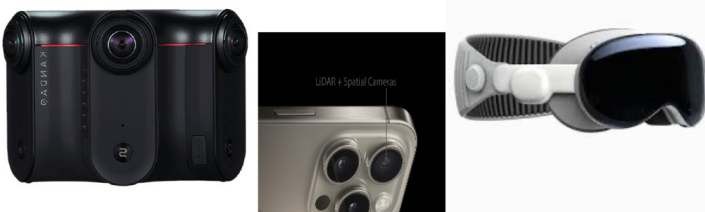


Fig. 1: Imaging platforms used for capturing and 3D data, shown from left to right: Kandao Obsidian Pro (Kandao Technology Co., Shenzhen, China), iPhone (Apple Inc., Cupertino, CA) using light detection and ranging (LiDAR), and augmented reality/virtual reality (AR/VR) visualization.



Fig. 2: Raw Static 3D output of a Pediatric Procedure Room scan.



Fig. 3: Raw Static 3D output of a MRI Room scan.

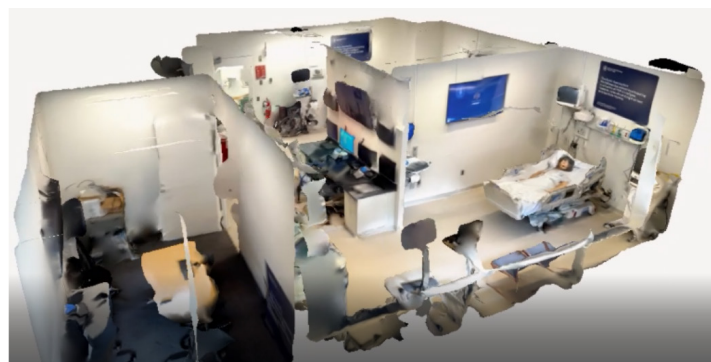


Fig. 4: Reconstructed 3D view of a suite of rooms.

Results: Different modalities for creating clinical immersive environments were identified.

Potential Clinical Impact: Immersive visualization of clinical spaces may help patients feel more comfortable during procedures and reduce the anxiety associated with hospitals.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

Total Skin Electron Beam (TSEB) Eye Shield Redesign

Johannes Hertrich¹, Karen Episcopia¹, Gary Lim¹, and Candy Reyes²

¹Department of Medical Physics and ²Radiation Oncology

Motivation: Total Skin Electron Beam (TSEB) therapy uses electron beam irradiation to treat patients with skin conditions such as mycosis fungoides, employing techniques and shields to reduce the radiation dose to the eyes, hands, and feet. At MSK, a pair of lead-based goggles was commissioned to shield radiation from the eyes; however, concerns over cross-patient contamination and poor fit across patients of different sizes necessitated a redesign of the goggles.

Methods: The engineering team was tasked with developing an improved eye shield design that would enhance patient comfort and radiation shielding, reduce contamination risk, and simplify setup operations. Using a combination of rapid prototyping techniques (3D printing, laser cutting, Cerrobend and silicone casting), the shop team was able to create a modular goggle design (Fig. 1) where each component can be optimized for discrete purposes and manufactured in large quantities onsite.

The reusable shields were constructed by injecting molten metal into a 3D-printed shell. With a lower melt temperature than the fused deposition modeling-printed nylon into which it was injected, Cerrobend provided ample radiation shielding without the need for complex machining or expensive tooling. The nylon casing provided a protective layer for the heavy metal while also offering an easy wipe-to-sanitize surface.

The 3D-printed flexible frames and bridge pieces provided enough sizing and adjustability to account for the wide range of anatomic variety seen in patient facial structures. The bio-safe material with which these components are printed is sanitized in an alcohol bath before being wiped down with a germicidal wipe.

The silicone cast headband (Fig. 2) provided a soft, compliant, sterile surface to interface with the patient's sensitive and delicate skin. It featured an overmolded laser-cut skeletal structure to help support and distribute the load of the shields across the crown of the head. The stretchy, sawtooth-shaped extremities allow for up to six inches of circumference adjustability. The headband is formed using the novel technique of modified two-part resin dispensers to inject resin on demand into custom 3D-printed molds.

Results: Since the initial rollout, the goggle design has been continuously improved for usability, range of adjustment, and mass manufacturability. Feedback from therapists, supervisors and patients alike was widely positive. Physician-prescribed use of goggles has continued to grow, and orders are expected to surpass 150 at MSK's main campus this year alone.

Scientific Significance: This project introduced the innovative technique of injection casting low-melt temperature metal alloys into 3D-printed shells. This novel manufacturing technique allowed for complex shielding to be manufactured with minimal time, cost, and equipment investment, while also eliminating the need to use traditional machining practices on heavy metals entirely.



Fig. 1: Prototype incorporating silicon, Cerrobend, and 3D-printed parts.



Fig. 2: Three-dimensional-printed mold for the strap.

Clinical Impact: This project improved patient comfort through use of soft-touch materials. It reduced contamination and infection transmission with patient-specific, disposable goggles. Such innovations also optimized treatment setup and reduced appointment times.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

Zeus MRgRT Motion Management QA Phantom Horizontal to Vertical Motion Translation Modification

Andre Deosaran¹ and Sean Trahan¹

¹Biomedical Engineering

Motivation: There is a need to translate the horizontal motion of the Zeus Magnetic Resonance-guided Radiotherapy (MRgRT) phantom (CIRS Inc., Norfolk, VA) into real-time vertical motion across imaging modalities to further research in MR-guided radiation therapy.

Methods: The Zeus MRgRT Motion Management Quality Assurance (QA) phantom (pictured in Fig. 1) is used in MR-guided radiation therapy for both quality assurance and research applications, primarily focusing on real-time motion management during radiation treatment. A limitation of this phantom is that it simulates movement solely along the horizontal axis; thus, research is limited to real-time motion management in a single axis. Our aim is to prototype an external modification to the Zeus MRgRT Motion Management QA phantom that translates the phantom's horizontal motion into real-time vertical motion, enabling use across imaging modalities to advance research in MR-guided radiation therapy. Here, we present a functional hydraulic system prototype fabricated using 3D printing and traditional manufacturing methods. This hydraulic system involves the use of a 3D-printed bearing attached to the phantom, which moves based on horizontal motion but independently of the rotational motion produced by the moving rod. The bearing is directly connected to a syringe filled with water, aligned parallel with the moving rod (Fig. 2).

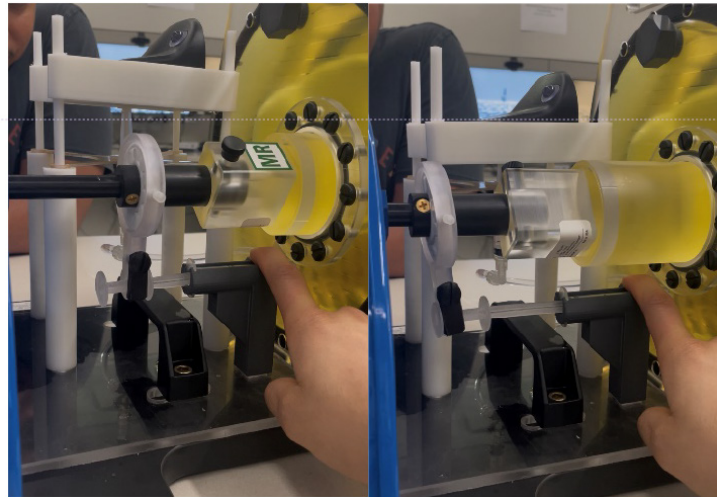


Fig. 2: Prototype demonstration displaying translation of horizontal to vertical motion. When the moving rod moves toward the horizontal syringe, the Respiratory Gating for Scanners (RGSC) (Varian Medical Systems, Palo Alto, CA) block is moved upward (left). Conversely, when the moving rod moves away from the horizontal syringe, the block is moved downward.

Scientific Significance: The visualization of horizontal and vertical motion in MR-guided radiation therapy can be researched across various imaging modalities.

Potential Clinical Impact: This prototype can improve treatment planning by advancing research in real-time motion management for both vertical and horizontal motion simultaneously in MR-guided radiation therapy.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

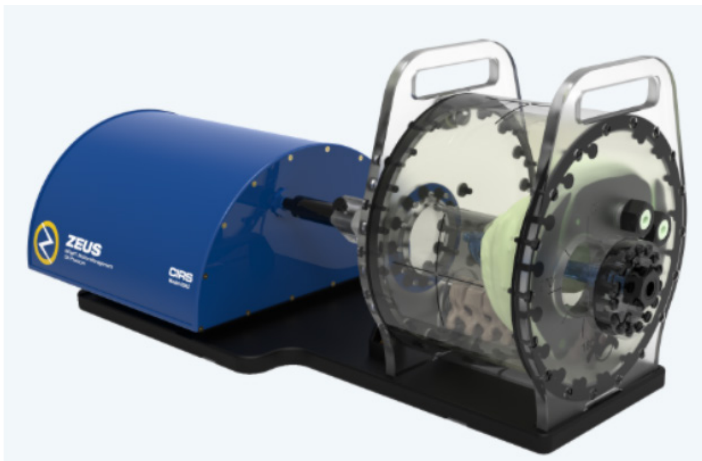


Fig. 1: Sun Nuclear Zeus Magnetic Resonance-guided Radiotherapy (MRgRT) Motion Management Quality Assurance (QA) Phantom (CIRS Inc., Norfolk, VA).

Results: Functional hydraulic system prototype. The manufactured prototype directly translates phantom motion along the horizontal axis into vertical motion of the RGSC gating block, enabling use across imaging modalities with minimal motion latency.

Computer Service



Anyi Li



Andrew
Brish-Guo



Darian
Pazgan-Lorenzo



Doorri Rose



Gary Aquino



Gourav Jhanwar



Hai Pham



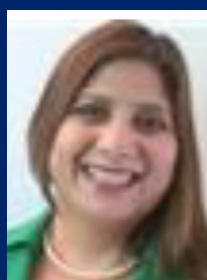
Jianping Xiong



Jie Yang



Masoud
Zarepisheh



Neerja Purang



Pengpeng Zhang



Ping Wang



Rob Smith



Roger Joseph



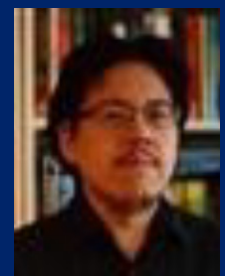
Ryan Kerslake



Seppo Tuomaala



Terry Li



Yu-Chi Hu

Computer Service

The Medical Physics Computer Service at MSK leads the integration of AI, advanced optimization, radiomics, and large-scale IT infrastructure to transform radiation therapy workflows from planning to delivery. Our multidisciplinary team of physicists, engineers, data scientists, and clinicians focuses on improving efficiency, patient safety, and decision-making through research, development, and clinical translation.

Goals: Our mission is to streamline radiotherapy operations by automating complex, time-consuming tasks, consolidating fragmented workflows, and enabling real-time, data-driven decision support. We aim to deliver high-quality treatment faster, reduce costs, and improve patient outcomes, while building scalable platforms for translational research and next-generation clinical innovations.

Research & Development Highlights:

We have pioneered clinical AI systems, optimization frameworks, and imaging analytics:

- **PlanQ:** AI-powered workflow platform integrating 11+ hospital systems, reducing coordination time by 70% and planning workload by up to 20%.
- **ECHO:** Automated treatment planning, used in > 10,000 cases, cutting planning time by 50%.
- **AWARE:** Automated adaptive radiotherapy monitoring for head and neck cancer, triggering replanning to reduce toxicity.
- **MKIG Motion Management:** Real-time MV/kV imaging for sub-millimeter tumor tracking in SBRT, lowering urinary toxicity.
- **RADAR:** Dose accumulation framework for re-irradiation with uncertainty correction, improving organ-at-risk safety.
- **CompressRTP & PortPy:** Open-source optimization tools enabling rapid, high-quality treatment planning and bridging research with clinical practice.
- **Radiomics Batch Effect Analysis:** Identify robust CT-derived radiomic biomarkers that are resistant to tube current and reconstruction kernel variation, quantify limitations of standard ComBat correction, and use the results to guide the development of ML-based correction methods.

- **Oncology AI Initiatives:** MSK-MATCH for 98.6% accuracy in trial matching with a 30 x speedup; Woollie, an open-source oncology LLM for cross-institutional cancer progression prediction.
- **Adaptive Radiotherapy Optimization:** “Primer shot” fractionation strategy yielding a simulated 24% improvement in tumor control.

Clinical Translation & Impact: Our platforms are fully integrated into daily operations, supporting 155 applications (53 in-house) across eight campuses and managing 31 LINACs plus hundreds of imaging devices. AI-driven segmentation (200,000+ organs processed) saves clinicians 131 hours/month. Seamless integration with Epic EMR and radiotherapy systems has improved interoperability and eliminated redundant steps. Collectively, these innovations have accelerated care for tens of thousands of patients, reduced errors, and enhanced safety through automated checks.

Future Directions: We will expand our platform as a unified hub for segmentation, planning, safety monitoring, radiomics integration, and cohort outcome analysis. Upcoming developments include agentic AI for workload optimization, multimodal AI for contouring, brachytherapy scheduling, and real-time operational dashboards. Research will extend into multi-agent clinical triaging, AI-powered trial matching, ML-driven batch correction in radiomics, and automated plan quality checks.

Conclusion: By combining AI innovation, radiomics analytics, and robust clinical infrastructure, the Medical Physics Computer Service has created a model for intelligent cancer care delivery — bridging cutting-edge computational research with direct patient impact, and positioning MSK at the forefront of AI-driven oncology.

Optimal and Adaptive Radiotherapy Dose Scheduling via Sequential Mixed-Integer Convex Optimization

Anqi Fu¹, Zeno Gouw², Jeho Jeong¹, and Joseph O. Deasy¹

¹Department of Medical Physics, Memorial Sloan Kettering Cancer Center, and ²Department of Radiation Oncology, Netherlands Cancer Institute

Motivation: Radiation therapy is typically delivered in consecutive equivalent dose fractions, but research suggests that a non-uniform dose schedule may produce better tumor control. We develop an optimization method for constructing dose schedules with variable fraction sizes and treatment breaks, accounting for the influence of cellular resource competition and hypoxia on dose-response.

Results: The optimal schedules adhere to a pattern consisting of an initial large fraction, which we dub the “primer shot,” followed by a one-week break and several small fractions, and concluded with a second large fraction. The primer shot kills off proliferating cells, freeing resources so that hypoxic cells can reoxygenate during the treatment break. These reoxygenated cells are more sensitive to radiation. To exploit this fact, our schedule waits until the majority of cells have reoxygenated before delivering its largest dose fraction. In our computational experiments, the primer shot schedule achieves a roughly 24% higher tumor control probability (TCP) than the standard weekday schedule with constant fraction sizes (see Fig. 1). Additionally, it remains the best dose schedule even when we vary treatment length and the upper bound on normal tissue BED₃.

Constant fractions (tumor control probability [TCP] = 0.83)

Primer shot schedule (TCP = 0.93)

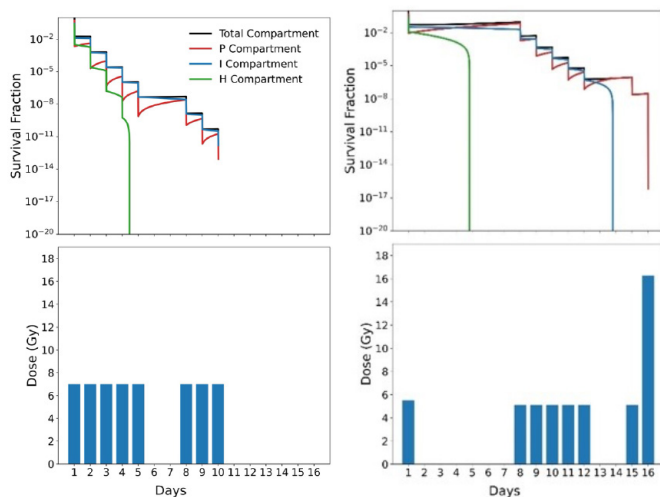


Fig. 1: Dose and Survival fraction in terms of days.

Method: We formulated the dose-scheduling problem as a finite-horizon optimal control problem, with the dose fractions as variables and the states determined by the numbers of proliferating, intermediately resourceconstrained, and extremely hypoxic cells at each time step. The state transition dynamics are based on a validated tumor dose-response model of radiation cell-kill, hypoxia-induced radioresistance, and cellular competition for oxygen and glucose. This problem is nonconvex; therefore, we employed a heuristic, called the convexconcave procedure (CCP), to construct and solve a sequence of mixed-integer convex approximations which converge to a good estimate of the solution. We compared the resulting schedules across different treatment lengths and normal tissue biologically effective dose (BED₃) values.

Scientific Significance: We formally define the dose scheduling problem as a mathematical optimization problem, which incorporates both tumor dose-response equations modeling hypoxia and reoxygenation as well as other clinical constraints. This definition allows us to leverage the machinery of optimization to efficiently solve for the best dose schedule with an arbitrary set of parameters.

Potential Clinical Impact: A Python software implementation of our dose-scheduling method can be used to automatically determine the optimal dose schedule for a patient. Our optimal primer shot schedule requires fewer treatment sessions to achieve the same or higher tumor control probability (TCP) than with the standard schedule used in the clinic.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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CompressRTP: Compressed Radiotherapy Treatment Planning Optimization

Masoud Zarepisheh¹, Mojtaba Tefagh², and Gourav Jhanwar¹

¹Computer Service, Department of Medical Physics, MSK, and ²The University of Edinburgh

Motivation: To develop a new paradigm, coined **CompressRTP** (Compressed Radiotherapy Treatment Planning), to enable rapid and high-quality treatment planning optimization. We are submitting a grant proposal to support this effort, and plan to integrate CompressRTP into clinical practice to enhance our in-house automated planning system, Efficient Comprehensive Hierarchical Optimization (ECHO).

Method: In our recent publications (NeurIPS'2024, MP'2025), we demonstrated that the large dosimetric datasets used in radiotherapy treatment planning — such as the influence matrix, which encodes the dose contribution of each beamlet to each patient voxel — are highly compressible due to inherent redundancies, including correlations among neighboring beamlets and voxels. This insight opens new avenues for leveraging data compression and dimensionality reduction techniques to construct compact representations of large-scale optimization problems, enabling faster solution times without sacrificing accuracy. Unlike traditional acceleration methods, such as data sparsification, which may degrade plan quality, our approach preserves data fidelity.

Results: Radiotherapy treatment planning optimization can be formulated as:

$$\min_x f(Ax, x) \quad s.t. g(Ax, x) \leq 0, x \in X,$$

where x represents the machine configurations (e.g., beamlet intensities) and A is the patient-specific dosimetric data matrix (dose influence matrix). The type of planning technique used (e.g., hierarchical, KPB, MCO, AI-based) determines the specific problems and parameters to be solved. As shown in Fig. 1A, matrix A demonstrates a low-rank, compressible structure, evidenced by the exponential decay in singular values. Similarly, the scattering matrix is even more compressible, evidenced by the sharper exponential decay in its singular values (shown in Fig. 1A). This suggests the use of a “sparse-plus-low-rank” compression, as shown in Fig. 1B. The low-rank nature of the scattering matrix enables its compression into two simpler matrices: HW , where H is a “long skinny” matrix with just a few columns, and W is a “wide short” matrix with just a few rows. Fig. 1C and 1D present the plans generated with and without compression for 10 prostate and 10 lung patients, demonstrating a significant plan quality improvement using compression.

Scientific Significance: CompressRTP enables rapid, high-quality treatment planning, supporting the needs of emerging online and future real-time radiotherapy systems. Its framework-agnostic design enables seamless integration with both AI-driven and traditional optimization methods.

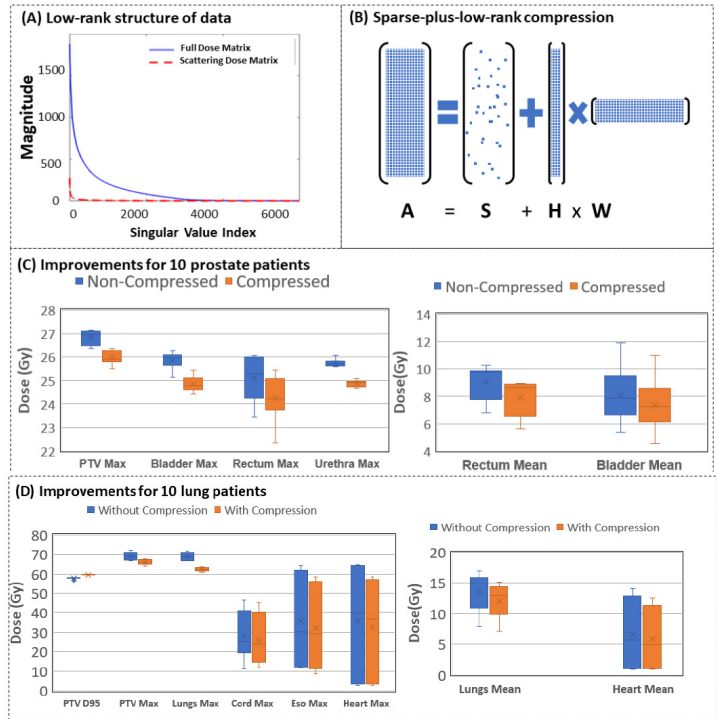


Fig. 1: (A) The distribution of singular values, showing exponential decay, reveals the data compressibility for the original matrix A (blue lines) and even more prominently for the scattering matrix L (red lines), (B) Schematic representation of the sparse-plus-low-rank decomposition of matrix A , (C,D) Comparison of plans generated using our in-house automated planning system, with compression (orange boxes) and without compression (blue boxes), evaluated on several clinically relevant metrics for 10 prostate patients (C) and 10 lung patients (D).

Potential Clinical Impact: Beyond enhancing our in-house automated planning system, ECHO, CompressRTP has the potential to significantly benefit our online treatment planning platforms, such as Ethos and MR-Linac, where rapid turnaround times are critical for clinical workflow and patient care.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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ECHO: MSK In-House Automated Treatment Planning System

Masoud Zarepisheh¹, Linda Hong², Ying Zhou², Qijie Huang², Jie Yang¹, Gourav Jhanwar¹, Hai D. Pham¹, and Joseph O. Deasy³

¹Computer Service, ²Division of Radiotherapy Physics, and ³Predictive Informatics

Motivation: To develop a fully automated treatment planning system for our clinic. The system has been successfully deployed in the clinic, used in the treatment of over 10,000 patients, and licensed by RaySearch Laboratories for broader dissemination.

Method: Expedited constrained hierarchical optimization (ECHO) leverages advanced mathematical techniques from operations research and optimization (e.g., hierarchical constrained optimization, convex approximations and Lagrangian methods) to fully automate the radiotherapy treatment planning process. It has been clinically implemented in our department, reducing average planning time by 50%.

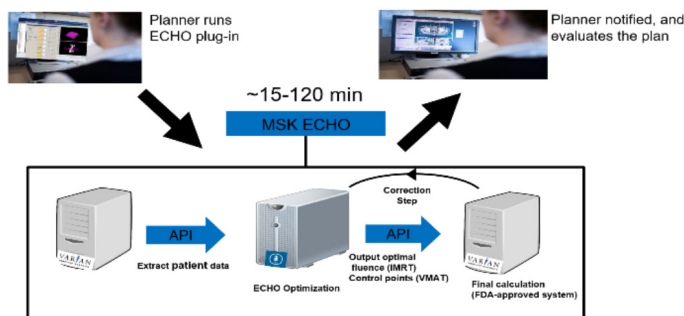


Fig. 1: Expedited constrained hierarchical optimization (ECHO) workflow is fully automated using application programming interface (API) scripting. IMRT: intensity-modulated radiotherapy VMAT: volumetric-modulated arc therapy

Results: Fig. 1 illustrates the system design and workflow of ECHO. Once structure contours and beams/arcs are defined, the user launches ECHO as a plugin within the Eclipse treatment planning system (TPS) (Varian Medical Systems, Inc., Palo Alto, CA), selecting the relevant structures for optimization. Through the Eclipse application program interface, ECHO retrieves all necessary patient data (e.g., beam geometry, influence matrices) to formulate and solve the underlying optimization problems. The derived machine parameters — such as fluence maps for intensity-modulated radiotherapy or control points for volumetric-modulated arc therapy — are automatically imported back into the Eclipse TPS for final dose calculation. Upon completion, the system sends an automated email notifying the user that the plan is ready for review. This workflow is fully automated, with user interaction required only for the initial setup of contours and beams.

ECHO has played a central role in spanning a wide range of disease sites, including the spine, prostate, and lung, as well as oligometastatic disease. Fig. 2 presents monthly statistics on plans generated using ECHO, along with their distribution across different disease sites.

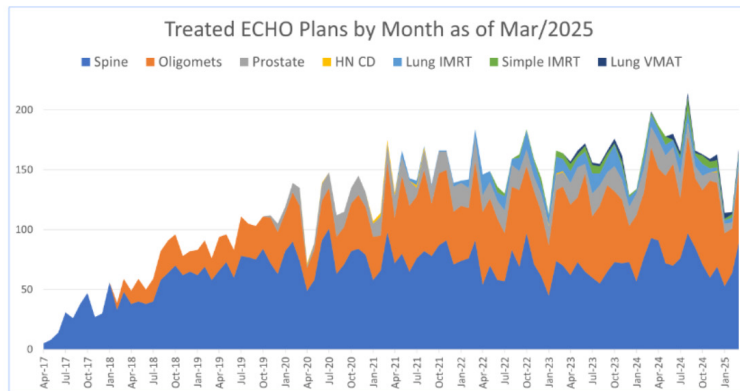


Fig. 2: About 180 plans are generated monthly using expedited constrained hierarchical optimization (ECHO).

HN: head and neck

CD: cone down

IMRT: intensity-modulated radiotherapy

VMAT: volumetric-modulated arc therapy

Scientific Significance: The project has resulted in over 11 publications in leading peer-reviewed journals, including *Medical Physics* (five articles) and *Physics in Medicine and Biology* (five articles), as well as two patents, both of which have been licensed by RaySearch Laboratories.

Clinical Impact: ECHO consistently delivers high-quality treatment plans while significantly reducing the workload for clinical staff.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Ensuring Tumor Coverage and Normal Tissue Sparing via On-Treatment Imaging and Motion Management

Pengpeng Zhang¹, Laura Happersett², Qiyong Fan², Yabo Fu², Hai Pham¹, Ping Wang¹, Sarah Burleson², Laura Cerviño², Antonio Damato², Joseph O. Deasy³, TianFang Li², and Xiang Li²

¹Computer Service, ²Division of Radiotherapy Physics, and ³Predictive Informatics

Motivation: To clinically implement an online motion management platform that corrects patient position during stereotactic body radiotherapy (SBRT) for prostate, lung, and paraspinal cancer, thereby mitigating the risk of missing the target and overdosing normal organs.

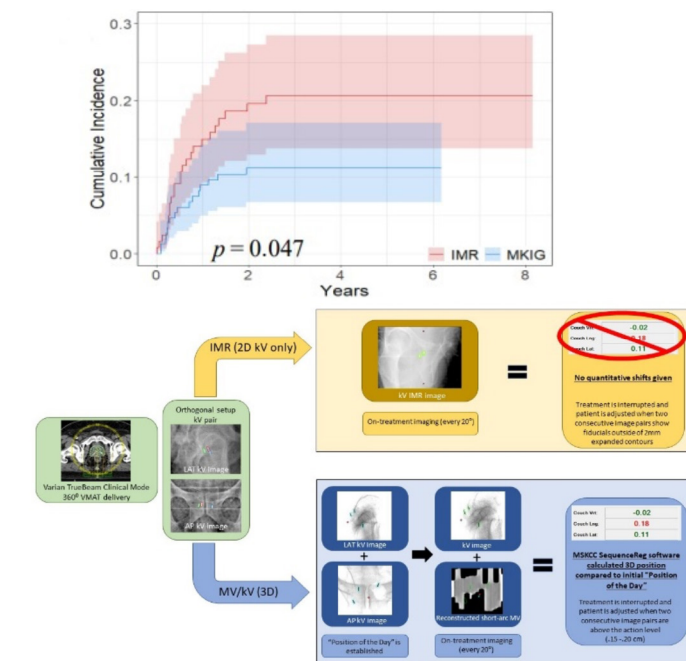


Fig. 1: Illustrations of the in-house megavoltage/kilovoltage (MV/kV) imaging system in comparison with a commercial intrafraction motion review (IMR) monitoring system.

Method: We developed an on-board 3D imaging guidance platform (megavoltage/kilovoltage image guidance, termed MKIG) that accurately tracks targets in real time. The system was clinically translated to replace the commercial intrafraction motion review (IMR) approach, which tracks the target only in two-dimensional (2D) imaging views. The key advancement of MKIG is its ability to continuously acquire megavoltage (MV) images during treatment and pair them with the orthogonal kilovoltage (kV) images to calculate the translational motion of the target every 3–4 seconds, as shown in Fig. 1. Shifts from the patient's initial treatment position are reported to the therapist and trigger an alert when a 1.5 mm action threshold is exceeded. Treatment is interrupted, and the position is corrected when the patient is off by the threshold for two consecutive imaging pairs. We further developed the MKIG platform and expanded its application to treat lung and paraspinal tumors (Fig. 2).

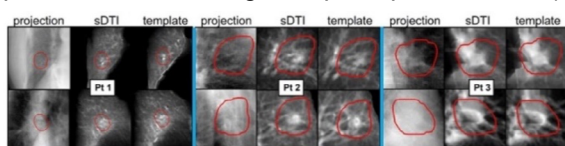


Fig. 2: Example of tracking lung (top) and paraspinal (bottom) tumors using the on-board imaging guidance system.

Results: During prostate SBRT, when compared with IMR, MKIG resulted in more treatment shifts (1.09 vs. 0.28) and a longer average delivery time per fraction (579 ± 205 s vs. 357 ± 117 s). Three-quarters (75%) of shifts resulting from MKIG were ≤ 3 mm, compared with 51% with IMR, indicating that MKIG detected and corrected smaller deviations. The incidence of grade ≥ 2 urinary toxicity was lower in the MKIG than in the IMR cohort, as shown in Fig. 3. On multivariate analysis of late urinary toxicity, only high (> 7) pre-RT International Prostate Symptom Score ($p < 0.043$) and the use of MKIG ($p < 0.029$) were selected. Excellent sub-millimeter localization accuracy was also achieved when using the image guidance system to monitor and correct target motion during lung and paraspinal SBRT.

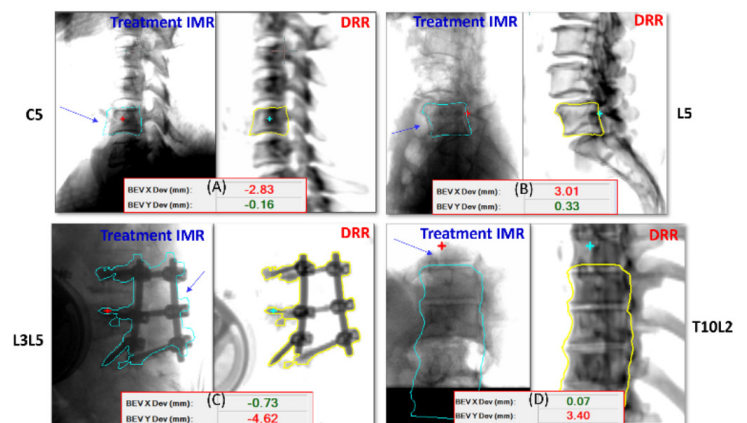


Fig. 3: Megavoltage/kilovoltage image guidance (MKIG) is a stronger platform for intrafractional motion management compared with intrafraction motion review (IMR) due to its association with reduced urinary toxicities.

Scientific Significance: Automated and quantitative MKIG had minimal impact on workflow and was superior to IMR in localizing the target during prostate, lung, and paraspinal SBRT, which was associated with a clinically significant reduction in late urinary toxicity.

Potential Clinical Impact: This technology provides a robust quality assurance tool for SBRT and paves the way for wide adoption of SBRT in a larger patient population, benefiting more patients through accurate dose delivery.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Human-AI Collaboration Enables Rapid, High-Fidelity Cancer Clinical Trial Eligibility Screening

Jacob T. Rosenthal¹, Emma Haehsy², Sulov Chalise², Menglei Zhu², Mert R. Sabuncu^{3,4}, Lior Z. Braunstein², and Anyi Li²
¹Tri-Institutional MD-PhD Program, ²Memorial Sloan Kettering Cancer Center, ³Cornell ECE and Tech, and ⁴Weill Cornell

Motivation: Clinical trials are essential for advancing cancer care, but patient enrollment remains low. A major bottleneck is the labor-intensive and errorprone process of eligibility screening, which involves reviewing unstructured data like clinical notes, labs, and imaging reports. There is a need for an automated, accurate, and scalable approach to identify eligible patients in real-world settings.

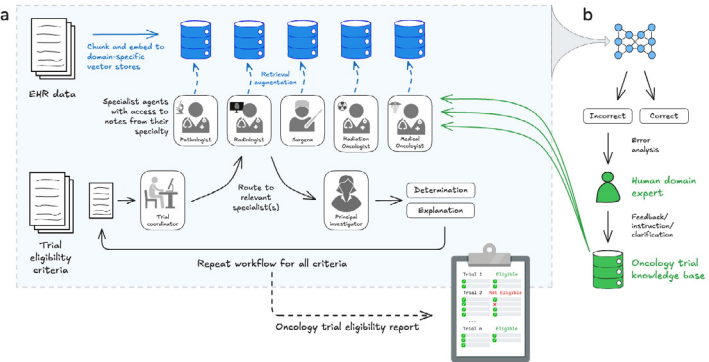


Fig. 1: Schematic diagram of the MSK-MATCH system and human-in-the-loop knowledge base curation. a) Clinical documents from the electronic health record (EHR) are categorized by domain, then split into chunks and embedded to create vector stores (solid blue arrow). b) The AI system was evaluated on all {patient, trial} pairs in the training dataset. Every incorrect prediction was manually reviewed by a clinical research coordinator, and feedback was provided in the form of instructions for the LLMs on how to avoid making the same error in the future.

Method: MSK-MATCH (Multi-Agent Trial Coordination Hub) is an AI-powered system developed to automate clinical trial eligibility screening. It integrates a generalpurpose large language model (LLM) with a structured oncology trial knowledge base. The system uses a multiagent framework: a general LLM performs unstructured data extraction, while a domain-specific agent assesses eligibility logic. MSK-MATCH was trained on 88,518 clinical notes from 731 patients across six cancer trials. It was benchmarked against human abstractors and evaluated for speed, accuracy, and scalability (see Fig.1).

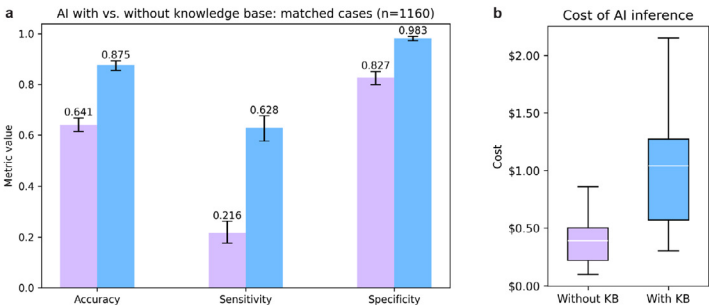


Fig. 2: Effect of including the oncology trial knowledge base (KB). a) Comparison of performance metrics on the test set, with and without inclusion of the KB. b) Comparison of cost per {patient, trial} pair, with and without inclusion of the KB.

Results: MSK-MATCH achieved high performance in identifying eligible patients: 98.6% accuracy, 98.4% sensitivity, and 98.7% specificity. Screening time was reduced from 20 minutes to 43 seconds per patient. The system demonstrated generalizability across diverse trial eligibility criteria. It enabled real-time patient-trial matching and trial accrual forecasting. The system also allowed clinicians to inspect intermediate steps for transparency and validation (see Figs. 2 and 3).

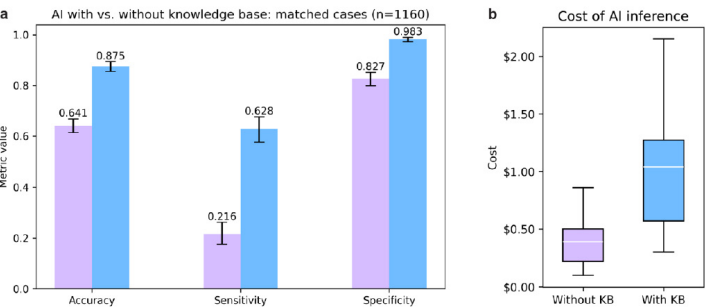


Fig. 3: Experimental design and overall results. a) Schematic of the experimental design. All {patient, trial} pairs are evaluated by the MSK-MATCH AI system (“AI alone”, n = 1160). All cases are also assigned to human review, either with the AI-assisted triage and workflow (“Human + AI”, n = 1100) or with the unassisted manual workflow (“Human alone”, n = 60). b) Comparison of performance metrics on the test set, by experimental group. c) Comparison of the time required to complete eligibility screening for a single {patient, trial} pair, with and without AI-assistance.

Scientific Significance: MSK-MATCH demonstrates the feasibility of high-fidelity, large-scale AI-enabled clinical trial matching and highlights the potential of LLMs in real-world oncology practice.

Potential Clinical Impact: By drastically accelerating and scaling clinical trial screening, MSK-MATCH may increase patient access to trials, improve accrual rates, and reduce clinician workload — bringing precision oncology trials to broader populations with greater efficiency.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

References: JT Rosenthal, E Haehsy, S Chalise, M Zhu, MR Sabuncu, LZ Braunstein, A Li. Human-AI Collaboration Enables Rapid, High-Fidelity Cancer Clinical Trial Eligibility Screening. *In review with Nature Cancer*. 2025.

Large Language Model Trained on Clinical Oncology Data Predicts Cancer Progression

Menglei Zhu¹, Hui Lin², Jue Jiang¹, Abbas J. Jinia¹, Justin Jee¹, Karl Pichotta¹, Michele Waters¹, Doori Rose¹, Nikolaus Schultz¹, Sulov Chalise¹, Lohit Valleru¹, Olivier Morin², JeanMoran¹, Joseph O. Deasy¹, Shirin Pilai¹, Chelsea Nichols¹, Gregory Riely¹, Lior Z. Braunstein¹, and Anyi Li¹

¹Memorial Sloan Kettering Cancer Center and ²University of California

Motivation: Large language models (LLMs) have shown promise in medicine but lack specialization in oncology and generalizability across institutions. There is an urgent unmet need for an oncology-specific, open-source LLM capable of predicting cancer progression using real-world clinical data.

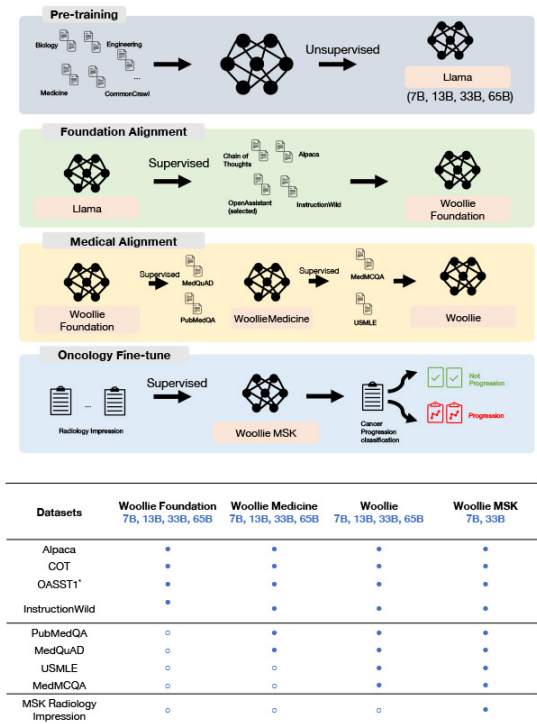


Fig. 1: Stacked refinement of Woollie models, from pre-training (a) to oncology domain fine-tuning (d).

Method: We have developed Woollie, an oncology-specific LLM based on Meta’s Llama architecture (Meta Platforms, Inc), trained using a stacked alignment strategy incorporating general, medical, and oncology datasets. The model was fine-tuned on 38,719 radiology impressions from 3,402 patients across five cancer types (lung, breast, pancreatic, prostate, and colorectal) at Memorial Sloan Kettering Cancer Center (MSK). Performance was evaluated in both binary and multi-class cancer progression prediction and externally validated on a University of San Francisco (UCSF) dataset of 600 impressions. The model’s outputs were further analyzed for interpretability using local interpretable model-agnostic explanations and topic modeling techniques (see Fig. 1).

Results: Woollie demonstrated strong performance in predicting cancer progression: MSK dataset: Area under the receiver operating characteristic curve (AUROC) 0.97 (33B model), with 0.98 for pancreatic cancer (see Fig. 2). UCSF dataset: AUROC 0.88 overall, with 0.95 for lung cancer.

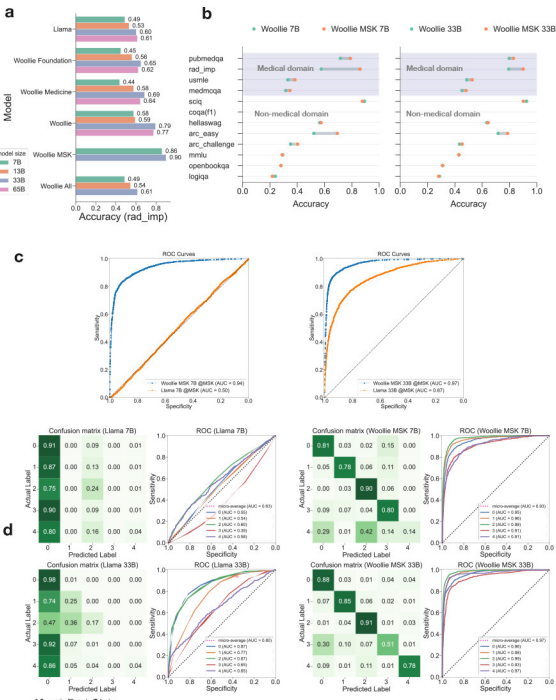


Fig. 2: High-performance cancer progression prediction models by Woollie MSK fine-tuned on MSK oncology data, including their performance metrics and comparisons with other models. ROC: Receiver Operating Characteristic. AUC: Area Under the Curve

Woollie outperformed ChatGPT and Llama across medical benchmarks (PubMedQA, USMLE). Smaller 7B models showed competitive performance and improved inference efficiency. Woollie also successfully identified tumor biology patterns and metastatic trajectories using unsupervised topic modeling.

Scientific Significance: Woollie is the first cross-institutionally validated, open-source oncology LLM. It achieves state-of-the-art performance in cancer progression prediction while maintaining explainability and adaptability for clinical tasks.

Potential Clinical Impact: Woollie could provide near-real-time progression risk estimates from radiology impressions, enabling earlier detection of likely progression and faster, better-targeted follow-up or treatment changes. By flagging high-risk cases for expedited review and supporting locally auditable deployment across institutions, it could improve triage and consistency of care.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

References: Zhu, M., Lin, H., Jiang, J. *et al.* Large language model trained on clinical oncology data predicts cancer progression. *npj Digit. Med.* 8, 397 (2025).

Evaluation of Deformable Image Registrations for Radiotherapy Dose Accumulation

Sebastian Meyer¹, LiCheng Kuo¹, Yu-Chi Hu², Lei Zhang¹, Ellen Yorke¹, James Mechalakos¹, Jue Jiang³, Harini Veeraraghavan³, Anyi Li², Laura Cerviño¹, and Pengpeng Zhang²

¹Division of Radiotherapy Physics, ²Computer Service, and ³Predictive Informatics

Motivation: Deformable image registration (DIR) is an essential technique used in various tasks for state-of-the-art radiation therapy. However, the ill-posed nature of DIR causes inherent uncertainties in the estimated deformation, e.g., due to the specific choice of DIR parameters for unknown anatomical changes. Understanding these uncertainties and integrating them into downstream applications, such as dose accumulation, is paramount for informed clinical decision-making.

Method: In this report, we propose an efficient methodology using principal component analysis (PCA) to compute the spatial distribution of the DIR uncertainty and directly integrate it into dose accumulation, and we demonstrate its feasibility through a use case in adaptive radiotherapy for lung cancer. We derived the dosimetric impact related to DIR uncertainty in a three-step procedure. First, we performed a series of 63 independent DIRs, each with slightly perturbed parameters that can noticeably affect the result (i.e., B-spline knot spacing, bending energy penalty weight, and optimizer step size), selected around the standard settings for thoracic CT-cone-beam CT (CT-CBCT) DIR. All results were validated using contour information available on each CBCT to ensure reasonable registrations.

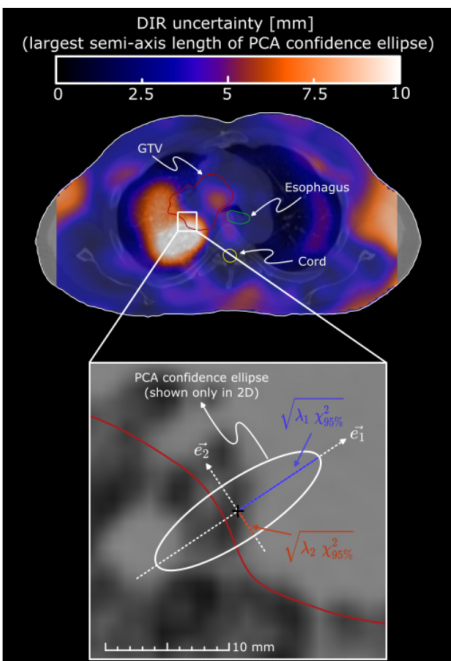


Fig. 1: Example case for principal component analysis (PCA)-based deformable image registration (DIR) uncertainty estimation. Planning CT with registration uncertainty overlay (i.e., the largest semi-axis length of the PCA confidence ellipse for the week 6 cone-beam CT [CBCT] DIR). The zoomed-in view shows the constructed ellipse of a single voxel obtained by the eigenvectors $\vec{e}$ and eigenvalues λ .

planning CT for dose accumulation, we mapped the largest and smallest dose values within the ellipsoids to estimate the upper and lower dose limits for each voxel.

Results: Robust dose accumulation with specified uncertainty for clinical decision-making: atypical weekly doses accumulations and the associated dose-volume histogram (DVH) uncertainty bands were calculated (Figure 2). Average dosimetric uncertainties derived from the confidence ellipsoids were mostly within 3 Gy, but were highly patient-specific due to interplay between DIR uncertainty and dose gradient. When the DIR uncertainty was considered within the dose accumulation, institutional organ-at-risk (OAR) dose constraints were exceeded in 30% of cases (6 / 20), indicating the importance of considering the inherent uncertainty associated with DIR. Automated integration into the clinical workflow: The average computational time for computing the DIRs, PCA confidence ellipsoids, and performing dose search via high-resolution interpolation was approximately 30 min, making the approach clinically feasible for automated offline evaluations.

Scientific Significance: We have developed a versatile probabilistic framework based on PCA for integrating registration uncertainty into dose accumulation and presenting it as DVH uncertainty bands. The use of the proposed DIR confidence ellipsoids has the potential to provide a more comprehensive understanding of the delivered dose distribution, which is vital for ensuring the effectiveness of adaptive radiotherapy and re-irradiation.

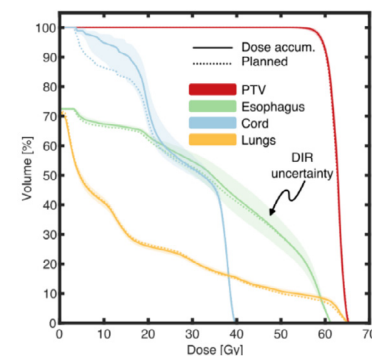


Fig. 2: Corresponding dose-volume histogram for the example case presented in Figure 1, showing the original plan (dashed line) and the dose accumulation (solid line) with its uncertainty (shaded area) due to deformable image registration (DIR).

Potential Clinical Impact:

We plan to develop an automated pipeline that computes DIR and its uncertainty for selected patients, and feeds the clinical dose accumulation script Radiotherapy Dose Accumulation Routine (RADAR), for quality assurance reviews and potential treatment

adaptation. This program will provide the essential information clinicians need to design adapted radiotherapy plans.

Acknowledgments: We appreciate our collaborators in Radiation Oncology, including Dr. Josh Yamada and Dr. Andreas Rimner. This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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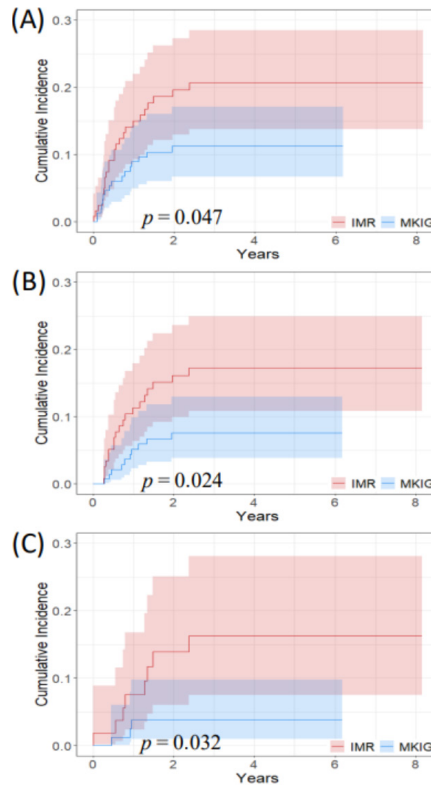
Reduction of Post-Radiotherapy Urinary Toxicity via Intrafractional MV-kV Prostate Location Monitoring

Pengpeng Zhang², Laura Happersett¹, Sarah Burleson¹, Jung Hun Oh³, Brian Leong¹, Maria Thor³, Antonio Damato¹, Andrew Jackson¹, Laura Cervino¹, and Joseph O Deasy³

¹Division of Radiotherapy Physics, ²Computer Service, and ³Predictive Informatics

Motivation: Stereotactic body radiotherapy (SBRT) for prostate cancer delivers a high tumoricidal dose in ≤ 5 fractions but is sensitive to organ motions because a sizable geometric miss in a single fraction would have a significant dosimetric impact and would be difficult to compensate for. We have developed a novel megavoltage-kilovoltage image guidance (MKIG) system that is seamlessly integrated into the radiation therapy (RT) delivery platform to enable SBRT by minimizing inter- and intra-fractional positional variations and accurately delivering planned doses to the intended locations. This report is the first to directly evaluate the clinical impact from the perspective of advanced technologies for managing intrafraction motions.

Method: We built a 3D MKIG platform (Fig. 1) that accurately tracks implanted prostate fiducials in real time and clinically translated the system to replace a commercial approach, intrafraction motion review (IMR), which only tracks fiducials in the 2D kilovoltage (kV) views. From 2017 to 2019, 150 prostate cancer patients were treated with SBRT and monitored by MKIG. The motion trace of the fiducials alerts therapists to interrupt and reposition the prostate when displacement exceeds a 1.5 mm threshold. A comparison cohort of 121 patients was treated with the same dose regimen and treatment technique but managed by IMR. Statistics on intrafraction patient shifts and delivery time were collected to evaluate the workflow efficacy. The incidence of grade ≥ 2 urinary toxicities was analyzed to assess clinical complications. The median follow-up time was 3.7 years (range, 0.2-8.2 years).



Scientific Significance:

Automated and quantitative 3D MKIG introduced minimal workflow impact and was superior to 2D IMR in localizing the prostate during SBRT. We have been one of the first groups to demonstrate in a clinical study that intrafraction motion management is correlated with a clinically significant reduction in late urinary toxicity.

Fig. 2: Cumulative incidence curves compare the risk of genitourinary (GU) grade ≥ 2 toxicity between the megavoltage-kilovoltage image guidance (MKIG) and intrafraction motion review (IMR)

cohorts for (A) the entire cohort, (B) a sub-group with late GU grade ≥ 2 toxicity (follow-up > 3 months), and (C) a sub-group with mild GU symptoms (International Prostate Symptom Score 0-7) at baseline.

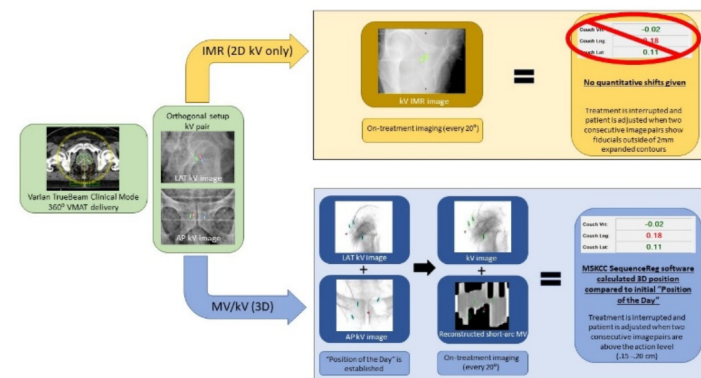


Fig. 1: Illustrations of differences in intrafraction motion review (IMR) and megavoltage-kilovoltage (MV-kV) image guidance.

Results: MKIG treatments had more treatment shifts (1.09 vs. 0.28) and a longer average delivery time per fraction (579 ± 205 s vs. 357 ± 117 s) than IMR treatments. Three-quarters (75%) of shifts resulting from MKIG were ≤ 3 mm, vs. 51% for IMR, indicating that MKIG detected and corrected smaller deviations. The incidence of grade ≥ 2 urinary toxicity was lower in the MKIG than in the IMR cohort: 10.7% vs. 19.8% ($p = 0.047$). On multivariate analysis of late urinary toxicity, only a high pre-RT International Prostate Symptom Score (IPSS) (IPSS > 7, $p < 0.043$) and the use of MKIG ($p < 0.029$) were identified as significant predictors (Fig. 2).

Potential Clinical Impact: In collaboration with Aarhus University, we are implementing a real-time dose tracker and a deep-learning network to provide a more relevant dosimetric-oriented signal for decision-making in motion management. We are also expanding the scope of this novel technology to other clinical use cases, such as paraspinal and lung SBRT. To overcome the limitations of this retrospective study, we hope to form a multi-institutional collaboration, test the improved MKIG platform in a randomized trial, and eventually benefit more patients with a robust and effective motion management system.

Acknowledgments: We appreciate our collaborators in Radiation Oncology, including Dr. Michael Zelefsky and Ahmed Elsayegh. We also want to thank Margie Hunt and Gig Mageras for their leading roles in designing and implementing the imaging-guidance platform at MSK before their retirement. This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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PlanQ: AI-Powered Radiation Therapy Workflow Management Platform

Doori Rose¹, Laura I. Cerviño², Joseph O. Deasy³, Sharif F. Elguindi², Gregory Niyazov², Jean M. Moran², Darian Pazgan-Lo-renzo¹, Yu-Chi Hu¹, Ellen Pinto², Shi Liu², Lakshmi Santanam², Niral M. Shah², Pengpeng Zhang¹, and Anyi Li¹
¹Computer Service, ²Division of Radiotherapy Physics, and ³Predictive Informatics

Motivation: Radiation therapy (RT) is essential for treating more than half of cancer patients, yet the current workflow is complex, fragmented, and inefficient. At large, patient data is dispersed across systems, causing delays and manual errors. Such challenges result in prolonged wait times before patients begin treatment, increasing psychological stress, and potentially compromising outcomes. There is an urgent need for a centralized, intelligent system that harmonizes workflows, improves care coordination, and accelerates treatment delivery.

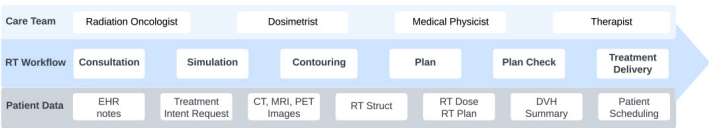


Fig. 1: PlanQ is a unified platform that connects disparate patient data and streamlines key tasks across the radiation therapy (RT) workflow, improving collaboration and efficiency for multidisciplinary care teams.

Method: PlanQ is an AI-based, vendor-neutral RT workflow platform developed at Memorial Sloan Kettering Cancer Center (MSK). It integrates data across 13+ hospital systems (e.g., MIM, Aria, Mosaic, Epic) using a flexible connector layer built on distributed data technologies. It consolidates diverse modalities, including unstructured clinical notes, structured treatment plans, radiology, pathology, and DICOM imaging, into a dynamic digital patient profile. The platform employs medical large language models (LLMs), knowledge graphs, and automated curation engines to standardize data, extract structured insights from clinical notes, and support real-time decision making (see Fig. 1). PlanQ features a centralized communication hub, automated safety checks, LLM-based treatment progression tracking, and AI-guided workload assignment (see Fig. 2).

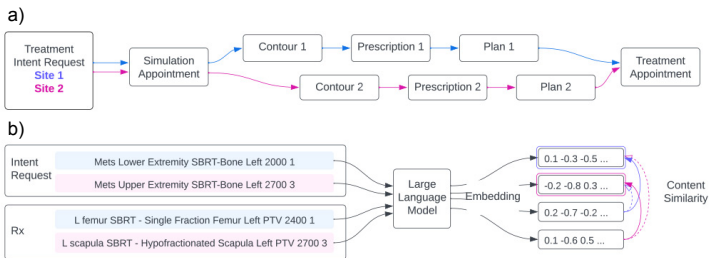


Fig. 2: a): The intelligent curation module uses AI to connect unstructured, non-standardized clinical notes at the site level when patients receive treatment at multiple sites simultaneously or on different timelines. b): We use an LLM trained on a medical knowledge base to link clinical events described using non-standardized medical terminology. We extract features from treatment intent reports and prescriptions using a sentence transformer, store the vector embeddings in an in-memory database, and calculate vector similarities to link the events at the site level. SBRT: stereotactic body radiation therapy

Results: PlanQ has significantly improved clinical efficiency, reducing treatment coordination time by 70% and the planning team's burden by up to 20%. It has been deployed in production at MSK with positive user adoption, with daily usage by more than 170 users. The platform (see Fig. 3) enables real-time treatment tracking and multidisciplinary coordination via an intuitive patient journal interface. It created the infrastructure for in-clinic AI model deployment and real-world evidence generation.

Scientific Significance: PlanQ represents the first large-scale application of LLMs and AI in clinical RT workflows. It addresses data fragmentation, enhances safety, and operationalizes clinical intelligence, making it a model for AI-integrated healthcare infrastructure.

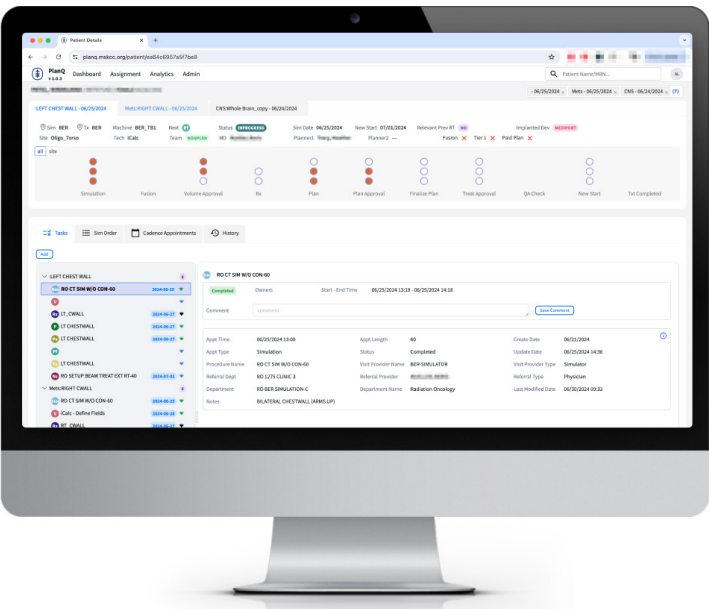


Fig. 3: The PlanQ patient dashboard displays real-time clinical events that are tracked using language models, enabling seamless handoffs between care teams. Tasks are dynamically generated from the patient journal, and curated information is presented to each care team member throughout the radiation therapy process.

Clinical Impact: PlanQ has already transformed radiation oncology by reducing errors, accelerating care, and relieving clinical burden. At scale, it could save millions in operational costs, improve patient outcomes, and serve as a blueprint for intelligent workflow systems in oncology and beyond.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

PortPy: Bridging Research and Clinical Practice with Open-Source Optimization Tools for Radiotherapy Treatment Planning

Masoud Zarepisheh¹, Mojtaba Tefagh², Vicki Taasti³, and Gourav Jhanwar¹

¹Computer Service, Department of Medical Physics, MSK, ²The University of Edinburgh, and ³Aarhus University

Motivation: To develop a Python-based open-source platform that accelerates research and innovation in radiotherapy treatment planning optimization. We are resubmitting a NIH grant proposal to support this effort (the initial submission received a promising impact score). The platform is scheduled for clinical deployment as the host system for our in-house automated planning solution, expedited constrained hierarchical optimization (ECHO).

Comprehensive tools: PortPy is designed for seamless integration with commercial treatment planning systems.

A benchmark dataset: Currently includes 100 curated lung cancer cases, featuring selected beam configurations, complete optimization data, and benchmark intensity-modulated radiotherapy plans generated using ECHO.

Benchmark algorithms: They include state-of-the-art optimization methods, such as mixed-integer programming, for generating globally optimal treatment plans. This ecosystem empowers researchers to develop, compare, and validate new algorithms with transparency and reproducibility, accelerating innovation in radiotherapy planning. Illustrated in Fig. 2 is the PortPy design and its three primary modules: "Data Management," "Plan Generation," and "Plan Evaluation."

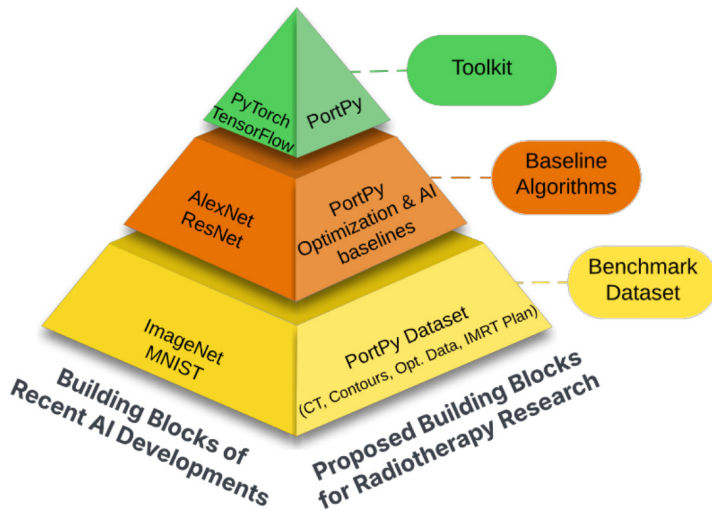


Fig. 1: A conceptual illustration of the development of the Planning and Optimization for Radiation Therapy in Python (PortPy) platform. Inspired by recent advancements in AI and facilitated by new tools, a benchmark dataset, and algorithms. Prog.: programming; TPS: treatment planning system; Opt.: optimization; IMRT: intensity-modulated radiotherapy

Method: We have developed Planning and Optimization for Radiation Therapy in Python (PortPy), an open-source software package designed to accelerate research and facilitate clinical translation of advanced treatment planning techniques in radiation therapy. PortPy addresses key limitations of existing tools by providing 1) interoperability with commercial systems, 2) access to benchmark datasets for standardized evaluation, and 3) integration of both advanced AI-based and classical benchmark optimization algorithms. Currently, PortPy has already been downloaded over 30,000 times on GitHub, reflecting strong engagement from the research community.

Results: Illustrated in Fig. 1 is the inspiration behind the development of PortPy, which is modeled on the success of open-source initiatives in the AI and computer science communities. Open-source frameworks such as PyTorch and TensorFlow, alongside a benchmark dataset such as ImageNet, and landmark algorithms (e.g., AlexNet), have transformed research and innovation in AI. With PortPy, we aim to bring a similar paradigm to radiotherapy treatment planning by providing the following:

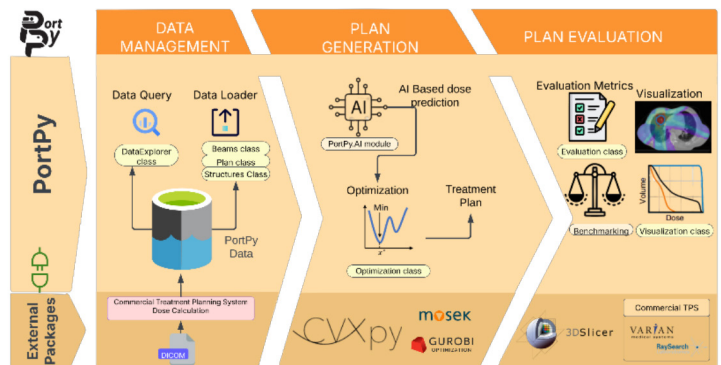


Fig. 2: The Planning and Optimization for Radiation Therapy in Python (PortPy) workflow. PortPy comprises three primary modules: 1) "Data Management," for accessing the benchmark dataset, 2) "Plan Generation," for creating treatment plans using either classical optimization techniques or AI-based planning, and 3) "Plan Evaluation," for visualizing and assessing the generated plans.

Scientific Significance: PortPy is designed to accelerate research in treatment planning optimization by bridging the gap between multiple scientific disciplines, including medical physics, computer science, and applied mathematics, thereby fostering interdisciplinary collaboration and innovation.

Clinical Impact: PortPy is the foundation for expanding our ECHO system, enabling more efficient, higher-quality treatment planning for patients beyond Memorial Sloan Kettering Cancer Center.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

References:

Jhanwar, G, Tefagh, M, Huang, Q, Taasti, VT, Tuomaala, S, Nadeem, S, Zarepisheh, M. (2024). PortPy: An Open-Source initiative for Radiotherapy Treatment Planning Optimization Including Benchmark Data and Algorithms and Integration with Commercial TPS. Proceedings of the 20th ICCR, 1-4.

Statistical Analysis and Control of Batch Effects in Cancer Radiomic Biomarkers

Elfried Salanon², Anqi Fu¹, Aditya Apte¹, Usman Mahmood¹, Zehor Belkhatir³, Amita Shukla-Dave¹, and Joseph O. Deasy¹
¹Department of Medical Physics, MSK, ²Université Clermont Auvergne, INRAE, UNH, Plateforme d'Exploration du Métabolisme, MetaboHUB Clermont, and ³Digital Health and Biomedical Engineering Group, University of Southampton

Motivation: Radiomics, the extraction of quantitative features from radiological imaging data, has the potential to revolutionize cancer care by enhancing image interpretation with personalized assessments. However, radiomic biomarkers are sensitive to non-biological factors that vary between batches of data, which introduce bias and obscure true relationships between features. We investigate the impact of two such batch effects on radiomic features and the challenges in controlling them using standard statistical methods.

Method: A total of 282 radiomic features were extracted from CT scans of a 3D-printed phantom with five imprinted pancreatic ductal adenocarcinoma tumors. We conducted principal component analysis (PCA) and computed statistical correlation measures to analyze the impact of batch effects due to integral tube current and reconstruction kernels on the extracted features. Robustness to batch effects was quantified using the Pearson correlation coefficient and the concordance correlation coefficient. We then applied the ComBat batch effects correction method and compared the pre- and post-correction datasets to assess its effectiveness in controlling for bias (see Figs. 1 and 2).

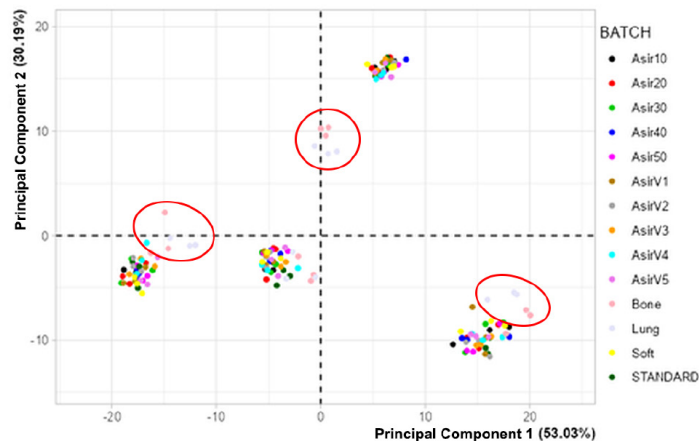


Fig. 1: Note: Red circles indicate bone- and lung-kernel batch effects, which were not completely corrected with the ComBat method.

Results: We found that 23.7% of the radiomic features were robust to tube current and 13.6% were robust to reconstruction kernel. Overall, only 39 features were robust to both sources of batch effects, with most of those being first-order statistics. The batch effects in our study were nonlinear and nonconstant, varying both by source and across specific regions of the image, which proved difficult

for general correction methods to handle. Data correction via ComBat yielded improvements in robustness, but clustering of batches remained, especially for reconstruction kernels. Specifically, ComBat removed batch effects due to the adaptive statistical iterative reconstruction (ASiR), ASiR-V, and the standard and soft kernels, but failed for the more complex lung and bone kernels.

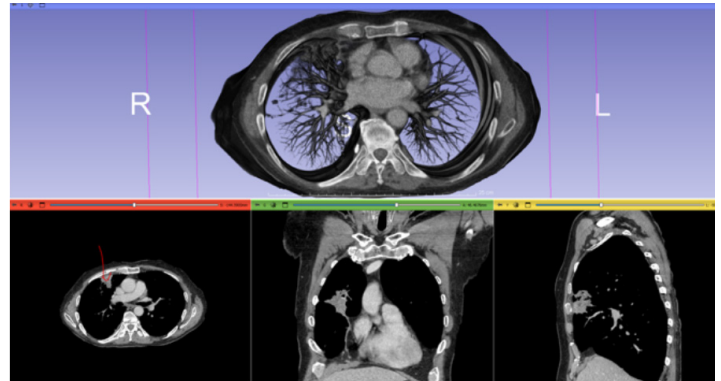


Fig. 2: Lung phantom design for a future machine learning (ML)-based batch effects correction method.

Scientific Significance: We quantified the impact of tube current and reconstruction kernel on radiomic features and identified those features that are robust to batch effects. In addition, we demonstrated that the commonly used ComBat correction method fails to correct for biases introduced by bone and lung reconstruction kernels in radiomic data.

Potential Clinical Impact: Our study identifies robust radiomic biomarkers that can be used to construct a mathematical model for cancer diagnosis and treatment, thereby reducing bias and improving accuracy. The results motivate future research into a new batch effects correction method built upon state-of-the-art machine learning (ML)-based models and novel 3D lung phantoms.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

References:

E. Salanon, A. Fu, A. P. Apte, U. Mahmoud, Z. Belkhatir, A. Shukla-Dave, J. O. Deasy. Cancer radiomic feature variations due to reconstruction kernel choice and integral tube current. bioRxiv preprint. 2024; doi: 10.1101/2024.06.04.596806.

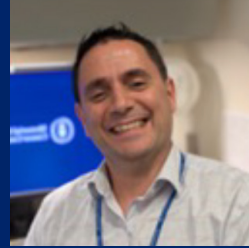
Medical Health Physics (Radiation Safety)



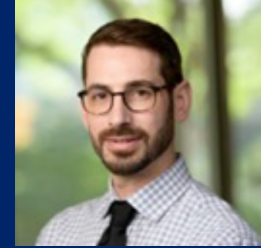
Lawrence Dauer



Michael Bellamy



Matthew Williamson



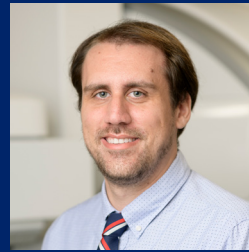
Brian Quinn



Bae Chu



David Bierman



Brian Serencsits



Daniel Miodownik



Joaquin Altamirano



Serene Waye



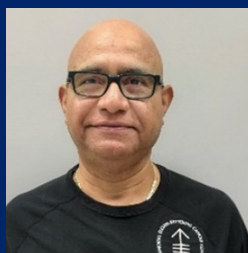
Natalie Abrahams



Grace Roemer



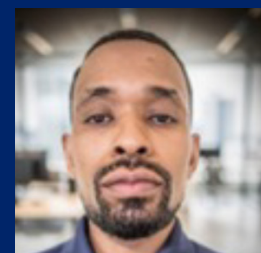
Mohammad Fahim



Julio Menendez



Julio Curiel



Antoine Parkinson

Medical Health Physics

Nearly every patient at MSK needs diagnostic imaging or therapeutic treatment/intervention, which utilizes radiation or radioactive material. The Medical Health Physics (MHP) section of the Department of Medical Physics implements a pivotal role in facilitating the safe, high-quality, and effective use of radiation and radioactive material for the overall benefit of MSK patients. The section provides guidance and oversight to all users of radioactive material and devices that produce radiation at all MSK locations to ensure the safe and effective application of radiation in patient care and research as well as facilitating ongoing compliance with applicable institutional, local, state, and federal regulatory requirements. In addition, MHP provides specific education and training on radiation benefit and risk as well as health physics policies, procedures, and implementation. MHP operates within seven critical radiation protection arenas:

Clinical Support: Ensure the safety, quality, and effectiveness of the use of radiation and radioactive material in all clinical settings. This includes annual volumes of nearly 1 M radiology procedures, ~150 K external beam procedures, > 50 K PET/CT imaging scans, > 3.3 K breast radioactive seed localization procedures, and an increasing 1.2-1.5 K radioactive material targeted theranostics procedures, which require direct patient and patient family interactions for radiation precaution discussions. Clinical support includes implementing/maintaining staff and patient radiation dosimetry programs (> 3.5 K) as well as staff, patient, and patient family training. In addition, MHP manages > 150 authorized user MDs and > 70 authorized physicists. MHP takes the lead on all radiation and radioactive material facility design, shielding evaluations, infrastructure, and final readiness approvals.

Research Laboratories and Research Core Support: Manage the MSK Committee on Radiation to review, amend and approve > 150 research protocols annually that utilize radiation and/or radioactive material. Support and audit ~100 research facilities for radiation use. Maintain radiation monitoring equipment. Facilitate radiochemistry research, supporting the Molecular Imaging and Therapy Service, including an active cyclotron and targeted alpha theranostics laboratory spaces.

Regulatory Agency Interactions: Manage all operations within the highly regulated environment of radiation protection, including 84 current local, state, and federal agency licenses and permits across MSK. Facilitate all inspection and response activities.

Radiation Emergency Response: Direct responses for all internal and community radiation events and managing MSK as founding partner of the National Radiation Injury Treatment Network.

Education: Provide radiation protection and radiation interaction (physics and biology) training for all individuals who utilize or encounter radiation or radioactive material in the institution, including MD residents, Medical Physics residents, radiation therapists, radiation technologists, nurses, researchers and all other staff.

National and International Reach: As the recognized radiation protection leaders of the industry, MHP plays an active role on national and international radiation protection professional guidance and policy setting.

Medical Health Physics Innovation and Research: MHP actively conducts ongoing research associated with the safety, quality, and effectiveness of the use of radiation and radioactive material in medical settings.

More Information:



The U.S. Million Person Study of Low-Dose-Rate Occupational Radiation Health Effects

Michael Bellamy¹, David Bierman¹, Serene Wayne¹, Grace Roemer¹, and Lawrence T. Dauer¹

¹Medical Health Physics



Motivation: There is a critical knowledge gap on the health consequences of exposure to radiation received gradually over time.

Method: MSK Medical Health Physics section scientifically directs and coordinates this study administered by the National Council on Radiation Protection and Measurements (NCRP). The epidemiologic study includes U.S. workers and veterans from 30 epidemiologic sub-cohorts and evaluates both cancer and non-cancer adverse outcomes. The MPS has published over 100 articles to date in the peer-reviewed scientific literature based on consistent epidemiologic methods while following precise dosimetry guidelines for determining organ-specific radiation doses from low-LET external radiation, neutrons and intakes of radionuclides. Innovations include the use of Medicare and Medicaid claims data to obtain individual information on smoking histories and disease occurrence, the use of the Virtual Pooled Registry Cancer Linkage System for cancer incidence, the development of open-source R-based software to handle big data with billions of data points, and the development of statistical approaches to optimize epidemiologic data harmonization.

Results: Early findings on > 600,000 workers and veterans include: 1) a potential association between occupational radiation and Parkinson's disease in some cohorts (consistent with Russian data), 2) a low risk of lung cancer and no difference in the risk between males and females (consistent with tuberculosis-fluoroscopy patient data), 3) a risk of leukemia excluding chronic lymphocytic leukemia (consistent with atomic bomb survivor data but with wide confidence limits), 4) little evidence for an association with ischemic heart disease (IHD), 5) inconsistent evidence of increases in all solid cancers combined due in part to the heterogeneity of the cancer sites and the influence of uncontrolled confounding due to asbestos exposure and cigarette smoking, 6) little evidence that contemporary radiation workers had higher risks than earlier workers, and 7) evidence that chromosomal damage could be detected 65 years after exposure to fallout from nuclear weapons testing.

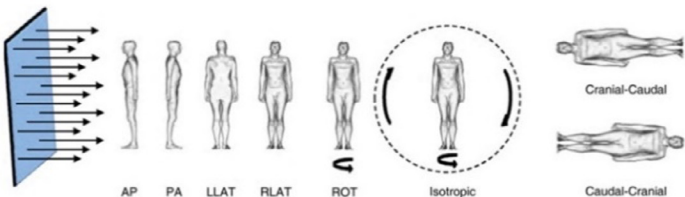


Fig. 1: Radiation exposure organ dosimetry geometries considered.

Scientific Significance: The plethora of studies on the risks of adverse outcomes from both acute and high-dose exposures, including the landmark study of atomic bomb survivors, are not characteristic of the chronic exposure to low-dose radiation encountered in occupational and public

settings. The MPS is the largest radiation occupational studies designed specifically to provide understanding of late health effects from chronic radiation exposures. Healthy American radiation workers and veterans are being evaluated for cancer and non-cancer (e.g., heart disease) mortality and morbidity (incidence) following exposures to low- (e.g., gamma) and high-LET (e.g., alpha, neutron) radiations, and intakes of radionuclides (e.g., uranium, plutonium, etc.). Importantly, rare cancers and differences between women and men are being examined. The study is directly relevant to U.S. radiation exposed worker populations: nuclear utility, medical, industrial radiographers, aircrews who fly at high altitudes, astronauts, cleanup workers of contaminated environments, radioactive waste management, emergency responders to nuclear incidents, nuclear submariners, and military personnel engaged in radiation activities.

Potential Clinical Impact: Adds critical information on cancer and non-cancer adverse outcome risks for U.S. radiation workers.

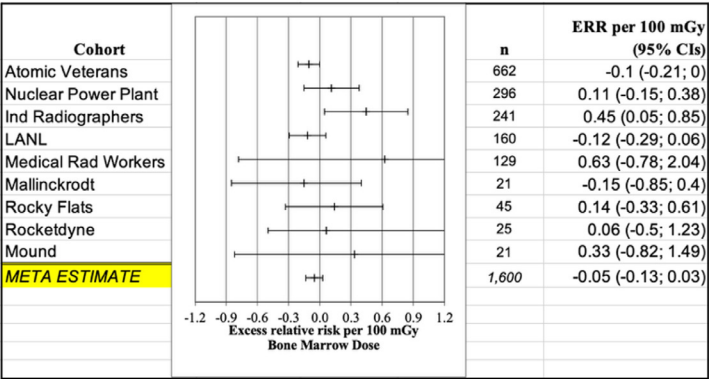
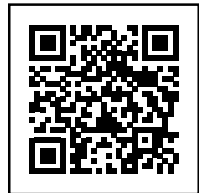


Fig. 2: Meta analysis Excess Relative Risk (ERR) / 100 mGy for non-chronic lymphocytic leukemia mortality
Los Alamos National Laboratory: LANL

Acknowledgments:

- Research grants from DOE and NASA. This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).
- MPS oversight by NCRP Advisory Committee - 1 with MSK's Dr. Jonine Bernstein, Department of Epidemiology & Biostatistics, as member.

References and More Information:



Radiation Protection for Targeted Theranostics and Therapeutic Nuclear Medicine Treatments

Medical Health Physics Team Members¹, Bae Chu¹, Brian Quinn¹, Brian Serencsits¹, Michael Bellamy¹, Matthew Williamson¹, and Lawrence Dauer¹

¹Medical Health Physics

Motivation: The implementation of novel targeted theranostics and therapeutic nuclear medicine treatments requires radiation protection evaluation and guidance.

Methods: The MSK Medical Health Physics (MHP) section conducts research on all aspects of radiation protection for targeted theranostics and therapeutic nuclear medicine treatments. MHP often publishes first-in-man evaluations of safe practices, recommendations, and guidance. In addition, MHP spearheads assessments of organ dosimetry for associated molecular and imaging scans (e.g., computed tomography [CT], positron emission tomography/CT). MHP evaluates all aspects of the delivery of targeted theranostics and therapeutic treatments, including patient radiation dosimetry, staff dosimetry, contamination potentials, family exposures, and exposures to members of the public as well as developing and implementing appropriate radiation protection precautions for patients, their families, and co-workers. As each protocol using an innovative targeted therapy is implemented, MHP staff specifically measure and evaluate all radiation exposure conditions, develop calculation methodologies for evaluating patient-release, and develop appropriately safe handling techniques and procedures. MHP regularly publishes these in peer-reviewed physics journals to further disseminate findings and facilitate FDA approvals as these treatments grow both nationally and internationally.

Results: Radiopharmaceuticals currently employed and evaluated include: Lu-177 Pluvicto, Lu-177 Lutathera, Lu177 Edotreotide, Lu-177 DOTA-related compounds, Lu177 Girentuximab, Lu-177 PNT6555, Ra-223 Xofigo, and I-131 for thyroid as well as I-131 MIBG, CLR, Omburtamab, other monoclonal antibodies, and increasingly targeted alpha therapies using Ra-223 Xofigo, and Ac-225 linked compounds. New and novel theranostic protocols are increasingly being introduced. With robust administrative and engineering controls, such novel treatments can be handled and administered safely for clinical use. Proper precautions, personal protective equipment (e.g., Fig. 1), training techniques, and radiation detection instrumentation (e.g., Fig. 2) are crucial for reducing exposures as well as contamination events while protecting clinical staff and the public. Patient release instructions can be developed to provide safety while often allowing patients to resume their activities (albeit with some restrictions for family and co-workers, other than for alpha-based theranostics where such restrictions are often minimal).

Scientific Significance: Targeted theranostics and therapeutic nuclear medicine treatments provide an effective means of delivering large radiation doses to targeted locations and have been shown by the MHP section to be safety and effectively administered.

Potential Clinical Impact: Evaluating, developing, implementing, and quality-checking the use of targeted theranostics and therapeutic treatment administrations for oncology and associated patients is a critical component of offering safe, high-quality, and effective treatments for patients and their families while ensuring the safety of staff and members of the public.

Instrument	Background (cpm)	Efficiency (cpm/dpm)	MDA	
			dpm	Bq
Portable survey meters				
α-probe (ZnS)	0	0.07	3	0.05
Thin window β-γ-probe (GM)	33	0.18	147	2.47
Low-energy γ-probe (NaI)	234	0.06	1,128	18.82
Radiometric detectors				
Liquid scintillation counter	36	0.97	13	0.22
γ-counter	288	0.13	547	9.13

cpm = counts per minute; dpm = disintegrations per minute.

Fig. 2: Removable contamination efficiencies and minimum detectable activity (MDA) for commonly used radiation detection equipment

Acknowledgments:

- Department of Radiology Molecular Imaging and Treatment Service.
- Molecular Imaging and Therapy Physics.
- Diagnostic Imaging Physics
- This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

References and More Information:

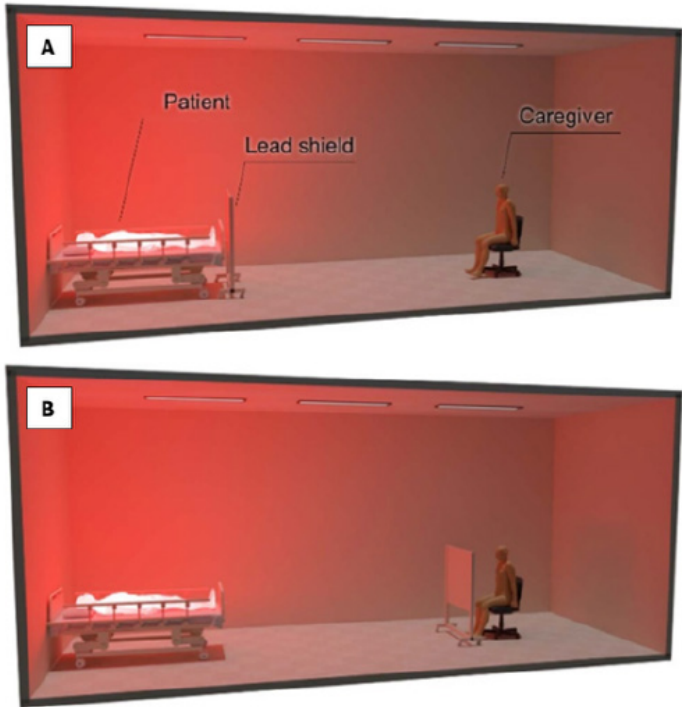


Fig. 1: Radioactive shielding configurations [(A) near patient and (B) near caregiver] for protecting families and staff during I-131 radiopharmaceutical theranostic therapy.

Molecular Imaging and Therapy Physics



John Humm



Pat Zanzonico



Adam Kesner



Joe O'Donoghue



Bradley Beattie



Assen Kirov



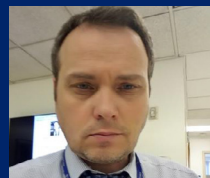
C. Ross Schmidtlein



Milan Grkovski



Lukas Carter



Daniel Lafontaine



Finn Augensen

Diagnostic Imaging Quality Assurance Section (DIQAS)



Yusuf Erdi



Yiming Gao



Usman Mahmood



Wei Tang



Daniel Long



Hung Ching



Dustin Lynch



Kevin Stiles



Andres Ruuge

Animal Imaging Core



Mihaela Lupu, Valerie Longo, Carl Lekaye, and Dov Winkleman

Molecular Imaging and Therapy Physics

Program Growth and Scope: The MITS physics section, alongside nuclear medicine physicians and radiochemists, provides one of the 3 cornerstones necessary to support a successful and innovative Molecular Imaging and Therapy program. Over the last 30 years, nuclear medicine has undergone rapid expansion resulting in the need for expert physics support to help usher this growth. MSK has long been a leader in PET imaging, in 1995 we saw the installation of the first clinical PET scanner, and since then we have grown to one of the largest PET programs: managing 17 PET-CT scanners and 1 PET-MR scanner across MSK, with more installations planned at the regional sites over the next year. The second area managed by nuclear medicine that is currently undergoing rapid growth is theranostics. For this too, MSK has been in the forefront of radionuclide therapies, since personalized radioiodine treatment for thyroid cancer began here in the 1960s. The field of cancer targeting radiopharmaceuticals has significantly expanded due to the recent approvals of the agents Lutathera™ and Pluvicto™, somatostatin- and PSMA-targeting peptides respectively, and continues to grow through company-driven research theranostic protocols, exploring a wide range of novel receptors labeled with gamma-, beta-, and alpha-emitting radionuclides for imaging and therapy. In response to growth in these two areas, the MITS physics team has developed our program and emerged as one of the strongest clinical support and research infrastructures in the world in this space.

MITS Physics Responsibilities: The MITS physics section oversees the quality assurance program for all of the nuclear medicine equipment and dose calibrators within OneMSK. Unique to MSK is the extensive repertoire of image acquisition protocols that support the more than 60 different PET radiotracers as part of the translational MSK radiochemistry and commercial clinical research program at MSK, alongside an increasingly large number of

SPECT procedures. MITS physics creates, oversees, and harmonizes all scanner acquisition protocols as well as the image reconstruction of processing steps that result in the final diagnostic images sent to PACS. With the recent (April 2025) installation of a Siemens total body 106 cm field of view Quadra PET-CT scanner, entirely new capabilities emerge to understand drug kinetics and uptake heterogeneity. The MITS physics team is engaged in over 50 clinical research protocols in support of radiology, medicine, pediatrics, cardiology, neurology, and radiation oncology, and in several instances produce innovative contributions. Some highlights include advances in respiratory motion management, hypoxia imaging in head and neck cancers, dosimetry for pediatric intra-ventricular and convective enhanced delivery of radiolabeled antibodies, microdosimetric analysis of PET-guided biopsy specimens, and cutting-edge reconstruction techniques.

The MITS physics team is assembled with individuals from diverse backgrounds that range from radionuclide dosimetry and digital autoradiography to PET physics and parametric imaging/analysis, mathematical image reconstruction techniques and AI, and creating customized novel and advanced software applications for MSK physicians and extended to community hospitals worldwide. In support of theranostics, Adam Kesner (MSK) and Wesley Bolch (University of Florida, Gainesville) have led the development of MIRDsoft (<https://mirdsoft.org/>), a suite of free, vetted, community software tools for calculating nuclear medicine, CT, and interventional radiology radiation dosimetry – funded by the NCI and endorsed by the Society of Nuclear and Molecular Imaging (SNMMI). This software has been downloaded by hospitals in 6 continents spreading the MSK logo and reputation. It is our history and critical mass of nuclear medicine physics expertise that has led to the group receiving global critical acclaim.

Diagnostic Imaging Quality Assurance Section (DIQAS)

Scope of work and responsibilities: DIQAS comprises eight ABR Diagnostic Physics certified medical physicists who provide QA services for medical imaging units throughout MSK. Departments served by the DIQAS group include Radiology, Radiation Oncology, Brachytherapy, Dental Service, PACU, ICU, Operating Rooms, and Pathology and Pain Management.

As of June 2025, there are 530 pieces of medical equipment under DIQAS QA management at 14 clinical locations and 32 private homes. The medical equipment comprises computed tomographs (CT), radiographic X-ray units, fluoroscopy and angiography units, mammography units, ultrasound units, primary diagnostic monitors, and mammography reading workstations.

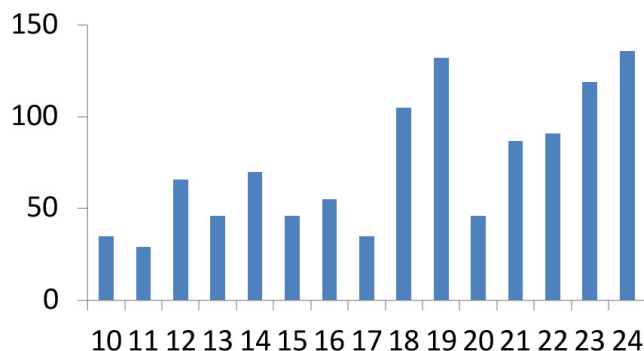


Figure 1: Number of unit acceptance testing performed annually 2010 - 2024.

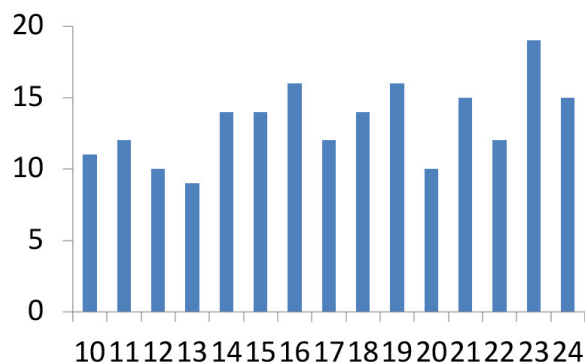


Figure 2: Number of inspections annually 2010 - 2024

The workload of the DIQAS group increased in-parallel to the rapid expansion of MSK services network in recent years. The number of new-unit acceptance testing across 15 years (2010 to 2024) is shown in Figure 1, and the number of diagnostic facility QA inspections requiring DIQAS active participation occurring per year is shown in Figure 2.

The QA policies mandated by the different regulatory agencies requires a varying degree of report generation (quarterly, semi-annual, annual, acceptance) during the life cycle of units. Generating a QA report requires testing various performance characteristics of a unit in regular time intervals. The number of unit-visits performed by the DIQAS group from 2010 to 2024 increased from 263 in 2010 to 679 in 2024.

Integration of new technologies and research: The three faculty within this section provide advanced protocol support, equipment evaluation, e.g., photon-counting CT, and research aimed at population analysis of the radiation burden from all diagnostic imaging procedures. One focus is the development of tools to extract CT and fluoroscopy scan parameters and to use Monte Carlo radiation transport codes to estimate realistic patient skin and organ doses, data essential for radiation epidemiology. Another focus is using 3D printing to create realistic variable density anthropomorphic phantoms derived from actual patient CT scans; phantoms that can be used for testing new AI software before clinical deployment. This section also provides the CT protocol expertise to work with radiologists to develop, test, and deploy advanced CT acquisition protocols as well as spectral CT imaging techniques. Such capabilities allow MSK to support both an efficient cutting-edge service and provide independence when evaluating manufacturer proposed solutions and imposed norms.



Diagnostic X-ray QA Lab (“DXQAL”)

Animal Imaging Core Facility

In vivo imaging of mice and rats is a critical component of preclinical and translation biomedical research. Non-invasive imaging allows serial assay of rodent models of human cancer and other diseases over the entire natural history of the disease and monitoring of treatment effectiveness. With each animal serving as its own control, not only is biological variability reduced, but the number of experimental animals required is minimized. With the ongoing development of genetically engineered rodent models of cancer and other diseases, such models are becoming increasingly realistic in recapitulating the natural history and clinical sequelae of the corresponding human condition and the ability to track these disease models long-term is therefore invaluable. In contrast to culture-based experiments, studies in intact animals incorporate all interacting physiological factors — neuronal, hormonal, nutritional, immunological, etc. — present in the complex *in vivo* milieu. Intact whole-animal models also facilitate investigation of systemic aspects of disease, such as cancer metastasis, which are difficult, or impossible, to replicate in *ex vivo* systems. Further, because many of the same imaging modalities — magnetic resonance imaging (MRI), computed tomography (CT), single-photon emission computed tomography (SPECT), positron emission tomography (PET), and ultrasound (US) — applied in the clinic are also used in the laboratory setting, the findings of small-animal imaging are readily translatable to patients. Thus, the Animal Imaging Core provides non-invasive, high-resolution quantitative imaging-based capabilities for metabolic, phenotypic, and genetic characterization of tumors and their microenvironment, including *in vivo* trafficking of tumor and immune cells in rodent models of human cancer. This is accomplished by monitoring directly targeting probes and the expression of single- and multi-modality reporter genes using optical (bioluminescence, fluorescence, and Cerenkov imaging), radionuclide (PET, SPECT, and autoradiography), MRI/magnetic resonance spectroscopy (MRS), CT, and US imaging.

The Core's major instrumentation (Figure 1) is as follows. **MRI:** a 7.0 tesla (T) 30-cm-bore, a 9.4 T 20-cm-bore, and a 11.7 T vertical-bore Bruker Avance NEO USR system (Bruker, Billerica, MA) for spectroscopic and special needs studies, and a 7 T-compatible PET insert for PET/MR. **PET and PET/CT:** a PET-only Focus 120 microPET and Inveon microPET/microCT system (Siemens, Knoxville, TN), with a new SuperArgus 6R PET/CT system (Sedecal, Niles, IL) funded by a recently approved NIH Shared Instrumentation (S10) grant (1S10OD036298-01) (installation Q4 2025). **SPECT/CT:** a NanoSPECT® SPECT/CT Plus system (Mediso, Boston, MA). **Optical:** IVIS® Lumina II, Spectrum (2) and Spectrum CT optical imaging systems (Caliper Life Sciences, Hopkinton, MA) capable of three-dimensional imaging. **US:** a Vevo F2 small-animal scanner (FUJIFILM VisualSonics, Toronto, Canada), recently upgraded from the no-longer-supported Vevo2100 model, with Doppler and Power Doppler capabilities. **Irradiator:** The SmART+ Biological Irradiator (Precision X-ray, Madison, CT) is a turn-key small-animal, image (CT)-guided, isocentric, and self-shielded radiation therapy unit. The Core also provides access to phosphor-plate digital autoradiography, digital fluorescence microscopy, a cryostatic microtome, and software for compartmental modeling, internal radionuclide dosimetry, and advanced image processing. The Core's comprehensive technical expertise is supported by a centralized management system that ensures efficient operation, regulatory compliance, and flexible user accessibility.



Figure 1: The Animal Core Facility's major instrumentation systems.

In its ongoing effort to maintain a state-of-the-art facility, the Core has recently submitted two (2) NIH S10 applications for new instruments: one for an NVISION ¹³C hyperpolarizer (Ulm, Germany) and a second for a VECTOr7CTUHR SPECT/CT system (MILabs, Houten, the Netherlands).

The scientific value and cost-effectiveness of our state-of-the-art Animal Imaging Core is documented by the following metrics: a perennially self-supporting (via chargebacks) balanced budget, > 1,000 peer-reviewed Core-supported publications, an "Exceptional" rating (the highest achievable) from reviewers of MSK's Cancer Center Support Grant, and 11 major instruments purchased, with funding support from S10 grants, including one for a new Super Argus 6R PET/CT (installation Q4 2025). The Animal Imaging Core is an indispensable resource, driving innovation and excellence in preclinical cancer research.

In summary, small-animal imaging provides a non-invasive means of assaying biological structure and function *in vivo*, yielding quantitative, spatially and temporally indexed information on both normal tissue and tumors *in situ*. By elucidating tumor biology and drug discovery in ways unachievable by *ex vivo* methods, small-animal imaging contributes to important advances in the diagnosis and treatment of human cancer.

High-Throughput Murine MRI

Carl LeKaye¹ and Jason Koutcher¹

¹Spectroscopic and Imaging Service and Small Animal Imaging Core

Motivation: There is a need to develop high-resolution high-Throughput murine magnetic resonance imaging (MRI) to meet the increasing demand for in vivo tumor detection in mice for cancer research.

Methods: MRI is a slow in vivo imaging modality compared with other in vivo imaging methods, such as bioluminescence imaging and computed tomography (CT). Generally, one subject is loaded and imaged at a time, even though MRI imaging speed has significantly improved due to the advances in parallel imaging and other fast scan methods. This conventional approach is a major under-utilization for the costly MRI scanner, especially for imaging mice where several mice can often be accommodated in an MRI bore. We have been developing the simultaneous multi-mouse MRI technology over the past years to increase both animal MRI utilization and throughput rate. High-resolution simultaneous multi-mouse MRI depends on individual radio frequency (RF) resonators for each animal to achieve the best acquisition sensitivity that is the same as imaging each animal sequentially. The current version of the 4-coil assembly is shown in Figure 1, where four identical volume coils are assembled to be positioned inside the magnet. Through the support of a NIH S10 Shared Instrumentation Grant, the 7T animal MRI console electronics has been upgraded recently to include the RF capability of simultaneous independent transmission, RF pulse amplification and MR RF signal receiving. This upgrade completes the hardware prerequisite for the new high-Throughput MRI technology at the Small Animal Imaging Core. Currently, we have adopted gradient-echo (FLASH) and fast spin-echo (RARE) imaging sequences and protocols for high-Throughput MRI. Initial post-processing scripts have been written to split the acquired images of all the animals into a separate folder for each animal for easy viewing, archiving, and further image processing. For testing parallel FLASH acquisition, the following acquisition parameters were used: 1 mm slice thickness, field of view (FOV) of 40 mm, matrix of 256, TR/TE of 100 ms and 4 ms, 1 average. For parallel RARE acquisition of phantoms, we used RARE factor of 8, 1 mm slice thickness, FOV 40 mm, TR/TE of 2000 ms and 30 ms, 1 average.

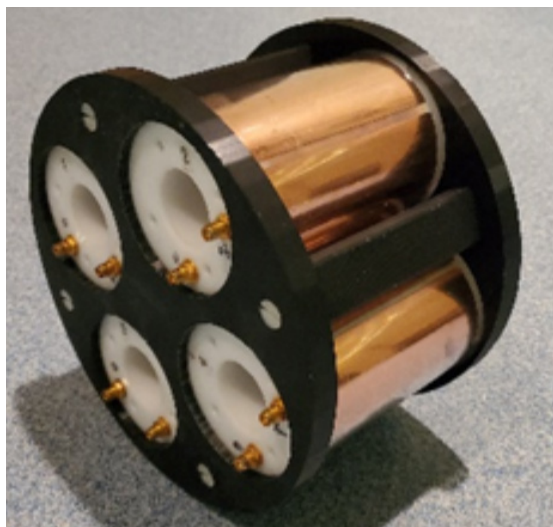


Fig. 1: The current 4-coil radio frequency detector assembly for high-Throughput magnetic resonance imaging.

Results: We have demonstrated that simultaneous MRI acquisition from four separate MR volume coils can be achieved for gradient-echo FLASH and fast spin-echo RARE sequences without sacrificing scan resolution and scan speed. Fig. 2 (a) shows axial FLASH images of four phantoms and (b) axial RARE images of the same phantoms.

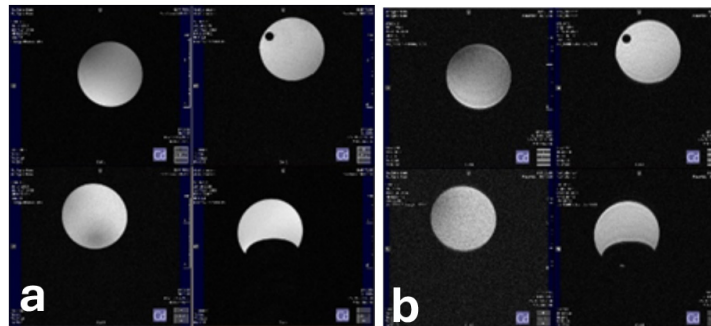


Fig. 2: Phantom (a) FLASH and (b) RARE magnetic resonance imaging of four phantoms acquired simultaneously

Scientific Significance: We have shown that high resolution high-Throughput MRI is feasible at the animal imaging core facility, and we will significantly increase MRI reach to MSK investigators.

Potential Clinical Impact: This development will improve the speed of pre-clinical trials for new therapies that require large cohorts of animals to be MRI screened for tumors. Newly developed fast scan MRI methods can also be readily translated for clinic application.

Acknowledgments:

- NIH SIG S10OD032202
- NIH CCSG P30 CA008748
- MSK Cancer Center Support Grant (P30 CA008748)

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Marc S. Ramirez, Stephen Y. Laic, and James A. Bankson, A throughput-optimized array system for multiple-mouse MRI, NMR Biomed. 2013; 26: 237-247

Implementation of a Clinical PET Traffic Controller

Brad Beattie¹ and Heiko Schöder²

¹Department of Medical Physics and ²Radiology

Motivation: MSK currently owns 18 positron emission tomography (PET) cameras encompassing eight different camera models falling roughly into four sensitivity categories (low: GE DSTE, medium: GE D690, D710, DMI_3-ring, high: GE DMI_5-ring, GE Signa, Siemens V600, and ultra-high: Siemens Quadra). Among them, there is a 340-fold difference in effective sensitivity. This means to get equivalent image quality on all of these cameras, one would need to scan 340 times longer on the low sensitivity system, 70 times longer on a medium sensitivity system, and 15 times longer on a high sensitivity system, relative to the ultra-high sensitivity Quadra. Moreover, high body mass index (BMI) patients require approximately 4-fold longer scan times (on a given PET camera) to achieve an image quality similar to that of a low BMI patient. Thus, the dynamic range of scan times to achieve equivalent image quality for all patients is over three orders of magnitude.

Methods: Enacting these patient- and PET camera model-specific scan parameters, is logistically quite complicated. However, this is where modeling and software can come to the rescue. The first step in this process was to model the impact of patient size (height and weight), injected dose, tracer type, and PET camera model, on image quality, to identify recommended scan durations for each PET scan. Note that this in and of itself does not impact overall patient throughput – it merely harmonizes image quality across all scans. Overall patient throughput (i.e., scan times) can be decreased or increased by specifying higher or lower target noise levels. The identified scan durations were then summarized into easy-to-use charts for each camera, specifying the adjustments in the scan parameters to be made by the PET technicians for each scan. Utilizing the tables, the PET tech can use patient-specific (and scan type-specific) scan durations based on the patient's height and weight. However, at sites with multiple PET cameras of differing sensitivities, there remains the issue of which scanner a given patient should be imaged on and when to inject that patient with a radiotracer so that their scan can commence at the proper time post-injection. At the main campus, this is particularly complicated in that there are three different PET cameras to which any given patient can be sent. In this instance, knowing when/if a patient should be injected requires knowing when the first of the three cameras will become free while a queue of six or more patients has already been assigned to cameras and are awaiting scans.

Results: This logistical nightmare is being managed by traffic control software written in the form of an Excel spreadsheet. The spreadsheet utilizes the same information provided to the PET technicians who are operating the individual PET cameras to arrive at estimates of the overall time needed to scan each patient (i.e., including patient setup, topogram, and computed tomography scan). This information is provided to the traffic controllers so that they can decide

the most appropriate scanner for a given patient (with high BMI patients generally going to the higher sensitivity cameras). It then allows patients to be assigned to queues maintained for each camera so that each has an associated time at which it becomes available, thereby informing the traffic controllers whether it is okay to inject the next patient.

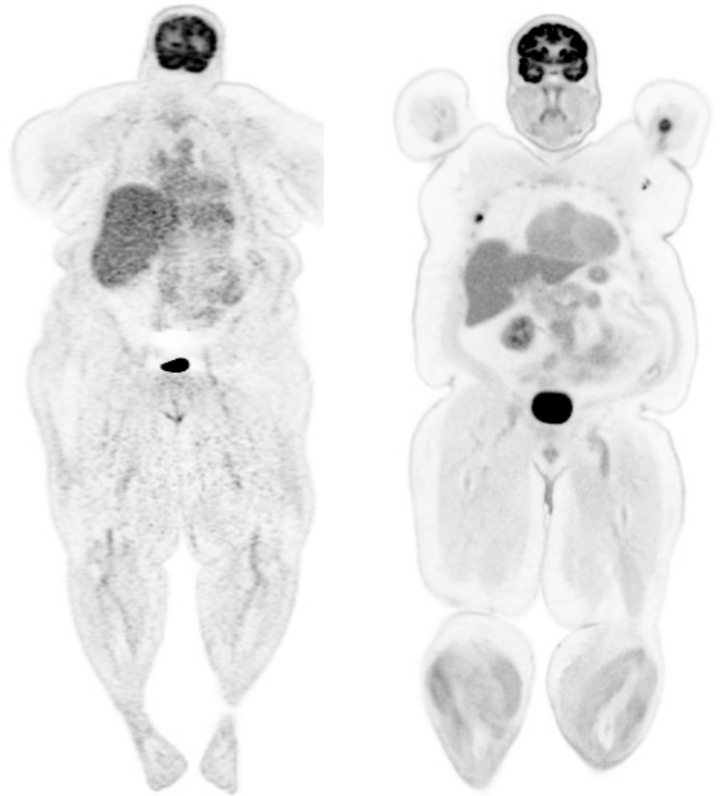


Fig. 1: On the left, the patient was imaged following the old procedures (i.e., fixed bed dwell times on a GE DMI_3-ring system) whereas on the right is an image of a patient acquired in less than half the time following the new procedures on a Quadra.

Potential Clinical Impact: This software and these procedures have been successfully applied and have been working well at the main campus. The improvement in image quality garnered by this approach with the higher sensitivity cameras, especially in larger patients, can be appreciated in the comparison of two patients both with BMI over 45 as shown in Figure 1.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

Autoradiography and Micro-CT Techniques for Investigating the Microdistribution of Radiopharmaceuticals in Biopsy Specimens

Assen S Kirov¹, Lukas Carter¹, Alexei Teplov², Eric Chan³, Olga Talarico¹, Yukako Yagi⁴, James Russell¹, Pat Zanzonico¹, John L Humm¹, Stephen Solomon⁵, and Constantinos Sofocleous⁵

¹MITS Physics, ²Sloan Kettering Institute, ³Molecular Cytology Core Facility, ⁴Pathology and Laboratory Medicine, and ⁵Interventional Radiology

Motivation: To understand the microdistribution of theranostic agents at resolutions below the scale of non-invasive imaging to determine the impact of radioactive source heterogeneity on treatment response.

Methods: A method for Quantitative Autoradiography (ARG) of Biopsy Specimens (QABS)¹ extracted under positron emission tomography/computed tomography (PET/CT) guidance has been implemented for various radionuclides, including ¹⁸F, ⁸⁹Zr, ⁶⁸Ga and ⁹⁰Y (Figs. 1 and 2). Applications range from interventional radiology (e.g., for evaluating specimen adequacy) to nuclear medicine (evaluating the efficacy of theranostic agents, and more recently alpha particle-emitting theranostics). Several digital **autoradiography devices**, including imaging plates, scintillator-CCD based and multiwire gas-filled proportional arrays have been tested and/or calibrated for performing quantitative ARG measurements of whole or sectioned biopsy specimens. In addition, for the case of trans-arterial radioembolization (TARE), scanning the samples with high-resolution micro-CT was adapted to visualize the ⁹⁰Y-loaded microspheres (Fig. 3). **Procedures for registration** of the obtained activity distributions with histopathology micrographs have been established. By applying Monte Carlo methods to the ARG images, the developed methodology provides a unique capability to estimate the microdistribution of the radiation dose from theranostic radionuclides at the biopsy locations.

Results: QABS measurements allowed determining radiotracer uptake per cell in-situ (Fig. 2) and can be further implemented for evaluation of specimen adequacy for diagnosis and genomic profiling. When applied to specimens obtained after ⁹⁰Y TARE, strong dose heterogeneity was observed leading to a factor of up to 100 dose variations in a single specimen. Such measurements allow studying biological effects as a function of absorbed dose and dose rate. Preliminary results supported by cumulative histograms for several specimens show increased inflammatory infiltration and non-uniform activation of double-strand break (DSB) within a few hours after TARE in the high dose regions around ⁹⁰Y microspheres (Fig. 3).

Scientific Significance: Microdosimetry around the targeted tumor cells at a histologic level is of immense importance when assessing the capability of new theranostic agents to deliver an adequate dose to the intended target and especially alpha-emitting radiopharmaceuticals, where successful treatment may be critically dependent upon delivering the targeting agents to within 80 microns of all tumor cells.

Potential Clinical Impact: Quantifying the microdistribution of theranostic agents in situ using ARG is essential for determining their efficacy. Microdosimetry – histology – treatment outcome correlations facilitate the development of biological response biomarkers.

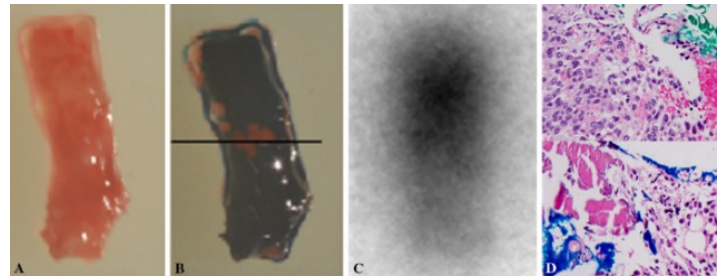


Fig. 1: Photograph of a bone specimen obtained with ⁶⁸Ga DOTATOC positron emission tomography/computed tomography-guided biopsy of tumor induced osteomalacia before and after staining (A, B), and corresponding autoradiograph (C) with pathology correlations (D) (Maybody et al., Cardiovasc Intervent Radiol, 39, 1352-7, [2016])

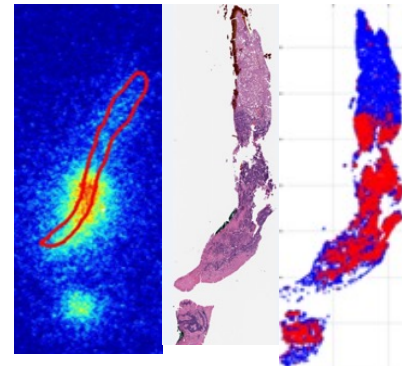


Fig. 2: Quantitative autoradiograph of a liver specimen extracted under ¹⁸F-FDG positron emission tomography-guided biopsy (left), hematoxylin and eosin stained section (middle) and identified tumor cells (red, right). Such measurements allow determination of radiotracer uptake per cell in situ,² and evaluation of adequacy of biopsy specimens for diagnosis and genomic profiling.

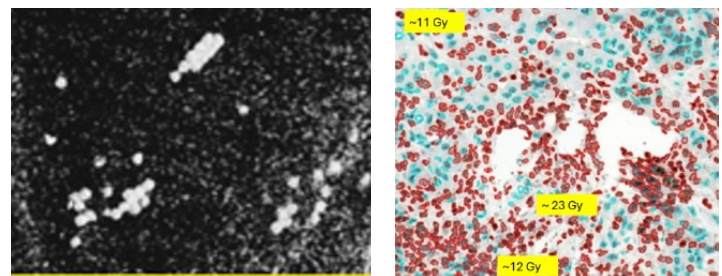


Fig. 3: Visualization of resin microspheres (~ 30 μ m diameter) in a biopsy specimen using high-resolution micro-computed tomography (left)³. Double-strand break staining (pH2AX) and automatic separation of stained cells (red and blue) (right). Dose levels at 4.3 h post-infusion are indicated (right) in the proximity of the microspheres (white spots) showing non-uniform response to dose (Kirov et al., EANM 2024)

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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MIRDsoft: Bridging Research and Patient Care with Open-Access Radiopharmaceutical Dosimetry Software

Adam L. Kesner¹, Harry Marquis¹, Gunjan Kayal¹, Lukas Carter¹, Juan C. Ocampo Ramos¹, and Pat Zanzonico¹

¹Molecular Imaging and Therapy Physics

Motivation: Radiopharmaceutical therapy (RPT) is advancing rapidly; however, personalized dosimetry has seen limited clinical adoption — largely due to a lack of accessible, transparent, and standardized tools. The MIRDsoft initiative aims to fill this gap by offering free, open-access, and vetted (i.e., peer-reviewed) software for radiation dosimetry. Such an approach supports consistent practice, enables community contribution, and fosters innovation.

Methods: MIRDsoft develops modular software tools tailored to the needs of the radiopharmaceutical community (Figure 1). These tools, delivered as Microsoft Excel-based applications and standalone executable programs, integrate established dosimetry models, accepted decay data, and a diverse library of anthropomorphic phantoms. The suite includes:

- MIRDcalc – Organ-level dosimetry software
- MIRDct – CT dosimetry simulator
- MIRDpvc – Partial-volume correction
- MIRDfit – Radiopharmaceutical biokinetic modeling
- MIRDy90 – Y-90 microsphere dosimetry
- MIRDprt – (In development) Clinically focused bioeffect dosimetry for Lu-177 and I-131 therapies

These tools and more are available at www.MIRDsoft.org.



Fig. 1: Screen captures of MIRDsoft program components.

Results: MIRDsoft has provided leadership in both the clinical and fundamental science aspects of radiopharmaceutical research, with its tools being used in over 30 countries (Figure 2), supporting clinical treatment planning, research, and education. Core programs, such as MIRDcalc and MIRDct, have been validated in peer-reviewed studies and are powered by a library of more than 750 computational phantoms developed as part of this project (Figure 3). To date, the initiative has produced five official MIRD Pamphlets in the Journal of Nuclear Medicine, with additional publications in preparation. The MIRDcalc pamphlet is among the journal's most cited publications, underscoring its wider impact. MIRDsoft has drawn interest from clinicians, researchers, educators, regulators, and industry seeking standardized and vetted dosimetry tools. The team has presented at international conferences, symposia, training schools, and seminars hosted by the Society of Nuclear Medicine and Molecular Imaging (SNMMI), the European Association of Nuclear Medicine, the International Atomic Energy Agency, the European Federation of Organisations for Medical Physics, and others.

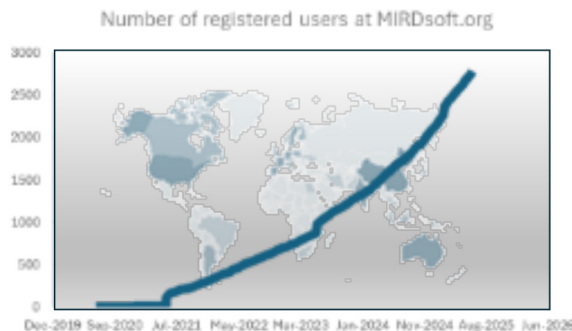


Fig. 2: Growth in registered users at MIRDsoft.org from 2020 to 2026, illustrating accelerating global adoption of the platform's free dosimetry tools.

Scientific Significance: MIRDsoft addresses critical barriers to progress in radiopharmaceutical research by delivering the infrastructure needed for standardized, reproducible dosimetry across institutions and applications. By providing accessible, rigorously validated tools, MIRDsoft accelerates the clinical translation of radiopharmaceuticals, supports regulatory harmonization, and enables quantitative benchmarking of commercial systems. The initiative plays a foundational role in advancing precision nuclear medicine by ensuring that dosimetry is accurate, transparent, and scalable.

Potential Clinical Impact: By providing accessible, accurate dosimetry tools, MIRDsoft helps lay a foundational infrastructure that advances the rapidly expanding field of theranostics and radiopharmaceutical dosimetry. This supports safer, more effective, and equitable treatment planning, aligned with the goals of precision medicine.

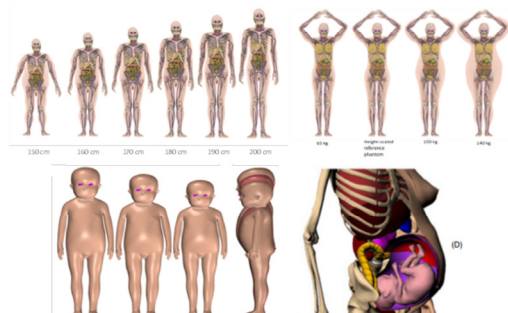


Fig. 3: Representative anatomical models from the University of Florida / Memorial Sloan Kettering Cancer Center (UF/MSK) computational phantom library, developed under a grant from the NIH/NIBIB. The library includes over 750 phantoms spanning pediatric, adult, and pregnant anatomies, guiding personalized dosimetry across diverse patient populations.

Acknowledgments: Supported by NIH NIBIB U01 EB028234, in part by the MSK Cancer Center Support Grant (P30 CA008748), and the SNMMI MIRD Committee. Special thanks to our collaborators at MSK, University of Florida, and international partners.

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TriDFusion (3DF) Image Viewer

Daniel Lafontaine¹, Heiko Schöder², Lukas Carter¹, Lisa Bodei², and John L Humm¹

¹Molecular Imaging and Therapy Physics, Department of Medical Physics, and ²Department of Radiology

Motivation: To address the complex clinical research needs within nuclear medicine, Daniel Lafontaine has developed a comprehensive user-friendly platform called TriDFusion (3DF). This integrated platform combines visualization, segmentation, image fusion, dosimetry, quantitative analytics, AI, and more within a unified environment. With 2,589 subscribers, TriDFusion is widely utilized by nuclear medicine physicians and physicists to efficiently streamline numerous analyses that would otherwise be labor-intensive, impractical, or not possible.

Methods: TriDFusion (3DF) was developed as a Vendor-Neutral multi-modal platform that can ingest tomographic datasets (PET, SPECT, CT, MRI) from any scanner vendor, automatically register them into a common spatial frame, and render synchronized axial/coronal/sagittal views alongside 3D volume (1). An example is shown in Figure 1.

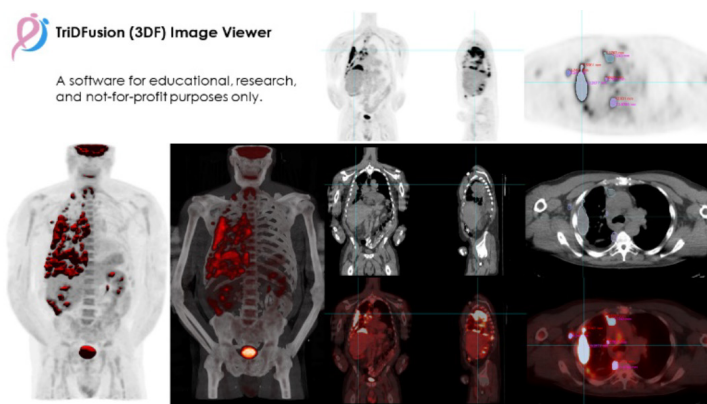


Fig. 1: TriDFusion coronal, sagittal, axial and MIP view.

The 3DF semi-automatic workflow is designed to segment metastatic tumor spread from whole-body PET-CT images, such as in patients receiving theranostic therapies such as 68Ga-DOTATATE. Such a workflow provides critical information for tracking individual disease foci in patients with multiple metastases, capturing their anatomical locations. Lesions are delineated using standardized uptake value-based thresholds, supported by user-friendly editing tools for manual adjustments, enabling high-Throughput analysis. The workflow helps accelerate patient image segmentation and is subsequently used for the development of an AI network tailored specifically to our needs.

Results: Below are the results of two projects accomplished using TriDFusion.

A. TriDFusion machine-learning was used to determine the lung shunt fraction (LSF). The LSF is an important measurement when performing 90Y-radioembolization to ensure that the radiation dose to lung is within tolerance. Traditionally, estimating the LSF from SPECT-CT images

has been too labor-intensive, and was commonly determined from 2D planar images. The introduction of semi-automated determination of the LSF using the 3DF analysis of SPECT-CT acquisitions has significantly improved accuracy, achieving results within 4%-12% of the ground truth as determined using a patient-specific CT-derived 3D-printed liver-lung phantom (2).

B. A semi-automatic, threshold-based 3DF workflow was used to segment brown adipose tissue (BAT) on 317 PET/CT scans. Brown fat is a frequent confounder in tumor detection. To minimize manual edits, we defined exclusion zones via machine-learning-based CT organ segmentation, and these organ masks were then used to assign each volume of interest (VOI) to its anatomical site. Three physicians then reviewed and corrected all segmentations using the 3DF contour panel. The final edited masks were used to train an nnU-Net V2 model, which we subsequently applied to 118 independent PET/CT scans. Across all anatomical sites, physicians reviewed the network's automated segmentations to be approximately 90% accurate (3).

Scientific Significance: TriDFusion (3DF) is becoming widely used for research in nuclear medicine due to its numerous clinical applications. However, it is also useful for addressing routine clinical issues. A practical use is in correcting acquisition errors, such as incorrect patient orientation entered by a technologist, or image acquisitions requiring mathematical operations such as anterior-posterior geometric mean calculations. At MSK, 3DF is integrated with Hermes, allowing to quickly correct these issues via 3DF.

Potential Clinical Impact: TriDFusion is an unprecedented all-in-one research tool that paves the way for new innovations and project support.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Computed Quantitative Planar Imaging for Targeted Alpha Therapy

C. Ross Schmidtlein¹, Joseph A. O'Donoghue¹, Lisa Bodei¹, Andrzej Krol², and Yuesheng Xu³

¹MSK, ²SUNY Upstate Medical, and ³Mathematics Old Dominion Universities

Motivation: Targeted Alpha Therapy (TAT) using alpha-emitting radionuclides (AERs), such as ²²⁵Ac, shows great promise for treating advanced and refractory cancers. However, current dosing protocols rely on body weight or surface area, without accounting for patient-specific biodistribution, pharmacokinetics, or patient genetics. Accurate, individualized treatment requires in vivo imaging of AER distributions; a major challenge due to the scarcity of detectable photons.

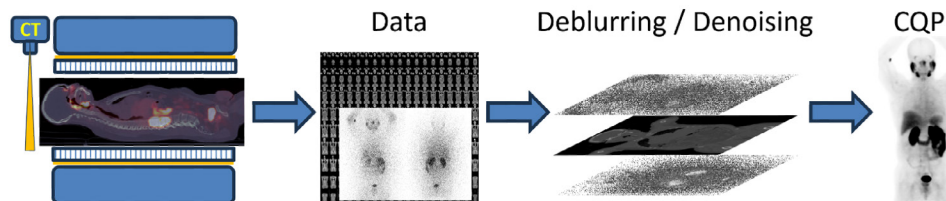


Fig. 1: Computed quantitative planar (CQP) imaging workflow. Showing patient scan, data, image reconstruction, and final image, from left to right.

Methods: In response, we developed a model-based image reconstruction technique, called "Computed Quantitative Planar" (CQP) imaging (**Figure 1**), which estimates coronal projections of three-dimensional AER distributions from anterior/posterior planar scintigraphy co-registered with CT. The method uses a physics-based model that accounts for attenuation, resolution loss, and scatter, and applies maximum a posteriori estimation to control noise while preserving resolution. To solve this we developed a fixed-point proximity algorithm and proved its convergence. Validation was performed using a novel modular epoxy slab phantom with vitrified ²²⁵Ac at known locations and concentrations. CQP was implemented on a clinical SPECT/CT system (**Figure 2**).

Results: CQP substantially improved image quality over conventional geometric mean (GeoM) methods, with lower bias and noise, enhanced spatial resolution, and higher signal-to-noise ratios (SNRs) (**Figure 3a,b,c**). Quantitative analysis showed improvements in mean squared error, structural similarity index, and task-based SNR. The results of Pareto analysis of noise-resolution tradeoffs (**Figure 3d**) revealed that even low-count CQP images outperformed high-count GeoM reconstructions.

Scientific Significance: Prior to the conception of CQP, the use of a physics-based model for the reconstruction of planar Images had not been considered by the research community.

Potential Clinical Impact: CQP enables quantitative planar imaging in low-photon count regimes where traditional methods fail by suppressing noise while preserving resolution, supporting patient-specific dosimetry for targeted alpha therapy (TAT). By facilitating clinical trials that compare personalized, dose-based regimens to fixed activity protocols, CQP could help shift clinical practice toward personalized treatment guided by routine, rapid biodistribution imaging, potentially supplemented by limited SPECT/CT or PET/CT. With continued validation, CQP has the potential to replace conventional planar imaging for both diagnostic and quantitative tasks.

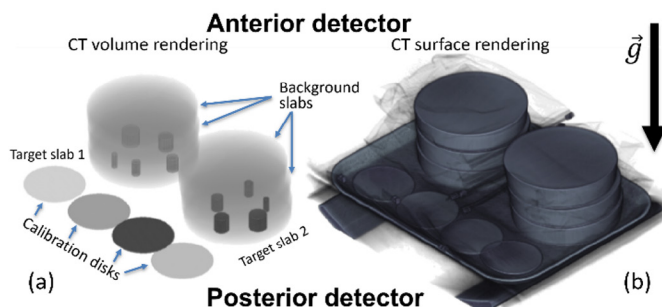


Fig. 2: Reference activity concentrations (a) and experimental setup (b) of the vitrified epoxy ²²⁵Ac phantom for validation of the CQP method.

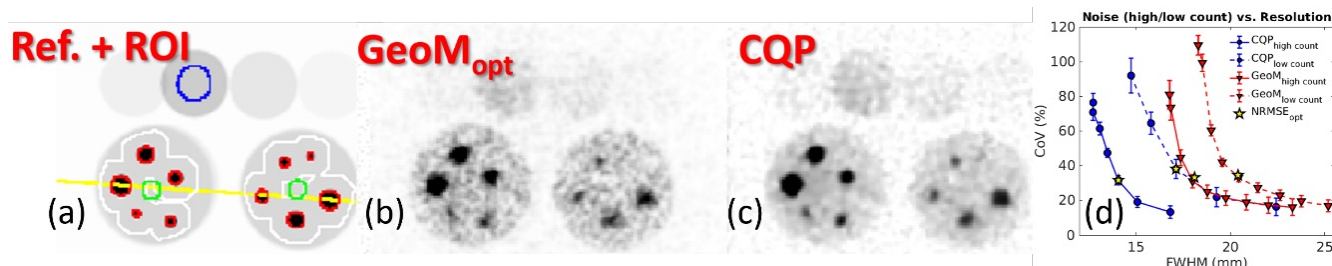


Fig. 3: Reference image with evaluation regions of interest (ROIs) (a), along with optimized geometric mean (GeoM) (b) and Computed Quantitative Planar (CQP) reconstructions (c). The plot (d) shows Pareto curves for high- and low-count data, demonstrating that low-count CQP images (one-third the counts) outperform high-count GeoM images in the noise-resolution tradeoff.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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A Parameterized Kernel Physics Model for Time-Of-Flight List-Mode PET Image Reconstruction

C. Ross Schmittlein¹, Erik Linghammar², Richard Nunstedt², Ida Häggström², Eric Harmon³, and Andrzej Krol⁴

¹Molecular Imaging and Therapy Physics, MSK, ²Chalmers University Sweden, ³Light Spin Inc., and ⁴SUNY Upstate Medical University

Motivation: In positron emission tomography (PET), the system model is central to image reconstruction, defining how the radiotracer distribution and detected coincidence events map to one another. With the design of sub-millimeter resolution PET detectors, the fidelity of the system model to the physical processes and system geometry is critical. Ad hoc, or empirical, approximations used by conventional models fail to capture these effects with sufficient accuracy, limiting the achievable performance of next-generation detectors. Thus, there is a growing need for high-resolution system models that fully leverage list-mode (LM) and time-of-flight (TOF) data while remaining compatible with emerging detector technologies capable of < 1 mm resolution.

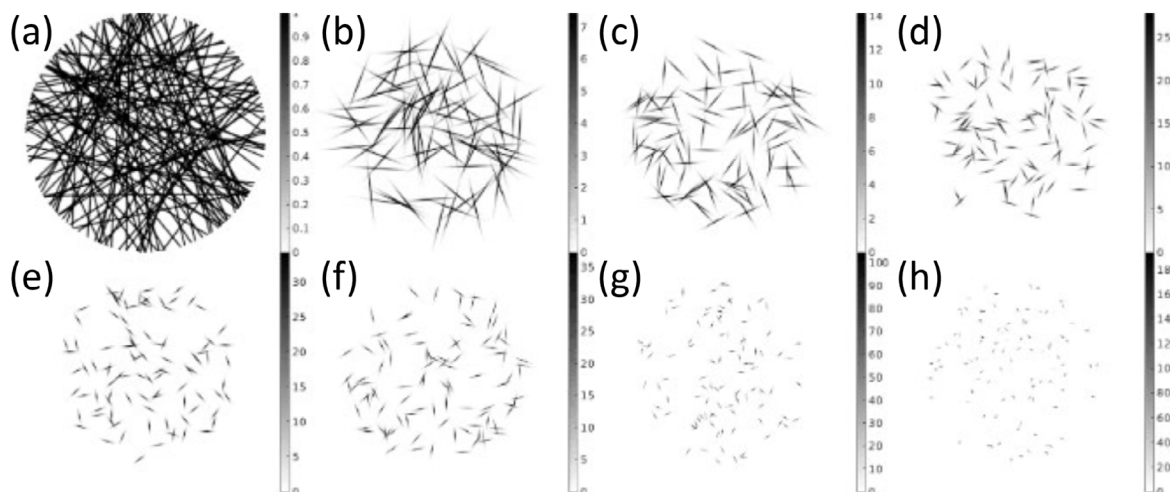


Fig. 1: Back-projection of 100 random coincidence events across varying positron emission tomography (PET) detector and timing resolutions within a 700 mm field of view. The spatial footprints of each event's probability density function are shown for systems with no time-of-flight [TOF], 5 mm (a), TOF = 675 ps, 4.5 mm (b), 385 ps, 4 mm (c), TOF = 215 ps, 3.5 mm (d), TOF 175 ps, 3.5 mm (e), TOF = 195 ps, 3 mm (f), (our design) TOF = 100 ps, 1 mm (g), and (theoretical limit of current scintillators) TOF = 60 ps, < 1 mm (h). As the image resolution improves, the footprints become increasingly localized.

Methods: We developed a novel system model for LM TOF-PET that explicitly accounts for key resolution-degrading effects, including positron range, non-collinearity, detector blur, and depth-of-interaction. The model operates on an event-by-event basis, mapping each coincidence event from a continuous domain to image space. It supports unsegmented detectors and satisfies the incoherence conditions required for compressed sensing, thereby enabling its application in high-resolution PET reconstruction.

Results: This event-by-event framework produced a probability density function (pdf)-based system model whose accuracy was determined by the fidelity of the physical modeling. Although originally designed for monolithic block detectors, the model can be adapted for conventionally segmented designs via modifications to the pdf.

In **Fig. 1**, projections of counts into image space are shown for several PET cameras, including a novel brain PET scanner under development by our team (lower center-right). The figure highlights the increasing localization of information with improved spatial and timing resolution.

Fig. 2 displays reconstructed brain images using maximum-likelihood expectation-maximization (MLEM) with the proposed model, showing progressive refinement over iterations.

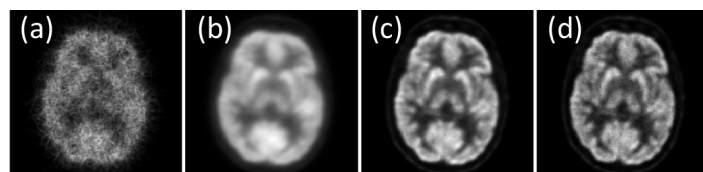


Fig. 2: Brain images reconstructed using maximum-likelihood expectation-maximization (MLEM) with the brain positron emission tomography (PET) projection model. A back-projection image (a), and images after 1 (b), 7 (c), and 20 (d) iterations of MLEM are shown.

Scientific Significance: This approach redefines the PET system model by directly incorporating key physical effects, offering a more natural and principled alternative to ad hoc point spread function modeling.

Potential Clinical Impact: Ongoing work includes comparisons with conventional system models and integration with compressed sensing techniques to further enhance resolution and reconstruction performance.

Acknowledgments:

This work was supported in part by NIH/NCI R01 EB032416, and the MSK Cancer Center Support Grant/Core Grant P30 CA008748.

References:

A provisional patent has been filed. A manuscript is in preparation.

Personalized Dosimetry for Radiopharmaceutical Therapy

Milan Grkovski¹, Joseph O'Donoghue¹, Daniel Lafontaine¹, Finn Augensen¹, and John Humm¹

¹Molecular Imaging and Therapy Physics

Motivation: Currently, there is intense interest in expanding the clinical applicability of radiopharmaceutical therapy (RPT), including treating earlier in the disease process, developing novel molecular vectors, and introducing new therapeutic radioisotopes. Although RPT dosimetry is possible via image-based quantification of biodistribution and kinetics, most clinical treatments are prescribed on a “one-size-fits-all” basis, more in line with a chemotherapeutic regimen. We anticipate that patient-individualized, dosimetry-driven treatments will improve, but it remains to be determined by how much, in terms of objective clinical endpoints. Dosimetry is of particular relevance when different radiation-based treatments are combined. Here we describe a clinical study featuring the radiopharmaceutical ¹⁷⁷Lu-PSMA-617 delivered in a neoadjuvant context in combination with stereotactic body radiotherapy (SBRT) for oligometastatic prostate cancer or used as a single agent for metastatic castration-resistant prostate cancer (mCRPC). In both cases, dosimetry provided key insights.

Methods: Patients with oligometastases (cohort 1; N = 16) received 2 cycles of ¹⁷⁷Lu-PSMA-617 followed by SBRT (3 x 9 Gy). Voxelize dose maps of combined biologically effective dose (BED) were generated as shown in Figure 1. Patients with mCRPC (cohort 2; N = 65) received up to 6 cycles of ¹⁷⁷Lu-PSMA-617.

Patient response was evaluated by changes in serum prostate-specific antigen (PSA) before and after cycle 1 of RPT. Lesion response was evaluated by the change in the maximum standardized uptake value (SUV_{max}) from ⁶⁸Ga-PSMA-11 PET/CT, acquired before, during, and after RPT.

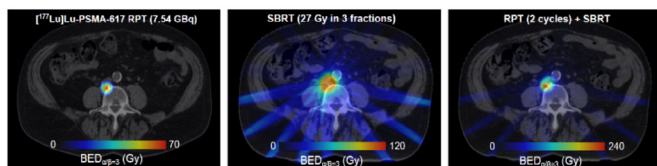


Fig. 1: Voxelized dose maps for a representative patient from cohort 1 BED: biologically effective dose; RPT: radiopharmaceutical therapy SBRT: stereotactic body radiotherapy; SUV: standard uptake value

Results: All cohort 1 patients completed combination therapy without complications or grade 3+ toxicities. There was a strong correlation between the combined BED and percentage change in PSMA SUV_{max} before and after therapy ($\rho = 0.88$, $p = 0.007$) as shown in Figure 2.

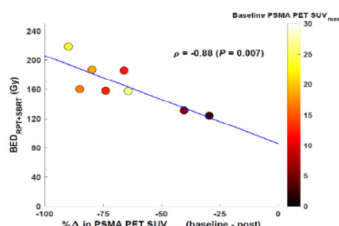


Fig. 2: Relationship between lesion biologically effective dose and PSMA positron emission tomography (PET)-assessed treatment response in N = 6 patients with oligometastatic prostate cancer undergoing radiopharmaceutical therapy (RPT) + stereotactic body radiotherapy (SBRT) combination therapy.

For patients in cohort 2, absorbed dose (AD)-response relationships were observed at both patient ($\rho = -0.33$; N = 63) and lesion ($\rho = -0.30$; N = 681) levels (Figure 3). Patients with higher mean AD (> 7.5 Gy) had longer (biochemical) PFS and OS compared to patients with mean AD < 7.5 Gy (Figure 4).

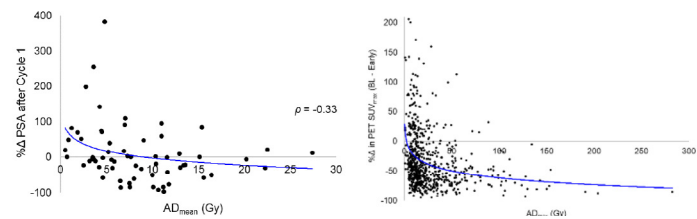


Fig. 3: Lutetium-177 absorbed dose (AD)-response relationship on a patient (left) and lesion (right) level. PET: positron emission tomography PSA: prostate-specific antigen SUV: standard uptake value

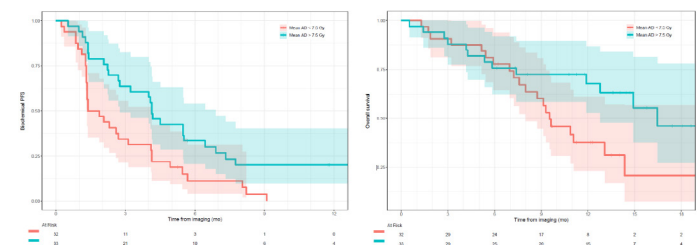


Fig. 4: Biochemical progression free survival (left) and overall survival (right) for patients dichotomized based on the mean absorbed dose (AD) from all lesions (cohort median = 7.5 Gy).

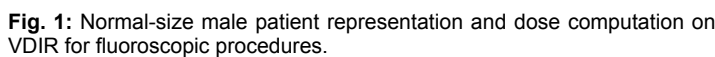
Scientific Significance: ⁶⁸Ga-PSMA PET-based prostate cancer lesion response following ¹⁷⁷Lu-PSMA-617 treatment is dependent on lesion absorbed dose. Patients who received higher mean lesion absorbed doses did better in terms of both biochemical progression-free survival and overall survival. However, most lesions do not show a complete response after the completion of standard ¹⁷⁷Lu-PSMA-617 treatment.

Potential Clinical Impact: These findings are suggestive of the value of personalized dosimetry-based radiopharmaceutical therapy. In particular, there is a dose-response relationship for lesion response, but higher doses need to be delivered to improve the clinical outcome. Careful monitoring of the radiation doses to normal tissues is the only way to accomplish this without causing excessive normal tissue toxicity. In the immediate future, ¹⁷⁷Lu-PSMA-617 therapy will be applied to castration-sensitive disease, where life expectancies are longer and long-term radiation toxicities more critical. As the field progresses, treatment personalization of dosimetry will allow it to achieve its full potential.

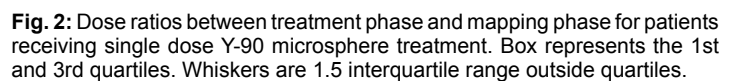
Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

Yiming Gao¹, Xingyu Nie², Wei Tang¹, Bae Chu¹, Usman Mahmood¹, Yusuf Erdi¹, and Lawrence Dauer¹
¹Department of Medical Physics, Memorial Sloan Kettering Cancer Center and ²Department of Radiology, University of Kentucky

Methods: A retrospective study was conducted on 500 patients undergoing Yttrium-90 (Y-90) radioembolization at two NCI-designated healthcare centers between 2019 and 2020. Institutional review board (IRB) approval was obtained with waived patient consent. Patient demographics, fluoroscopy parameters, and radiation dose metrics were collected from DICOM headers. Y-90 administration data were obtained from written directives. Fluoroscopic irradiation events were modeled using VirtualDoseTM IR (VDIR) for body mass index (BMI)-specific phantom simulations and batch processing capability. For each exam, a phantom with the closest BMI was used to simulate the patient. Fluoroscopic guidance fields were assumed to be at the liver center on average, and relative field locations to the liver center were computed using table horizontal and lateral positions from DICOM header. Irradiation event level parameters were then organized for organ dose computation in batches by VDIR. The results from VDIR included organ doses, patient-specific effective doses, and peak skin dose (PSD) and were compared between mapping and treatment phases. Statistical analysis included Wilcoxon's rank-sum test and ANOVA for multi-factor effects.



The organs included in the dose assessment focused on radiation exposure field, and the potential for dose deposition in surrounding tissues that include the liver, lungs, red bone marrow (RBM) and skin. Mapping phases showed twice as much radiation dose, on average, compared with treatment phases in lung dose, RBM dose, PSD, most other organ doses and effective dose (E103) as shown in **Figure 2**. The highest PSD was 3.7 Gy in mapping and in treatment.



Potential Clinical Impact: This study can clarify radiation dose from fluoroscopy guidance in Y-90 radioembolization and facilitate protocol optimization in radiation usage.

- This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).
- IRB #16-1589 "Patient-specific radiation dosimetry for oncology radiopharmaceutical and X-ray procedures", PI Dr. Lawrence Dauer.
- Internal collaboration: DIQAS and Radiation Safety.
- External collaboration: MSK and the University of Kentucky.
- Paper draft in progress for Journal of Vascular and Interventional Radiology.

PET/MR Enables High Spatial Resolution, Quantitative Imaging of Amyloid Plaques in an Alzheimer's Disease (AD) Mouse Model

Georgia R. Frost¹, Valerie Longo², Jason Koutcher³, Carl Lekay², Pat Zanzonico², and Yue-Ming Li¹

¹Chemical Biology, ²Small Animal Imaging Core, and ³Spectroscopic Service

Motivation: To image and quantify A β plaques in 5xFAD mice using the PET tracer fluorine-18 [18F]-Florbetapir uptake.

Methods: Alzheimer's disease (AD) animal models that express a FAD mutation (APP and/or PS1) have been widely used for investigation of β -amyloid plaques (A β) and AD pathogenesis. However, PET imaging of plaques in mouse models is limited by relatively coarse spatial resolution (1 to 2 mm full-width half-maximum [FWHM]) and therefore cannot reliably define specific regions within the mouse brain. To overcome this, PET/CT images may be manually co-registered with a sequential MRI scan or to an MRI template. The radiotracer [18F]-Florbetapir has been used to analyze amyloid load as well as its spatial distribution in APP/PS1-21 mice both *ex vivo* by autoradiography and *in vivo* by microPET. Furthermore, although too low to be demonstrable visually, localization of [18F]-Florbetapir was 14.5% greater in 5xFAD mice, which coexpress five FAD mutations that drive A β production, compared to WT mice.

We first assessed amyloid load in the whole brains (identified as intracranial activity) of 5xFAD mice compared with WT (wild type) mice by measuring [18F]-Florbetapir uptake by PET/CT. We next identified 6 regions of interest (cortex, hippocampus, thalamus, caudate, cerebellum, and brainstem) in the brain using the high structural resolution of the MRI scan and the Allen Brain Atlas. Applying the MRI-defined anatomical regions to a PET image allows visualization and quantitation of uptake of [18F]-Florbetapir within these regions.

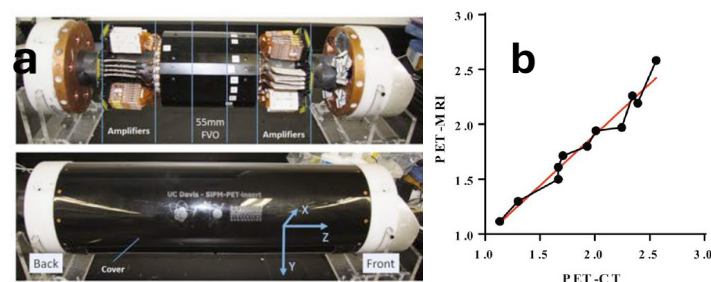


Fig. 1: 7T-compatible PET insert (a) inside and outside pictures; (b) Correlation of whole brain %ID/gm for individual mice measured by PET/MR (y-axis) versus PET/CT (x-axis) ($R^2 = 0.96$). PET: positron emission tomography; MRI: magnetic resonance imaging; CT: computed tomography

Results: The cortex and hippocampus had high uptake in the 5xFAD mice compared with WT mice whereas the differences in uptake between the two groups in the brainstem and the cerebellum were much less. In fact, when normalized to average uptake in the WT mice, the thalamus had the highest ratio of uptake in 5xFAD.

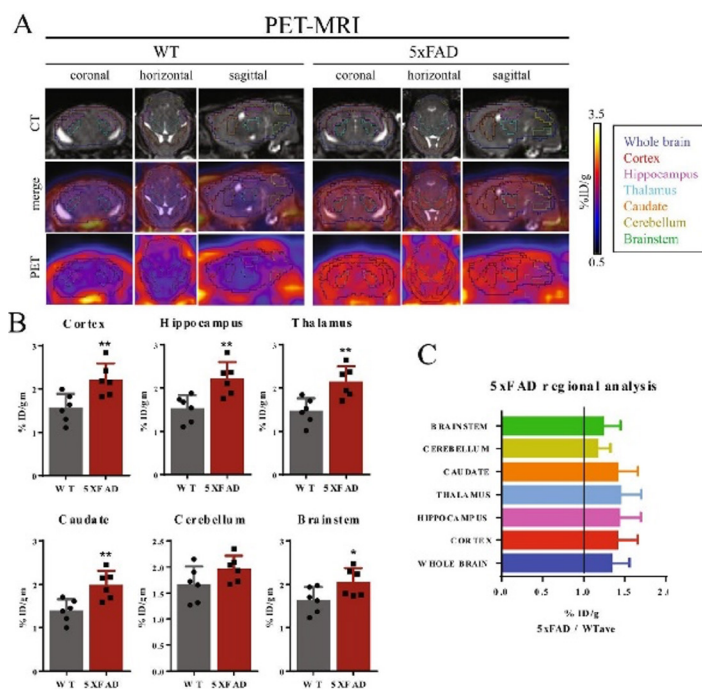


Fig. 2: PET/MR enables brain region-specific quantification of [18F]-Florbetapir uptake. (A) Representative images of [18F]-Florbetapir uptake for wild-type (WT) and 5xFAD mice by PET/MR. (B) Uptake was quantified within each region of the brain as (%ID/g). (C) Average [18F]-Florbetapir uptake in each brain region of 5xFAD mice normalized to average WT uptake.

Scientific Significance: We are the first to utilize small-animal PET/MR for amyloid plaque imaging in an AD mouse model.

Potential Clinical Impact: This study demonstrates the enormous potential of PET/MR, which combines MRI's spatial resolution and PET's high sensitivity for molecular brain measurements that contribute to the development of new and effective treatments for AD.

Acknowledgments:

- NIH R01NS096275, RF1AG057593, R01AG061350, RC2 CA148971
- NIH CCSG P30 CA008748

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Imaging-Based Monitoring of Non-Invasive Mechanical Interventions to Enhance Drug Delivery to Bone Tumors

Pat Zanzonico¹, John Healey², and Susannah Fritton³

¹Molecular Imaging and Therapy Physics, MSK, ²Department of Surgery, MSK, and ³Department of Bioengineering, City College of New York

Motivation: The objective of this study is to develop and validate a clinically translatable mechanical intervention that can be used to enhance drug delivery to cancerous bone tumors.

Methods: This on-going multi-institution pre-clinical study utilizes a clinically realistic rat model of breast cancer metastatic to the tibia and includes intra-animal comparisons before and after application of a mechanical intervention, cyclical loading and more recently treadmill exercise or vibration plate. The drug distribution and tumor uptake of iv-administered radiotracer drugs surrogates (such as fluorine-18 [¹⁸F]-fluorodeoxyglucose [FDG] and [¹⁸F]-sodium fluoride [NaF]) as well as clinically relevant drugs (e.g., paclitaxel and trastuzumab radiolabeled with zirconium-89 [⁸⁹Zr]) are being investigated using small-animal PET/CT (Inveon, Siemens) in the MSK Animal Imaging Core. The MDA-MB-231 human breast cancer cell line is being used, with cells injected directly into the right proximal tibia of anaesthetized immunocompromised female rats. The cells are genetically transduced to express firefly luciferase (FLuc) prior to injection, and bioluminescence imaging is subsequently used to verify the viability and orthotopic location of the engrafted cells. Reproducible mechanical loading of the tumor-bearing rat tibia was performed using a customized loading device to apply controlled forces that simulate treadmill walking (Fig. 1). (Mechanical loading is now accomplished by a vibration plate and clinical translatable treadmill exercise). Rats were divided into four groups: two groups were injected with ¹⁸F-FDG, and the right tibia was either mechanically loaded (n = 5) or sham-loaded (n = 5); the other two groups were injected with ¹⁸F-fluoride, and the right tibia was likewise either mechanically loaded (n = 5) or sham-loaded (n = 5). Rats in the two loading groups received cyclical compression/de-compression to the right, cancer cell-injected tibia for 10 min immediately after injection of the tracers. Sham-control rats were placed in the loading device with no load applied.

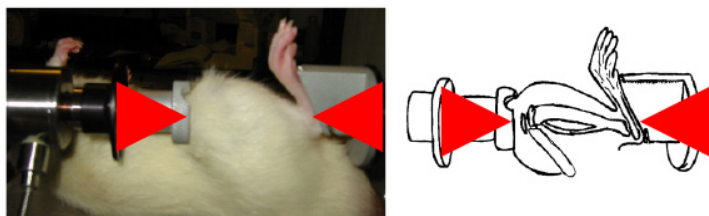


Fig. 1: With the non-invasive loading device (ElectroForce TestBench), the rat tumor-bearing tibia is constrained by foot and knee holders, while the actuator applies a cyclical mechanical load in the direction of the arrows, simulating the effect of a patient walking on a treadmill.

Results: Mechanical loading increases radiotracer delivery to orthotopic bone tumor

The mean percent of the injected dose / ml (%ID/ml) of ¹⁸F-FDG and ¹⁸F-NaF, radiotracer surrogates of anti-cancer drugs, was determined for the right (cancer cell-injected) and left (normal contralateral) tibia using 3D volumes of interest that were segmented on the co-registered serial PET/CT images (Fig. 2). Uptake of ¹⁸F-fluoride in the right, tumor-bearing tibia was significantly influenced by mechanical

loading. ¹⁸F-fluoride uptake in the tumor region was 47% higher in the loaded tibia compared to the sham-control, a clinically relevant increase. By contrast, uptake of ¹⁸F-FDG in the tumor region was not influenced by mechanical loading, but only by the presence of tumor.

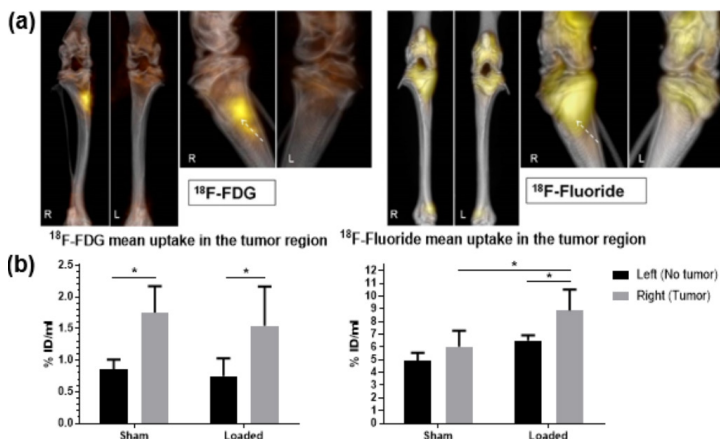


Fig. 2: Fused positron emission tomography/computed tomography images of iv injected ¹⁸F-FDG (left panel) and ¹⁸F-NaF (right panel) demonstrated that tumor growth was contained within the right (R) tibia, where the cells were originally inoculated, with predictably higher uptake in the bone lesion than in the contralateral normal bone. (b) Mean uptake ± standard deviation (in percent of the injected dose / ml, %ID/ml) of ¹⁸F-FDG (left panel) and ¹⁸F-NaF (right panel) in the tumor-bearing proximal tibia versus the contralateral normal proximal tibia with and without mechanical loading. Uptake of ¹⁸F-fluoride in the right, tumor-bearing tibia was significantly influenced by mechanical loading. * p < 0.05.

Scientific Significance: Non-invasive PET/CT imaging detects enhanced delivery to bone tumors of systemically administered agents.

Potential Clinical Impact: Clinically translatable bone loading may increase delivery of anti-cancer drugs to bone tumors and thereby enhance drug effectiveness.

Acknowledgement:

- Valerie Longo, MSK Animal Imaging Core
- MSK Cancer Center Support Grant (P30 CA008748)

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Gatti, V., Gelbs, M.J., Guerra, R.B., Palacio-Mancheno, P.E., Longo, V.A., Rajasekhar, V.K., Zanzonico, P.B., DiResta, G.R., Healey, J.H. and Fritton, S.P., "Physiological Mechanical Loading Enhances ¹⁸F-Sodium Fluoride Uptake in a Rat Model of Bone Metastasis," submitted to J Orthopaedic Res, 2025.

Total-Body PET at MSK: Capabilities, Challenges, and the Technical Work Behind the Promise

Bradley J. Beattie¹, Lukas M. Carter¹, and Heiko Schoder²

¹Department of Medical Physics and ²Department of Radiology

Motivation: The Siemens Biograph Vision Quadra represents a major advance in positron emission tomography (PET) imaging technology, offering a 106 cm axial field of view and astronomical sensitivity that can dramatically reduce scan times, enable late-time point imaging, and support total-body dynamic protocols. However, its clinical and research value cannot be fully realized without extensive technical expertise and support. Unlike a simple hardware upgrade, implementing total-body PET at MSK has required a substantial investment in physics oversight, ongoing protocol and workflow development, and inevitable occasional systems-level troubleshooting.

Methods: Compared with traditional PET systems, including those from GE and standard Siemens Vision models, the Quadra offers clear imaging advantages: full-body coverage in a single bed position, time-of-flight resolution < 230 ps, and a monumental increase in sensitivity and image quality (Fig. 1, Fig. 2). However, these benefits come with tradeoffs in system complexity and operational limitations that affect daily use and research scalability.

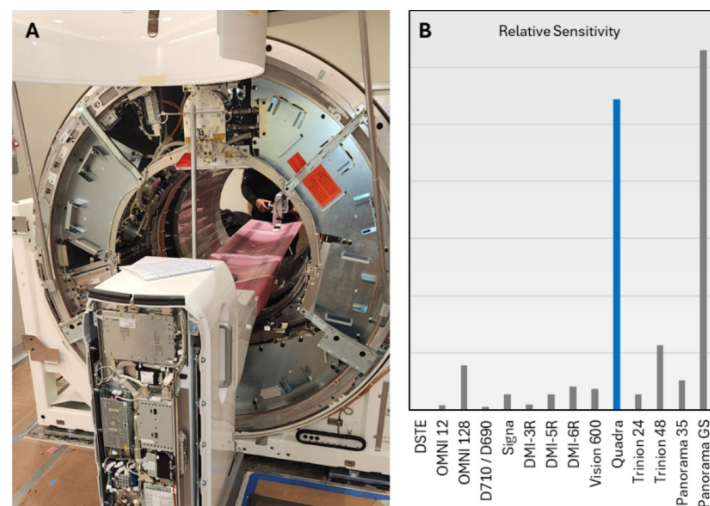


Fig. 1: A) Installation of MSK Quadra. B) Relative sensitivity of Quadra vs. conventional and total-body positron emission tomography (TB-PET) scanners.

The introduction of the Quadra has exposed technical and workflow issues that require active physics support:

- **Support & Maintenance:** Siemens' quality assurance (QA) and calibration infrastructure is less responsive and more cumbersome than systems from other vendors. Daily QA is fully automated but occasionally fails and takes > 90 minutes to re-run. Full PET detector setup and quarterly calibration routines are time-intensive (up to 6 hours), with limited granularity and poor remote support (due in part to a locked-down operating system).
- **Operational Constraints:** Despite fast acquisition times, reconstruction delays limit real-time assessment of patient motion – particularly problematic for continuous bed motion acquisitions. No step-and-shoot mode translates to different axial sensitivity profiles depending upon the

height of the patient. Users must scan ≥ 106 cm in PET and computed tomography (CT) mode, and there is no efficient way to reconstruct or export partial datasets. Although the introduction of tin filter for the CT subsystem represents a significant advance, insufficient guidance from Siemens has necessitated independent evaluation to determine appropriate use cases and technique parameters.

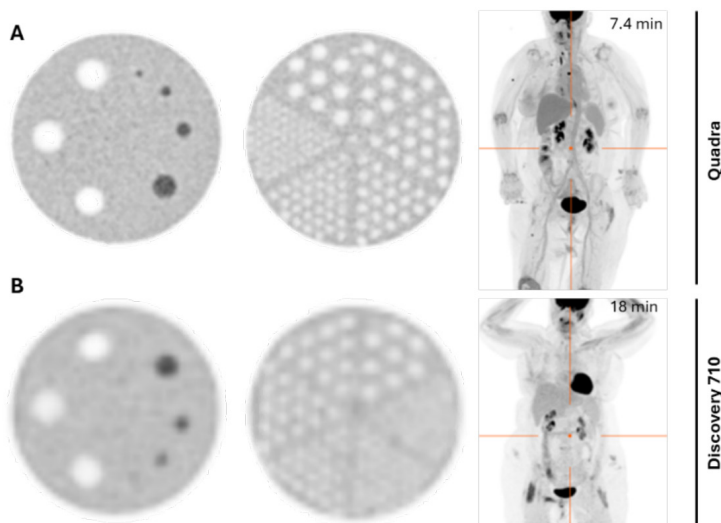


Fig. 2: A) Quality assurance images of the ACR PET phantom (left, middle), and patient images (right) for Quadra. B) Same as (A) for the GE Discovery 710 conventional PET camera.

Results: Our physics team has taken an active role in addressing these issues:

- **QA and Calibration Improvements:** Developing tools to extract and analyze QA output files, pushing Siemens for modularized quality control routines, and working to streamline fault detection and setup validation.
- **Reconstruction and List Mode Processing:** Implementing customized reconstruction workflows and list mode reprocessing strategies to enable flexible imaging protocols and improve/expedite motion detection.
- **Protocol Optimization:** Investigating and refining the use of CT filter options (e.g., tin filters) and optimizing scan protocols for pediatric imaging, multi-tracer studies, and low-dose applications.

Scientific Significance: This work establishes the technical and physics framework needed to translate the unprecedented sensitivity of total-body PET into new research capabilities.

Potential Clinical Impact: This work is essential not only to maximize the scientific value of the Quadra, but to prepare for a future where total-body PET may be the clinical standard. By addressing the real-world limitations of this powerful but complex system, MSK's physics team is playing a central role in ensuring that total-body PET delivers on its promise – for oncology, theranostics, and our patients.

Acknowledgments: This work was supported in part by the MSK Cancer Center Support Grant P30 CA008748.

Transforming Oncology Imaging with Total-Body PET at MSK

Lukas M. Carter¹, Bradley J. Beattie¹, and Heiko Schoder²

¹Department of Medical Physics and ²Department of Radiology

Motivation: Conventional positron emission tomography (PET) scanners are constrained by limited sensitivity, short axial field of view, and motion artifacts that impair image quality and quantitative accuracy. The recently installed Biograph Vision Quadra total-body PET (TB-PET) scanner at MSK features a 106 cm axial field of view providing whole-body imaging with tremendously improved effective sensitivity (Fig. 1); the sensitivity gain enables rapid acquisitions, late-time point imaging, and reduced injected activity – unlocking clinically and scientifically meaningful PET protocols that were not previously possible.

- Drug Delivery Quantification and Theranostic Applications (Aim 3): We will use radiolabeled analogs of therapeutic agents to perform dynamic and delayed imaging of tumor uptake. This will support personalized treatment planning by quantifying drug delivery and biodistribution. The Quadra's design also supports multi-tracer imaging within a single session, opening new possibilities for theranostic studies that combine imaging and therapy.

Results: By enabling whole-body dynamic imaging, late-time point scans, and ultra-fast acquisitions (Fig. 2), and high image quality, this program pushes the limits of what is possible with PET.

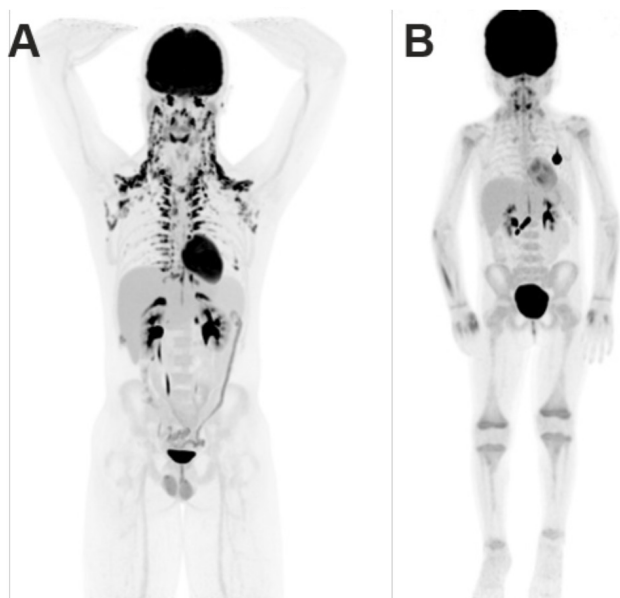


Fig. 1: Notable early images acquired with MSK's new Biograph Vision Quadra total-body positron emission tomography (PET) scanner. A) First patient imaged on the Quadra (¹⁸F-FDG; 12 mCi, 5-minute acquisition duration); extensive uptake present in normal physiologic brown fat. B) Short acquisition duration enabled pediatric patient to be imaged without anesthesia (¹⁸F-FDG; 2.2 mCi; 2.2 minutes).

Methods: Our research program is designed to leverage these strengths to advance diagnostics, therapy planning, and theranostic development. We are launching a set of clinical research initiatives to evaluate high-impact applications of TB-PET.

- Breath-hold Imaging (Aim 1): We will test whether the Quadra enables diagnostic-quality PET during a single deep-inspiration breath-hold (DIBH), reducing respiratory motion artifacts and improving image sharpness. Imaging results will be compared with Siemens' OncoFreeze AI motion correction.
- Late-Time Point Hypoxia Imaging (Aim 2): The Quadra's sensitivity allows us to explore [¹⁸F]fluoromisonidazole PET imaging at up to 6 hours post-injection, enabling improved assessment of tumor hypoxia status – an important biomarker for treatment resistance – leveraging background clearance and intrinsic contrast gains at timepoints that were previously inaccessible with conventional scanners.

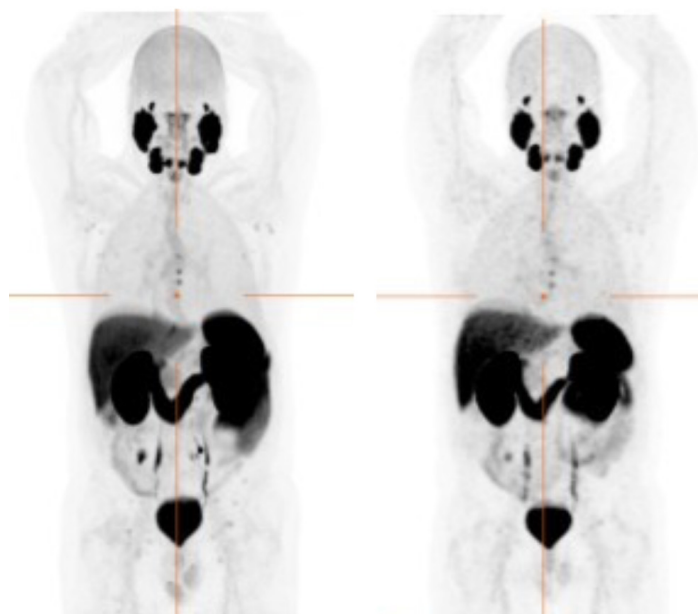


Fig. 2: Patient initially scanned on conventional PET camera (right image; GE Discovery 710; 5 mCi ⁶⁸Ga-PSMA-11, 34 minutes) agreed to be rescanned on Quadra (left image; 5 mCi ⁶⁸Ga-PSMA-11, 10.6 minutes), demonstrating tremendous reduction in acquisition duration possible while still achieving improved image quality.

Potential Clinical Impact: These innovations promise to improve diagnostic accuracy, reduce scan duration, and minimize radiation exposure. The ability to acquire high-quality scans in seconds also creates new opportunities for pediatric imaging (e.g., imaging without anesthesia, imaging of long-lived radionuclides such as ⁸⁹Zr-labeled monoclonal antibodies), reducing risk and streamlining workflow. In addition, this work lays the groundwork for theranostic approaches that integrate imaging and treatment and multi-tracer imaging protocols that streamline early-phase drug development. MSK is well-positioned to lead in defining clinical applications for total-body PET and translating them into meaningful patient benefits.

Acknowledgments: This work was supported in part by the MSK Cancer Center Support Grant P30 CA008748.

Inside Digital Twins: High-Fidelity Mesh Anatomic Models for Macro- and Microscale Radiopharmaceutical Dosimetry

Lukas Carter¹, John Humm¹, Wesley Bolch², and Adam Kesner¹

¹Department of Medical Physics, MSK, and ²Department of Nuclear Engineering, University of Florida

Motivation: The most sophisticated commercial patient-specific radiopharmaceutical dosimetry software applications rely on voxel-based anatomic models that cannot efficiently represent small/thin structures or fine anatomical boundaries, leading to large dosimetric uncertainties in many radiosensitive anatomical regions. Improved mesh-type models with anatomical fidelity at small scales opens up an important realm needed for establishing radiation dose-biological effect relationships.

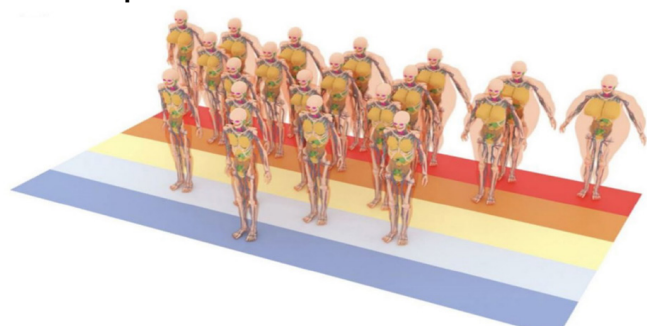


Fig. 1: Selection of representative phantoms of different body morphometries from a 357-member adult mesh phantom library. Dark blue = underweight; light blue = healthy weight; yellow = overweight; orange = obese; red = morbidly obese.

Methods: We have generated extensive libraries of anatomically realistic mesh phantoms by combining anatomic imaging data (e.g., of patients, animal subjects, tissue specimens) with computer-aided modeling and animation software (Fig. 1). These techniques enable creation of high-fidelity digital twins that capture dosimetrically relevant anatomy, from whole-organ structures down to microanatomy such as skeletal spongiosa (Fig. 2), renal subregions, radiosensitive mucosa of the gastrointestinal and respiratory tracts, vasculature, and even smaller structures, including individual cell components (Fig. 3) or molecular targets of DNA. These mesh models resolve many limitations of voxel phantoms and are readily adapted for diverse research and clinical applications by integration with Monte Carlo radiation transport simulations.

Scientific Significance: The short particle ranges and microscopic activity concentration gradients typically present in radiopharmaceutical therapy may yield profoundly steep dose gradients that cannot be accounted for by voxel-based models used by current commercial dosimetry software. The accompanying uncertainties may translate to critical limitations in radiopharmaceutical therapy such as overly conservative dose limits, leading to the underdosing of most patients to avoid dose limiting toxicities in only a few patients. Similar limitations apply in other subspecialties in radiopharmaceutical science and medicine, including preclinical animal studies, basic radiobiology, and radiation safety.

Mesh phantoms can capture complex anatomy with submicron-scale precision, enabling dose reconstruction in fine radiosensitive anatomy. They are especially powerful when paired with ex vivo tissue imaging to analyze

microscopic activity, dose distributions, and associated biological effects. Their flexible format also allows facile modeling of diverse radiation exposure scenarios encountered in clinic, preclinical development, and radiation protection settings. Ultimately, access to such models may improve predictions of biological effects from radiation dosimetry.

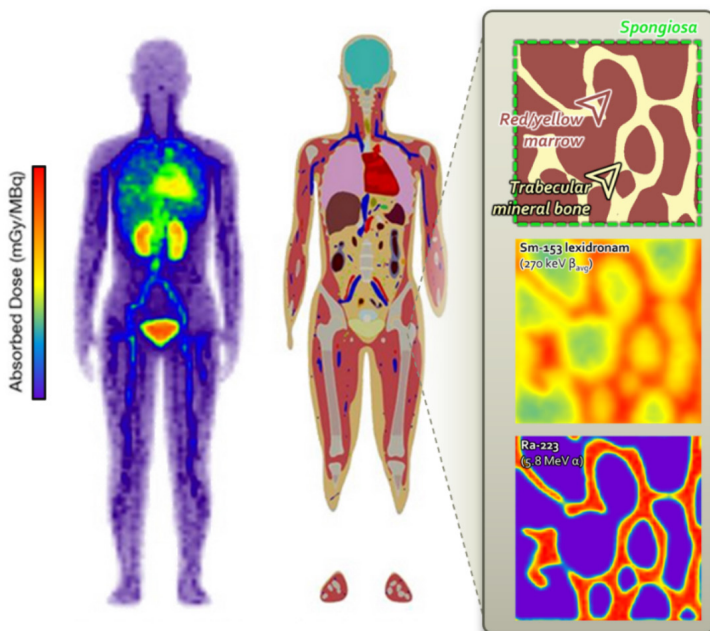


Fig. 2: Macro- and micro-scale dosimetry possible with mesh phantoms. Left: Macroscopic dose distribution in whole body. Right: Microscopic dose distribution in marrow and trabecular mineral bone regions of the skeletal spongiosa for different radionuclides localized in mineral bone.

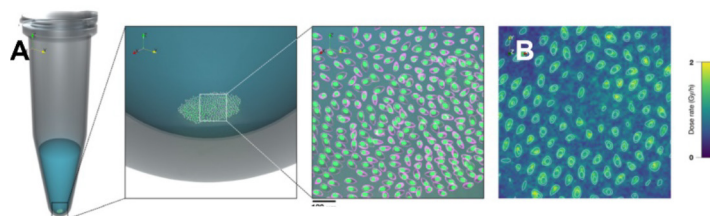


Fig. 3: Cell-level dosimetry for in vitro radioassay. (A) Three-dimensional rendering of radiolabeled cell model. (B) Cell-level dose rate map.

Potential Clinical Impact: By combining high-fidelity anatomical models with fine-scale activity mapping, mesh-based workflows can improve the accuracy and reliability of radiation dose estimates, enhance toxicity and/or efficacy predictions, and refine treatment planning for both established and emerging radiopharmaceuticals. Expanded mesh phantom libraries and integration into tools such as our *MIRDsoft* platform (www.mirdsoft.org), will make these capabilities widely accessible, accelerating the adoption of precise, biologically informed dosimetry across the radiation sciences.

Acknowledgments:

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A Statistical Model for Dosimetry for Radioactive Iodine Therapy

John Humm¹, Laura Boucai², Heiko Schöder³, Audrey Mauguén⁴, Binsheng Zhao³, Finn Augensen¹, Harry Marquis¹ and Steve Larson³
¹Department of Medical Physics, ²Medicine, ³Radiology, and ⁴Epidemiology-Biostatistics

Motivation: The incidence of thyroid cancer in the U.S. has tripled in the past four decades. Radioactive iodine (RAI) therapy has been shown to stabilize disease and prolong life in patients with metastatic thyroid cancer. It is widely recognized that acquiring four imaging timepoints for accurate dosimetry is desirable for all radionuclide therapies; however, such a practice is resource intensive. Therefore, methods to predict lesion and normal organ radiation doses from a reduced number of imaging timepoints (one or two) are needed by the theranostics community.

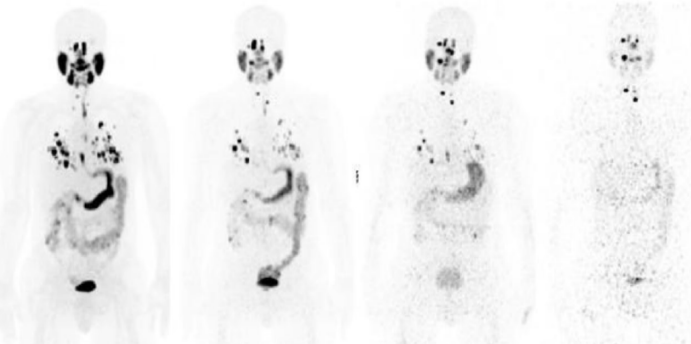


Fig. 1: Iodine-124 positron emission tomography (¹²⁴I PET) images of a patient showing individual lesion uptake at 24, 48, 72, and 120 hours, respectively, following radioactive iodine administration.

Methods: The kinetics of RAI in individual thyroid cancer lesions were measured using four-timepoint iodine-124 positron emission tomography (¹²⁴I-PET) images (see example patient in Fig.1).

Dr. Mauguén created a generalized estimating equation model which fits a linear model using one- or two- timepoint imaging data. Using the estimated regression parameters, a prediction interval (PI) is constructed to predict absorbed radiation doses of metastatic lesions and normal organs based on the measured uptake from a single or two images.

Results: The correlation between lesion standardized uptake value (SUV) at 48 hours and lesion absorbed radiation dose was shown to depend on lesion location, differing among bone, lung, and soft tissue is shown in Fig. 2. Precise lesional dosimetry estimates, combined with volumetric segmentation tools developed by Dr. Zhao in her Computational Image Analysis Laboratory, will allow for establishment of the first dose-response relationships for RAI therapy. An example analysis of one patient is shown in Fig. 3.

Scientific Significance: This will be the first comprehensive analysis correlating individual lesion and normal organ radiation absorbed doses and RAI avidity with changes in lesion volume, enabling assessment of overall patient response normal organ toxicity.

Potential Clinical Impact: The development of a new imaging biomarker that can predict lesion and normal organ doses from a limited number of imaging timepoints is of high importance to the theranostics field because it can mitigate the logistical challenges and costs associated with repeated imaging.

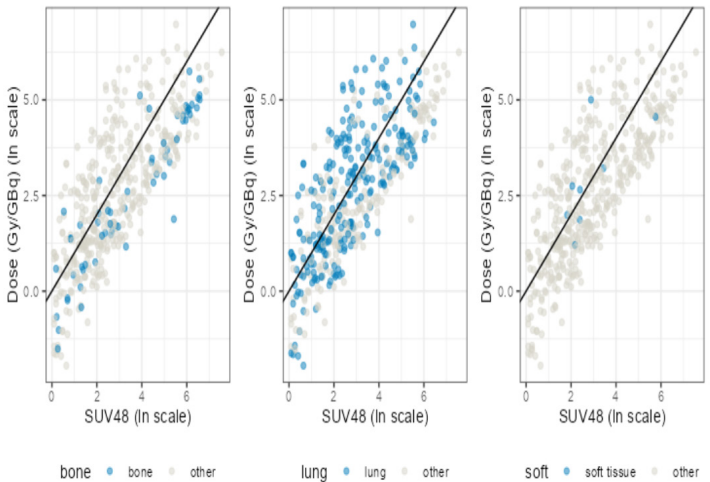


Fig. 2: Correlation between iodine-124 (¹²⁴I) standardized uptake value at 48 hours and the lesion absorbed radiation dose (Gy/GBq). Colored circles represent lesions in bone (left), lung (middle), and soft tissue (right).

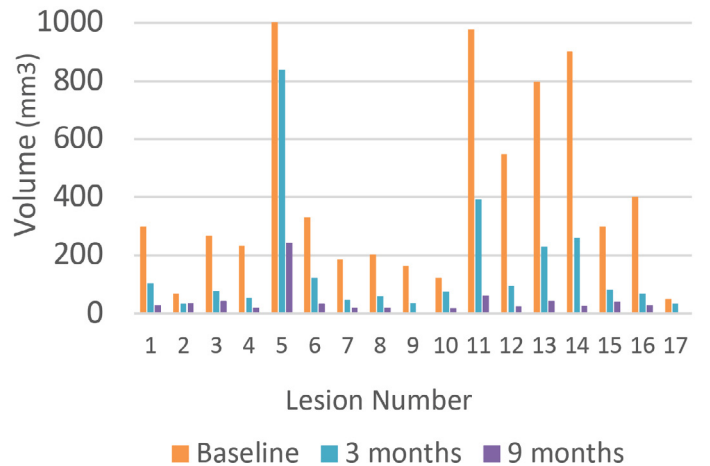


Fig. 3: Volumetric response data for a patient with 17 individual metastatic cancer lesions, measured at the pre-treatment baseline and at 3- and 9-month follow-up using CT images.

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Magnetic Resonance Imaging and Spectroscopy Physics



Faculty: Mark Burgess, Ouri Cohen, Carl Lekaye, Yousef Mazaheri, Victor Murray, Ricardo Otazo, Kyung Peck, Sunitha Thakur, and Can Wu.

Staff: Anthony Mekhanik (MRI engineer)

Postdoctoral fellows: Tamer Abdelrehim, Spencer Brinker, Subin Erattakulangara, Aniket Pramanik, Enlin Qian, Melanie Schellenberg, and Ethan Tu.

Magnetic Resonance Imaging and Spectroscopy Physics

The Service brings together physicists and engineers to develop new acquisition and reconstruction techniques for magnetic resonance imaging (MRI) and ultrasound imaging (US) to improve cancer detection, diagnosis and treatment. Technical development is oriented to clinical translation and driven by clinical needs. The Service collaborates with radiologists, radiation oncologists, and other clinicians at MSK to define and solve the problem and validate the developed technology. There is also strong collaboration with industry to implement the developed technology into clinical scanners with the overall goal of clinical translation. Representative projects include:

Accelerated MRI acquisition using AI reconstruction: designed to reduce scan time without degrading image quality by leveraging AI to acquire less data and reconstruct images without undersampling artifacts. This project also employs simultaneous acceleration of multiple sequences within a single protocol to exploit additional inter-sequence correlations.

Motion-tolerant MRI scans using a combination of non-Cartesian k-space acquisition, AI-based auto-navigation, and motion-resolved reconstruction: analogous to taking a live photo on a cell phone, this approach captures motion as a short-video using AI to sort data into frames and minimize the scan time.

Fast and motion-robust pediatric MRI with reduced anesthesia: the combination of radial k-space acquisition and AI reconstruction enables us to make MRI robust to both patient and respiratory motion, which will reduce, and in some cases, remove the need for anesthesia.

MR fingerprinting for fast quantitative mapping of tissue parameters: to enable access to new contrast, such as the acidity level of tumors, for improved characterization of brain metastases and differentiation of tumor progression from treatment related effects.

MRI-guided adaptive radiotherapy on an MR-linear accelerator (MR-Linac) system: real-time 3D MRI to adapt radiation delivery according to motion of the tumor and organs at risk. This development would enable safe delivery of curative doses to tumors affected by motion, such as pancreatic tumors.

Quantitative perfusion MRI to predict radiation therapy outcomes of metastatic spine tumors: the plasma volume parameter estimated from dynamic contrast-enhanced MRI is more sensitive and specific than conventional size measurements for predicting whether treatment will be successful.

Quantitative multiparametric endoscopic ultrasound imaging: a combination of quantitative US measurements and endoscopy for early detection of pancreatic cancer.

The Service consists of seven MRI faculty members and one US faculty member, one MRI engineer, and several NIH-funded postdoctoral fellows. Faculty members participate in various educational programs at MSK, including the PhD in Cancer Engineering program, and the joint Cornell-MSK MSc in Biomedical Imaging program.



Ricardo Otazo, PhD, Service Chief

End-to-End Deep-Learning Auto-Navigation and Reconstruction For Fast Free-Breathing Abdominal MRI

Victor Murray¹, Yan Wen², Subin Erattakulagara¹, Oguz Akin³, Richard Do³, Gerald Behr³, Amaud Guidon², and Ricardo Otazo^{1,3}

¹Department of Medical Physics, MSK, ²GE HealthCare, and ³Radiology, MSK

Motivation: To improve acquisition speed and motion tolerance of abdominal MRI using deep-learning auto-navigation and reconstruction.

Methods: This project aims to capture motion in a short movie rather than reject, or correct, for motion using deep learning for auto-navigation and motion-resolved reconstruction. The end-to-end deep-learning approach uses data continuously acquired during free-breathing with a stack-of-stars k-space trajectory and consists of an auto-navigation network called “RANGR” to extract a motion signal directly from the acquired data and to sort the acquired data into motion frames as well as a reconstruction network called “Movienet” that can produce a movie without aliasing artifacts using accelerated k-space data, as shown in Fig. 1. Data from 40 patients with abdominal cancer were employed to train the networks. Data were collected using the DISCO-STAR sequence on 3T scanners (Signa Premier, GE Healthcare) with in-plane resolution of 1.25-1.5 mm and slice thickness of 4-5 mm. k-space data were automatically transferred to a Linux computer (Intel Xeon Platinum 8380, NVIDIA A-100 GPU) for RANGR auto-navigation and Movienet reconstruction. RANGR estimated a 1D respiratory motion signal using z-projection for each angle. The k-space data were sorted into 4 motion states, and 3D NUFFT generated 5D aliased images (x, y, z, time, coil). Movienet reconstruction removed aliasing artifacts, resulting in motion-resolved 4D MRI output (the MRI video). The end-expiration images were then converted to DICOM format using standard GE Healthcare post-processing techniques. Lastly, two experienced radiologists qualitatively assessed 5 test datasets to compare the proposed RANGR + Movienet against the standard DISCO-STAR reconstruction.

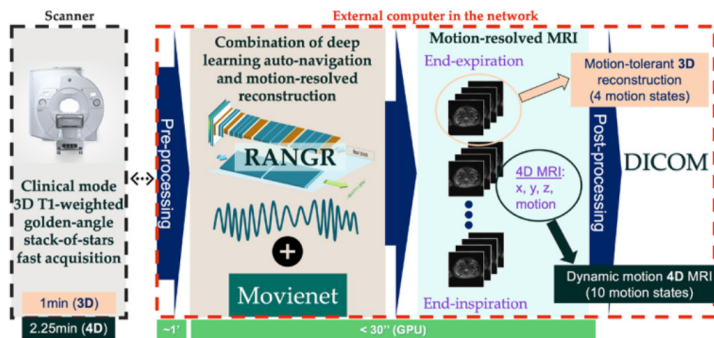


Fig. 1: The end-to-end approach begins with a three-dimensional (3D) T1-weighted golden-angle stack-of-stars acquisition, which takes only 1 min. The raw data is compressed into 8 virtual coils. Deep-learning (RANGR) and motion-resolved reconstruction (Movienet) generate a 4D motion-resolved magnetic resonance image (MRI). Lastly, vendor post-processing produces Digital Imaging and Communications in Medicine (DICOM) using only the 3D end-expiration volume.

Results: RANGR and Movienet enable robust free-breathing abdominal MRI with only 1 min of scan time. Pre-processing lasted about 1 min whereas the combination of RANGR and Movienet with DICOM conversion required 22-30 s on a GPU (4 min on a CPU). The deep-learning motion-resolved reconstruction outperformed the conventional DISCO-

STAR method, providing better delineation of anatomical structures and improved lesion visibility, as noted by expert radiologists. The deep learning system achieved higher scores compared with DISCO-STAR in anatomical structure discernment, lesion conspicuity, artifacts, and overall image quality. Enhanced motion compensation was observed for both adults (as shown in Fig. 2) and children. Additionally, RANGR-based sorting improved Movienet’s performance, and the system can be applied to various MR contrasts, with potential for managing 4D MRI and planning radiotherapy for tumors affected by motion.

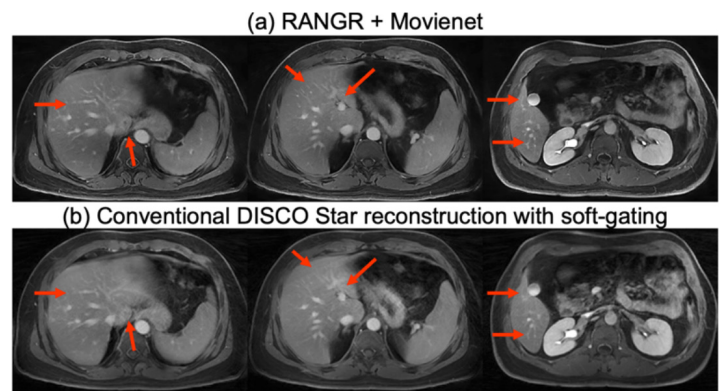


Fig. 2: Motion-resolved three-dimensional magnetic resonance image of an adult case using (a) Movienet with RANGR versus (b) conventional DISCO Star reconstruction.

Scientific Significance: The combination of radial k-space acquisition and deep-learning motion-aware reconstruction enables motion capture in a short video rather than rejecting or explicitly correcting for motion.

Potential Clinical Impact: Deep-learning-based RANGR+ Movienet can improve both image quality and efficiency compared to traditional breath-holding and respiratory gating techniques.

Acknowledgments: R01-CA255661, R01-CA244532. This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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- Nario J J, Murray V, Mekhanik A and Otazo R 2024 RANGR: deep learning autonavigation of free-breathing golden-angle radial abdominal MRI. ISMRM 2024.

AI-Powered Reconstruction For Highly-Accelerated 3D MRI of Brain Tumors

Anthony Mekhanik¹, Robert Young², and Ricardo Otazo¹

¹Department of Medical Physics, and ²Radiology, MSK

Motivation: To highly accelerate the acquisition of 3D brain MRI with high spatial resolution using AI.

Methods: A deep learning-based image reconstruction technique named “Accelerated Deep Modular Image Reconstruction” (ADMIRE) was developed to reduce k-space data and thus accelerate the acquisition. ADMIRE consists of two independently trained convolutional neural networks (CNNs) to first unalias multicoil coronal images (acceleration plane) and then enhance axial slices (the clinical evaluation plane), as shown in Figure 1. ADMIRE was trained with brain tumor patient data acquired with T1-weighted 3D sequences (BRAVO and magnetization-prepared rapid acquisition with gradient echo [MPRAGE]) and is able to reconstruct any of them. Cancer imaging protocols acquire multicontrast data to examine complementary features. Thus, both intra- and inter-contrast correlations are available to exploit. Three-dimensional pre- and post-contrast T1 MPRAGE share considerable mutual information at short and long pixel ranges that can be efficiently explored by a Transformer. A Transformer, mimicking a Unet structure named “Joint-Uformer”, was trained on concatenated coil images from both contrasts to exploit additional inter-contrast correlation and further improve acceleration or image quality.

Results: AI reconstruction enables 8-fold acceleration (2 to 3-minute scan time savings) of 3D MRI with 1 mm isotropic resolution for brain tumor patients

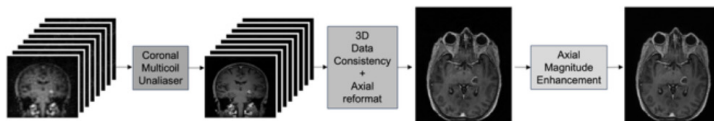


Fig. 1: Accelerated Deep Modular Image Reconstruction (ADMIRE) technique featuring two independently trained convolutional neural networks, where the first network unaliases multicoil coronal slices (the acceleration plane), and the second network enhances coil-combined axial images (the clinical evaluation plane). Single fixed k-space data consistency block in between is used to remove hallucinations.

ADMIRE enabled 8-fold acceleration without degrading image quality of the current clinical standard that uses lower acceleration factors of 3-5, as shown in Fig. 2, representing scan time reductions of 2-3 mins. Neuroradiologists found statistically nonsignificant differences in diagnostic image quality. Joint-Uformer jointly reconstructs 3D pre- and post-contrast MPRAGE at comparable quality to the longer clinical acquisitions, representing a promising direction for acceleration of the whole imaging protocol that consists of multiple sequences with different contrasts, as shown in Fig. 3.

Scientific Significance: Deep learning reconstruction of undersampled k-space data can increase the acceleration rate of clinical techniques. The main advantage is to learn directly from the data, resulting in more realistic image models and robust reconstruction methodology.

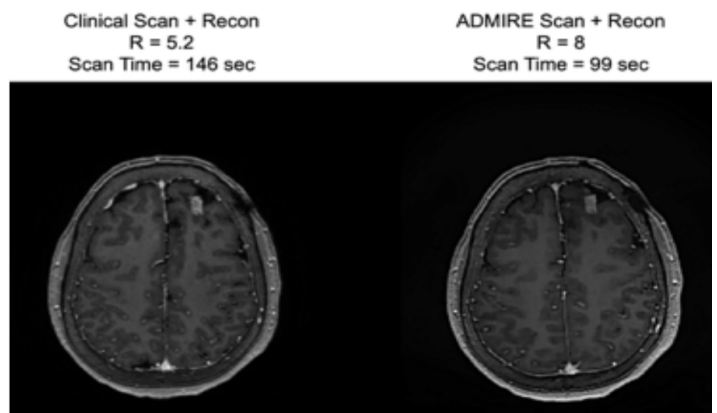


Fig. 2. Clinical standard with 5.2-fold undersampling (R factor) (left) and Accelerated Deep Modular Image Reconstruction (ADMIRE) with 8-fold undersampling (right) on a patient with reactive enhancement around anterior left frontal resection cavity using ADMIRE achieves similar diagnostic quality to the clinical standard despite the reduction in scan time.

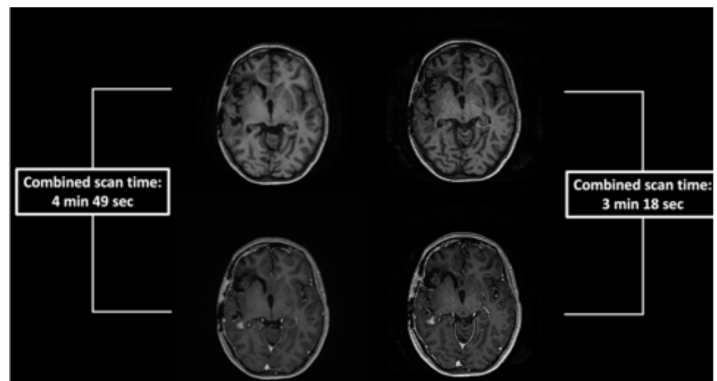


Fig. 3. Reconstruction results for a patient with history of grade IV astrocytoma using clinical acceleration with 4 min 49 s total scan time (left) and proposed Joint-Uformer with 3 min 18 s total scan time (right).

Potential Clinical Impact: ADMIRE and Joint-Uformer can reduce scan times and allow scanning more patients in an efficient manner. The higher acceleration can be potentially used to achieve higher spatial resolution.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Mekhanik A, Stember JN, Yildirim O, Naveed MA, Zhang Z, Young RJ, Otazo R. Highly-accelerated 3D MRI of brain tumors using deep modular reconstruction networks. NMR Biomed. Submitted in October 2025

SELFIE: Self-Supervised Reconstruction Learning For Fast Dynamic Golden-Angle Radial MRI

Melanie Schellenberg¹, Anthony Mekhanik¹, Victor Murray¹, Oguz Akin², and Ricardo Otazo¹

¹MRI Physics, and ²Radiology

Motivation: The properties of golden-angle radial k-space acquisition (consecutive spokes are separated by 111.25°) can be exploited to self-supervise training of a space-time reconstruction network to improve performance over compressed sensing.

Methods: SELFIE (Self-supervised Learning for Fast reconstruction of dynamic golden-angle radial MRI) leverages two key properties of golden-angle radial acquisition to enable fully self-supervised network training, as shown in Fig. 1. First, the flexible k-space ordering allows for variable temporal resolution, enabling automatic extraction of anatomical and temporal image representations — low and high temporal resolution, r^A and r^T , respectively — directly from the acquired data. Second, SELFIE exploits the intrinsic temporal sparsity of dynamic MRI, a principle also central to compressed sensing (CS). The network operates slice-wise in the image domain, taking complex multicoil dynamic input images ($\tilde{x}$, 2D + time + coils) and reconstructing dynamic magnitude coil-combined images (x , 2D + time). During training, the output x is guided by the extracted self-references r^A and r^T , along with a temporal total variation constraint, eliminating the need for external labels or fully sampled references. Once trained on a multi-subject dataset, SELFIE generalizes to unseen test data without the need for retraining.

Results: Highly-accelerated dynamic contrast enhanced (DCE) MRI of gynecological tumors

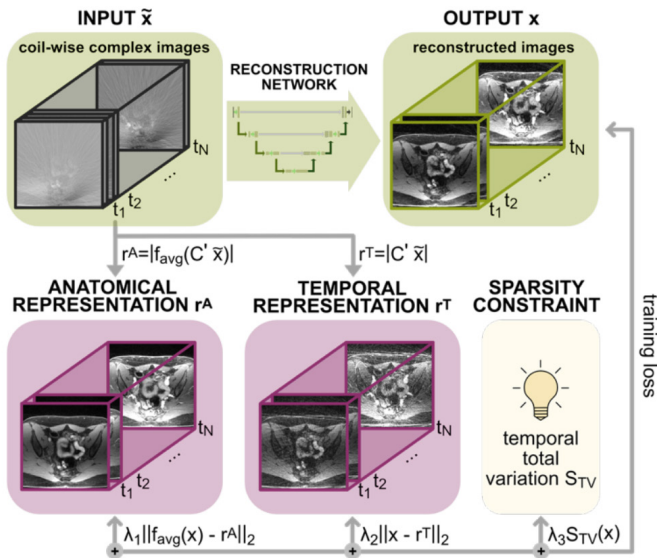


Fig. 1: Self-supervision of SELFIE (Self-supervised Learning for Fast reconstruction of dynamic golden-angle radial MRI). A dynamic accelerated multicoil input image $\tilde{x}$ with N frames ($t_1, t_2, \dots, t_N$) is reconstructed to a coil-combined dynamic image x . The loss function compares the output x with the anatomical (r^A) and temporal (r^T) representations and enforces temporal sparsity. Representation r^A are fully sampled coil-combined magnitude images with low temporal resolution, constructed by averaging N_{avg} frames of the input image with periodic boundary conditions (operator $f_{avg}(\cdot)$). Representation r^T are coil-combined magnitude images with the target temporal resolution. The temporal sparsity constraint is a temporal total variation S_{TV} .

SELFIE reduces residual streaking artifacts (due to k-space undersampling) compared with compressed sensing (golden-angle radial sparse parallel [GRASP]) and improves image sharpness compared with supervised deep learning (DCE-Movienet), as shown in Fig. 2. These improvements enable performing DCE-MRI with 5 s temporal resolution and 1.5 mm spatial resolution with high spatial and temporal quality. In addition, SELFIE offers significant reductions in reconstruction times by approximately two orders of magnitude (min to seconds) compared with compressed sensing, which is attractive for clinical implementation.

Scientific Significance: Self-supervised reconstruction for dynamic golden-angle radial MRI removes the need for a reference during training and can outperform compressed sensing and supervised learning methods.

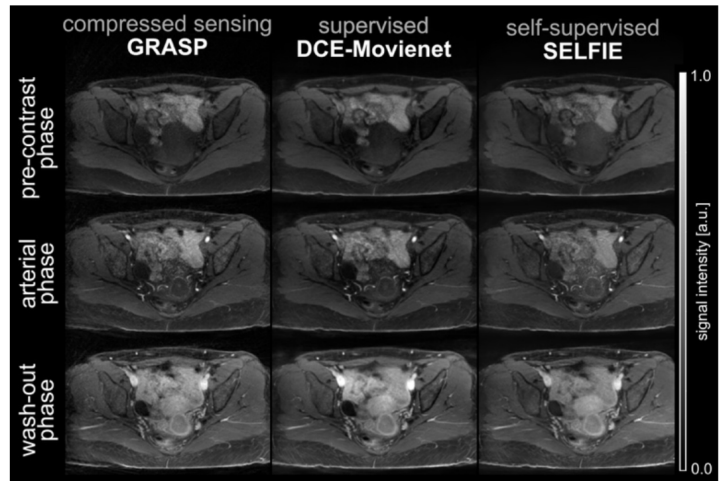


Fig. 2: Comparison of golden-angle radial sparse parallel (GRASP) (compressed sensing), dynamic contrast-enhanced (DCE)-Movienet (supervised deep learning) and SELFIE (Self-supervised Learning for Fast reconstruction of dynamic golden-angle radial MRI, self-supervised deep learning) for reconstruction of 8-fold accelerated DCE-MRI of cervical cancer. SELFIE presents lower streaking artifacts compared with GRASP, reduced blurring compared with DCE-Movienet. SELFIE presents an effective alternative for accelerated dynamic MRI in cases where the acquisition of a fully-sampled reference to train the network is impractical, such as DCE-MRI with high spatial and temporal resolution.

Potential Clinical Impact: SELFIE can enable dynamic MRI with superior image quality and quantification performance for improved diagnosis and treatment response evaluation.

Acknowledgments: NIH grant R01-244532 This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Schellenberg, M., Mekhanik, A., Murray, V., Otazo, R. SELFIE: Self-supervised Learning for Fast dynamic golden-angle radial MRI reconstruction with auto-extracted representations. Proc. Intl. Soc. Mag. Reson. Med. 33. 2025; p.1188.

Dynamic Contrast-Enhanced MRI for Clinical Outcome Prediction of Metastatic Spinal Tumors after Radiation Therapy

Kyung K. Peck¹, Atin Saha², Sasan Karimi², Eric Lis², Yoshiya Yamada³, and Andrei Holodny²

¹MRI Physics, ²Radiology, and ³Radiation Oncology

Motivation: To improve the differentiation between treatment success and failure in radiation therapy of spinal metastases using quantitative perfusion parameters derived from dynamic contrast-enhanced (DCE)-MRI instead of size measurements on anatomical images.

Methods: An accelerated DCE-MRI acquisition tailored to the spine was implemented using the DISCO sequence on clinical 1.5T and 3T GE scanners. Perfusion analysis was performed using the 2-compartment Tofts model with an arterial input function defined on the aorta. The plasma volume perfusion parameter (V_p) was employed for treatment response evaluation. The Ktrans was also computed, for comparison. The study included 49 patients (mean age, 63 [SD, 13] years; 29 men) with metastatic lesions treated with radiation therapy. The median time between radiation therapy and follow-up DCE-MR imaging was 62 days. Patients were divided into 2 groups: clinical success ($n = 38$) and failure ($n = 11$). Failure was defined as positron emission tomography recurrence ($n = 5$), biopsy-proven ($n = 1$) recurrence, or an increase in tumor size ($n = 7$) whereas their absence defined clinical success. A Mann-Whitney U test was performed to assess differences between groups.

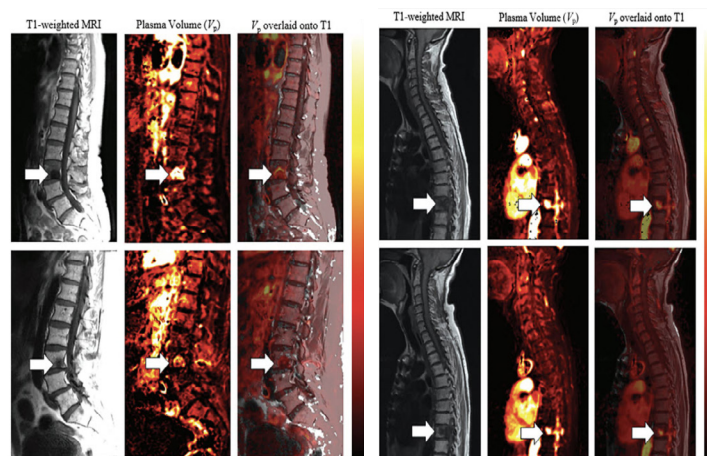


Fig. 1: (Left) Patient with metastatic pancreatic neuroendocrine cancer demonstrating successful treatment response of lesion at L3. The middle column shows fractional plasma volume (V_p) maps (a reduction of 87.8%). (Right) Patient with metastatic thymoma demonstrating unsuccessful treatment response of lesion at T9 (an increase of 64.8%). The patient experienced progression of disease, particularly the epidural associated portion of the tumor. Additional RT therapy was required from T8-T10 14 months after the secondary imaging study.

Results: The plasma volume parameter correlated well with treatment response and there was a significant reduction for successful treatment and an increase for unsuccessful treatment, as shown in Fig. 1. The changes in V_p were more statistically significant than those of Ktrans and presented higher sensitivity and specificity than size measurements performed on anatomical contrast-enhanced images, as shown in Fig. 2.

Scientific Significance: The sensitivity and specificity of the plasma volume parameter was higher than conventional size measurements, suggesting that DCE-MRI is a powerful tool to discriminate between treatment success and failure.

Potential Clinical Impact: Quantitative DCE-MRI is a promising tool to predict treatment outcome in radiation therapy of metastatic spine tumors.

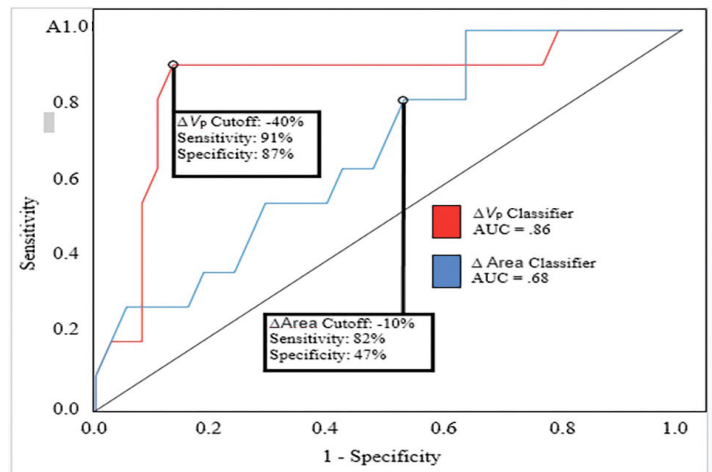


Fig. 2: Receiver operating characteristic (ROC) curve of the ΔV_p (area under the ROC curve, 0.86; 95% CI, 0.717-1) and change in lesion area (Δ area; area under the ROC curve, 0.68; 95% CI, 0.505-0.846). The optimal ΔV_p cutoff is -40%, which yields a sensitivity of 91% and a specificity of 87%. The optimal Δ area cutoff is -10%.

Acknowledgments:

Grant funding: Bayer Healthcare This work was also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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2-Hydroxyglutarate MR Spectroscopy for Characterization of IDH-Mutant Adult Gliomas and Brainstem/DIPG Tumors

Sunitha Thakur^{1,2}, Robert Young², Andrew Lin³, Sofia Haque², and Ingo Mellinghoff³

¹Department of Medical Physics, ²Radiology, and ³Neurology

Motivation: Isocitrate dehydrogenase (IDH) mutations define a large subset of adult gliomas and a proportion of diffuse intrinsic pontine gliomas (DIPGs). These mutations lead to accumulation of the oncometabolite 2-hydroxyglutarate (2-HG), which serves as a tumor-specific biomarker. Tissue biopsy is invasive and carries significant risk in brainstem tumors, underscoring the need for noninvasive methods to establish IDH status and monitor treatment response.

Methods: Clinical translation of 2-HG magnetic resonance spectroscopy (MRS) was achieved by optimized single-voxel PRESS/semi-LASER and 3D magnetic resonance spectroscopic imaging protocols on 3T scanners, introducing broadband refocusing pulses, spectral filtering, and quantum mechanical fitting to improve sensitivity and reproducibility. Protocols were validated in phantoms, healthy controls, and glioma patients, then integrated into the MSK clinical workflow. A retrospective study of brainstem gliomas combined MRS, cerebrospinal fluid cell-free DNA sequencing (“liquid biopsy”), and tissue biopsy (when available) to confirm IDH status.

Results: Adult gliomas: The results of a landmark neuro-oncology study demonstrated the feasibility and reproducibility of 2-HG MRS for IDH detection and disease monitoring, correlating with tissue-based assays. The method is now routinely applied in clinical practice and incorporated into multi-center trials of IDH inhibitors as a pharmacodynamic biomarker, as shown in Fig. 1.

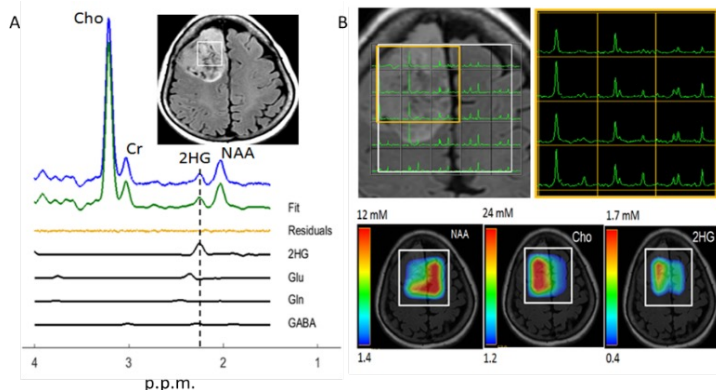


Fig 1: Metabolite color maps using multivoxel magnetic resonance spectroscopy. Data were obtained from a subject with a World Health Organization grade III oligodendroglioma using (A) single-voxel indicated in white box, and (B) 10 mm-thick 2D slab across the tumor selected from 3D multi-voxel spectroscopic imaging data overlaid on the T2w-FLAIR image.

Brainstem/DIPG gliomas: MRS proved sensitive for detecting a 2-HG peak in addition to other major brain metabolites at baseline and was most reliable when performed prior to radiotherapy. In patients rescanned after treatment, the 2-HG peak disappeared, consistent with therapeutic response. These findings confirm that MRS can provide critical diagnostic and monitoring information in brainstem tumors where biopsy is often unsafe.

Scientific Significance: This work establishes 2-HG MRS as a noninvasive molecular imaging biomarker that bridges tumor genetics and neuroimaging in both adult and pediatric brainstem gliomas.

Potential Clinical Impact: By enabling safe and reliable detection of IDH mutations in both adult gliomas and brainstem/DIPG tumors, 2-HG MRS reduces the need for invasive biopsies, offers a means to longitudinally monitor tumor biology and treatment response, and provides a validated biomarker for clinical trials of IDH inhibitors. These capabilities position MRS as a critical tool for advancing precision neuro-oncology and improving patient care.

Acknowledgments: This work is supported in part by the Society of MSK, the Dana Foundation, the B*Curad Foundation, the MSK Brain Tumor Center (MPI), and by the MSK Cancer Center Support Grant (P30 CA008748).

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Deep Neural Network IVIM Analysis and Ensemble Machine Learning of DCE-MRI Pharmacokinetics for Breast Cancer Response Prediction

D. Basukala^{1,2}, A. Bhowmik³, C. Lin³, S. Eskreis-Winkler³, M. Marrow⁴, D. Giri⁵, E. Sigmund², and S. Thakur^{1,3}

¹Department of Medical Physics, MSK ²Radiology, NYU, and ³Radiology, MSK, ⁴Surgery, MSK, and ⁵Pathology, MSK

Motivation: Intravoxel incoherent motion diffusion-weighted imaging (IVIM-DWI) provides biomarkers for breast cancer characterization, but variability across methods and limited external validation underscore the need for standardized, independent comparisons to ensure reliable clinical translation. Separately, tumor permeability and interstitial fluid pressure influence drug transport and neoadjuvant chemotherapy (NAC) response, yet predictive models are limited. Using pre-NAC dynamic contrast-enhanced (DCE) breast MRI-derived parameters, we developed a model predicting pathologic complete response with areas under the curve (AUCs) of 0.78 (internal) and 0.95 (external).

Methods: In this retrospective IRB-approved, HIPAA-compliant study, breast MRI from 186 patients (65 benign, 137 malignant) at 3T with 13 b -values was analyzed, as shown in Fig. 1. Lesions were segmented, IVIM parameters (perfusion fraction [f_p], pseudodiffusivity [D_p], tissue diffusivity [D_t]) were estimated using least-squares, and Bayesian and deep learning methods, with histogram features were extracted. Statistical tests and receiver operating characteristic (ROC) analysis were used to evaluate performance. Separately, pre-NAC DCE-MRI from 70 breast cancer patients (internal) and 10 public cases (Quantitative Imaging Network breast DCE-MRI) were analyzed. Tumors were segmented by a fellowship-trained radiologist, and permeability maps (K^{trans} , k_{ep} , v_p , v_e) were generated using the extended Tofts model. A steady-state fluid flow equation estimated interstitial fluid pressure and velocity. From all maps, 572 radiomic features were extracted, followed by feature selection (recursive feature elimination [RFE], least absolute shrinkage and selection operator), six classifier training with hyperparameter optimization, and ensemble prediction, as shown in Fig. 2A.

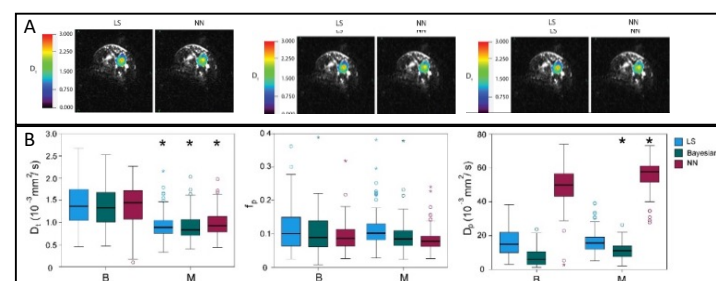


Fig 1: (A) Intravoxel incoherent motion (IVIM) parametric (D_t , f_p , D_p) maps overlaid on diffusion-weighted imaging in a patient with malignant breast lesion. (B) Tissue diffusivity (D_t), perfusion fraction and pseudodiffusivity values for benign (B) and malignant (M) lesions from Firevoxel (least squares [LS]), Bayesian (Olea) and IVIM-NET (neural network [NN]). *Indicates significant B/M differentiation.

Results: IVIM analyses showed excellent least squares neural network (NN) correlations for D_t , good for f_p , and poor for D_p . D_t mean consistently differentiated benign from malignant lesions (AUC > 0.80) whereas additional D_t and D_p metrics had moderate performance. Perfusion fraction was less diagnostic but improved with Bayesian or NN fitting. Separately, the optimal DCE-MRI model, built from RFE-selected features across classifiers, as shown in Fig. 2B, achieved AUCs of 0.78 (internal) and 0.95 (external).

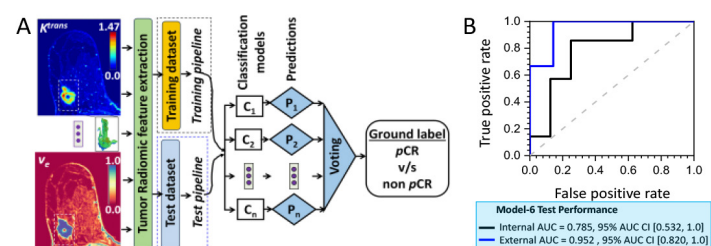


Fig 2: (A) Workflow of quantitative image analysis and radiomic machine learning model. (B) Receiver operating characteristic of internal and external test datasets. AUC: area under the curve

Scientific Significance: Reproducible IVIM metrics, particularly D_t , reliably distinguished benign from malignant lesions, supporting robust biomarker potential. Separately, our DCE model integrates permeability, fluid pressure, and radiomics from pre-NAC DCE-MRI to noninvasively predict treatment response.

Potential Clinical Impact: Reproducible IVIM-derived D_t shows promise as an early response marker, with prospective evaluation advancing precision oncology adoption. Separately, our DCE-MRI based machine learning model enables early prediction of NAC response, supporting timely treatment adjustments.

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Ultrashort Echo Time (UTE) and T1-Weighted 4D Lung MRI Using 3D Radial Acquisition and Deep Learning Reconstruction

Can Wu¹, Victor Murray¹, Victoria Yu², Andreas Rimner³, and Ricardo Otazo¹

¹MRI Physics, ²Division of Radiotherapy Physics, and ³Radiation Oncology

Motivation: To improve the contrast and motion-tolerance of lung MRI using a combination of radial acquisition and AI reconstruction for treatment planning and motion monitoring in lung cancer radiotherapy.

Methods: Data acquisition: Free-breathing three-dimensional (3D) half-spoke ultrashort echo time (UTE) and full-spoke T1-weighted 3D radial acquisitions were performed in eight healthy volunteers and eight patients with lung tumors on a clinical 3T Philips MRI scanner. Fig. 1 illustrates the k-space trajectories and the corresponding kx-ky projections for these acquisitions.¹ A back-and-forth k-space ordering was employed to minimize eddy-current-related artifacts caused by large angular rotations of the radial spokes between two consecutive interleaves.

Results: 4D MRI of lung cancer patients Fig. 2 shows the end-exhale and end-inhale phases of 4D MRI (half-spoke UTE and full-spoke T1-weighted contrasts) from a lung cancer patient, reconstructed using XD-GRASP and HD-Movienet. The reconstruction time for XD-GRASP is approximately 10 mins, which is substantially reduced to 11 seconds using HD-Movienet.

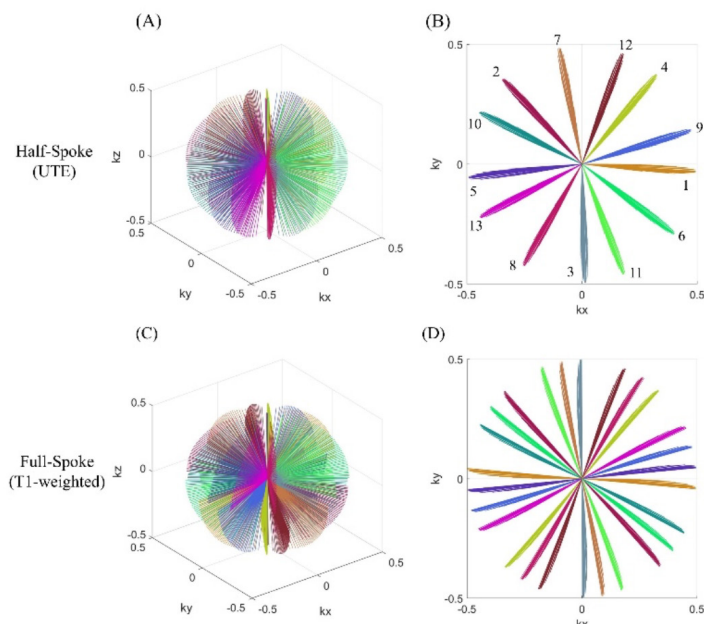


Fig 1: The k-space trajectories of ultrashort echo time (UTE) (A, B) and T1-weighted (C, D) acquisitions (example for 13 interleaves) with 3D golden-angle radial sampling following a spiral phyllotaxis trajectory. The kx-ky projections (B, D) demonstrate that the interleaves are spaced relatively uniform in the azimuthal direction according to the golden-angle rotation. The numbers in (B) indicate the interleaf ordering for the half-spoke acquisition, and the same color-coded order is used for the full-spoke acquisition shown in (D).

4D MRI Reconstruction: Four-dimensional (4D) MRI were reconstructed from k-space data using two methods: 1) compressed sensing (Extra-Dimensional Golden Angle Radial Sparse Parallel [XD-GRASP]) and 2) a deep-learning approach. A high-definition Movienet (HD-Movienet)² was developed to reconstruct high-isotropic-resolution 4D MRI from UTE and T1-weighted 3D radial acquisitions. HD-Movienet first sorts the data into motion states to form an aliased 5D image (x, y, z, motion, coil) and then applies a reconstruction network (a variant of the original Movienet without k-space data consistency) to generate unaliased, coil-combined, motion-resolved 4D images.

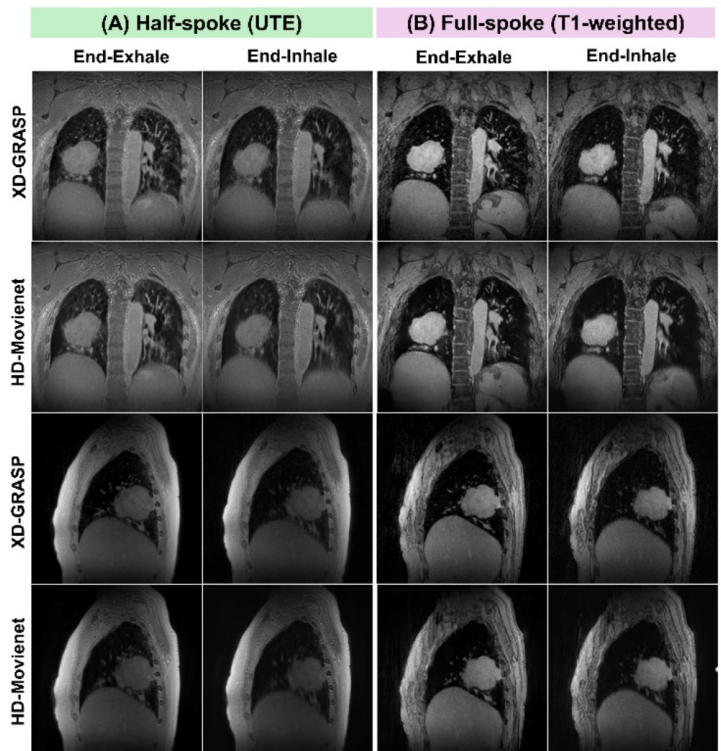


Fig. 2: Motion-resolved four-dimensional (4D) lung MRI using half-spoke (ultrashort echo time: UTE) (A) and full-spoke (T1-weighted) 3D radial acquisitions (B), reconstructed with Extra-Dimensional Golden Angle Radial Sparse Parallel (XD-GRASP) (10 min) and the proposed High-Definition Movienet (HD-Movienet) (11 s), in a clinical patient with a large lung tumor (7.7 cm × 5.0 cm).

Scientific Significance: The combination of 3D radial acquisition and deep learning-based 4D reconstruction enables high-isotropic-resolution, multi-contrast, motion-resolved 4D lung MRI.

Potential Clinical Impact: UTE and T1-weighted 4D lung MRI enable accurate motion assessment for treatment planning and treatment monitoring in lung radiotherapy.

Acknowledgments: This was supported by Philips Healthcare, and in part by the MSK Cancer Center Support Grant (P30 CA008748).

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T1rho (T1p) Imaging: A Novel Quantitative MRI Biomarker for Assessing Tumor Treatment Response in Radiotherapy

Sandeep Panwar Jogi¹, Victoria Yu², Vonetta Williams³, Nancy Lee³, Ricardo Otazo¹, and Can Wu¹

¹MRI Physics, ²Division of Radiotherapy Physics, and ³Radiation Oncology

Motivation: T1rho imaging, which measures T1 relaxation in the rotating frame, is a promising quantitative MRI biomarker with potential for early tumor detection and for monitoring tumor treatment response to radiotherapy.

Methods: The T1rho sequence is based on the magnetization-prepared angle-modulated partitioned k-space spoiled gradient echo snapshot (MAPSS).¹ The MAPSS sequence incorporates phase cycling and a variable flip-angle scheme, enabling fast and accurate T1rho quantification. To overcome the limitation of prolonged scan times, an unpaired phase-cycling approach — referred to as fast-MAPSS — was developed, achieving approximately a two-fold acceleration.^{2,3} Building on this, we recently developed a motion-robust, free-breathing three-dimensional (3D) T1rho technique for abdominal imaging by combining variable-density radial sampling (i.e., a diamond pattern) with fast-MAPSS.

Results: Quantitative 3D T1rho imaging in the head and neck, cervix, and abdomen

T1rho imaging has been applied in patients with head and neck cancer (Fig. 1)⁴ and cervical cancer (Fig. 2)⁵ to assess treatment response during radiotherapy.

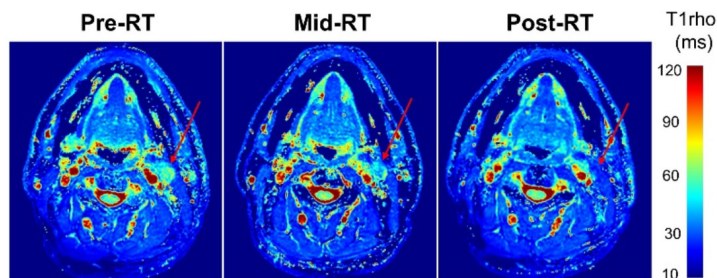


Fig 1: T1rho (T1p) mapping for radiotherapy (RT) treatment response assessment in a head and neck cancer patient with a left metastatic lymph node (1.6 cm × 1.3 cm), shown from left to right at pre-treatment, mid-RT (2 weeks), and post-RT (4 weeks).

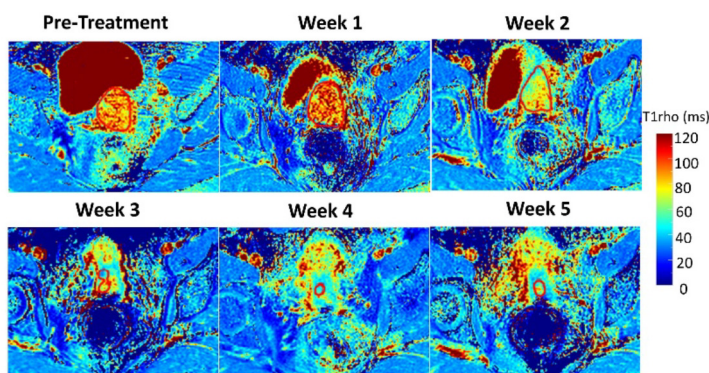


Fig. 2: T1rho (T1p) mapping for radiotherapy treatment response assessment in a cervical cancer patient, shown at pre-treatment, and during weekly scans throughout treatment.

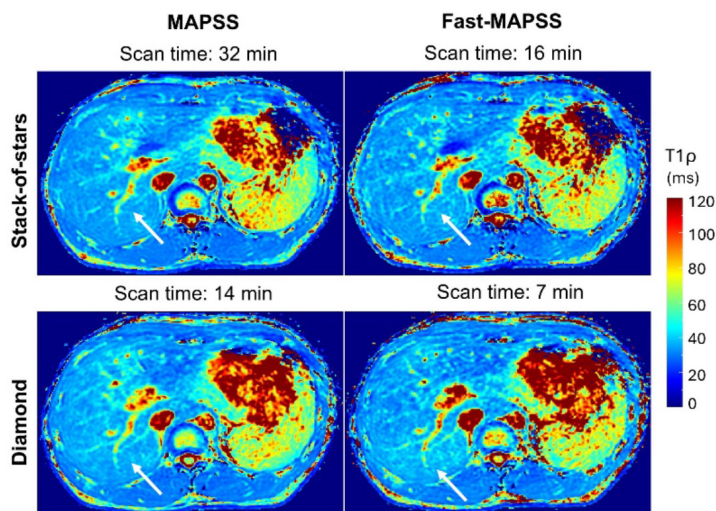


Fig. 3: Fast and motion-robust free-breathing three-dimensional (3D) T1rho (T1p) mapping of the abdomen in a healthy volunteer, using diamond-patterned radial sampling combined with fast-magnetization-prepared angle-modulated partitioned k-space spoiled gradient echo snapshot (MAPSS) compared with stack-of-stars radial sampling. The total scan time for diamond fast-MAPSS is seven minutes, representing a 2.2-fold acceleration compared with the stack-of-stars approach.

Additionally, the feasibility of the radial T1rho imaging technique was demonstrated in a healthy volunteer for abdominal tissue characterization — specifically of the liver and pancreas — under free-breathing conditions (Fig. 3).⁶

Scientific Significance: The combination of radial sampling and the fast-MAPSS technique enables quantitative, rapid, and motion-robust T1rho imaging.

Potential Clinical Impact: Quantitative T1rho imaging enables accurate assessment and monitoring of treatment response in patients undergoing radiotherapy.

Acknowledgments: This was supported by Philips Healthcare, and in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Magnetic Resonance Signature Matching (MRSIGMA) for Real-Time, Free-Breathing 3D Imaging on a MR-Linac

Saad Siddiq¹, Can Wu¹, Victor Murray¹, Neelam Tyagi², Christopher Crane³, and Ricardo Otazo¹

¹MRI Physics, ²Division of Radiotherapy Physics and ³Radiation Oncology

Motivation: Real-time, free-breathing three-dimensional (3D) MRI with a total imaging latency of less than 300 ms on the MR-Linac would enable safe delivery of curative radiation doses for abdominal tumors.

Methods: Methods: MRSIGMA pre-learns 3D motion states and 1D motion signatures in the motion learning phase and acquires and matches signatures in the signature matching phase (shown in Figure 1). The majority of the acquisition and reconstruction burden occurs in the motion learning phase, leaving fast signature-only data acquisition and correlation-based matching in the signature matching phase to minimize latency. The motion signatures are 1D projections along the z-dimension (head-foot) that uniquely represent the position of the liver dome. Data acquisition is performed using a golden-angle stack-of-stars k-space trajectory (radial kx-ky, Cartesian kz), where motion signatures can be extracted directly from the kz-line formed from the central kx-ky positions. During motion learning, hundreds of spokes are acquired, and data are sorted into motion states. To minimize scan time, motion states are undersampled, and our deep learning Movienet technique reconstructs the motion-resolved images by removing undersampling artifacts. Movienet operates in the image domain by exploiting space-motion-coil correlations constrained by motion consistency rather than k-space data consistency, which significantly speeds up the reconstruction process and allows for greater scan-time reduction than compressed sensing. Once the dictionary of 3D motion states and 1D motion signatures is ready, the real-time signature matching phase proceeds with the same acquisition, but data from each angle are processed separately to compute and match the incoming signature. MRSIGMA reconstruction was implemented on a high-performance computer connected to the Elekta Unity 1.5 T MR-Linac (Elekta AB, Stockholm, Sweden) via Ethernet.

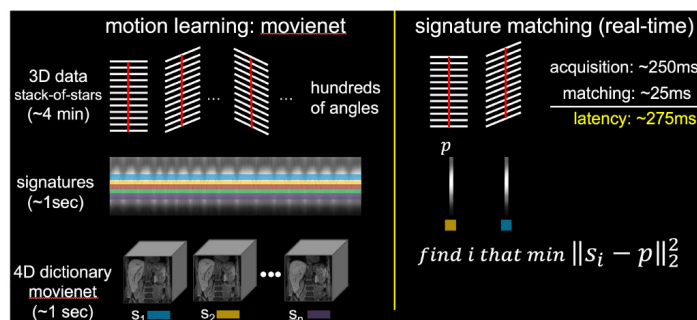


Fig. 1: Magnetic resonance signature matching (MRSIGMA) involves two steps per imaging session. Motion learning computes a motion dictionary with three-dimensional (3D) motion states and 1D signatures (a z-projection that encodes the position of the liver dome) using a golden-angle stack-of-stars k-space acquisition, amplitude-based motion sorting, and the deep learning Movienet reconstruction. Signature matching uses the same acquisition but processes each angle independently to compute a corresponding signature and match it to the closest signature in the motion dictionary. Implementation on the Elekta Unity MR-Linac (Elekta AB, Stockholm, Sweden) requires ~250 ms to acquire one angle and ~25 ms for signature calculation and matching, resulting in a total imaging latency of 275 ms, sufficient to track anatomical changes due to breathing.

Results: Real-time, free-breathing MRI of patients with pancreatic cancer on the Elekta Unity MR-Linac Motion learning can be accomplished in approximately four minutes, with almost negligible data transmission overhead. Signature acquisition is about 250 ms, and data transmission plus signature matching only takes about 25 ms, which results in a total latency of approximately 275 ms (below the target of 300 ms). Motion-related volumetric changes in the tumor and organs at risk (duodenum, stomach, and small bowel) were properly imaged in patients with pancreatic cancer using MRSIGMA (shown in Figure 2). Current work in progress includes the use of MRSIGMA for multileaf collimator (MLC) tracking to adapt radiation delivery in real time, and the development of an adaptive MRSIGMA version with continuous motion learning.

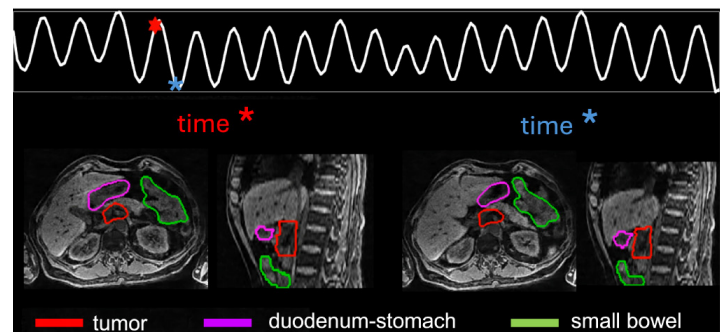


Fig. 2: Free-breathing, real-time three-dimensional (3D) magnetic resonance signature matching (MRSIGMA) with a total imaging latency of 275 ms on the Elekta Unity 1.5 T MR-Linac (Elekta AB, Stockholm, Sweden) for a patient with pancreatic cancer. Motion-related 3D deformation is captured in the tumor and organs at risk (duodenum, stomach, and small bowel) for adaptive radiation delivery.

Scientific Significance: The combination of radial imaging, deep learning reconstruction, and signature matching enables real-time, free-breathing 3D MRI on the MR-Linac, with a total imaging latency of less than 300 ms, allowing adaptive radiation delivery based on motion.

Potential Clinical Impact: MRSIGMA can enable the safe delivery of curative radiation doses to regions affected by respiratory motion.

Acknowledgments: This was supported by the NIH (R01-CA255661), and in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Multiparametric Ultrasound for Improved Pancreatic Cancer Screening and Characterization

Tamer Abdelrehim¹, Tuomas Tamella², Mark Schattner³, Carlie Sigel⁴, Vineet Rolston³, and Mark Burgess¹

¹Department of Medical Physics, ²Biology and Genetics, ³Gastroenterology, Hepatology and Nutrition, and ⁴Pathology

Motivation: Early detection of pancreatic cancer in high-risk individuals can enable curative treatment before malignant progression. Although most pancreatic cancers are sporadic, familial and hereditary pancreatic cancers can represent up to 25% of cases in high-risk individuals (HRIs) (shown in Figure 1). Endoscopic ultrasound (EUS) is routinely used for imaging-based pancreatic screening in HRIs, but it is highly operator-dependent and qualitative. The goal of this research project is to develop a system and methodology for multiparametric endoscopic ultrasound (mpEUS)-based assessment of pancreatic tissue in a non-subjective, quantitative manner.

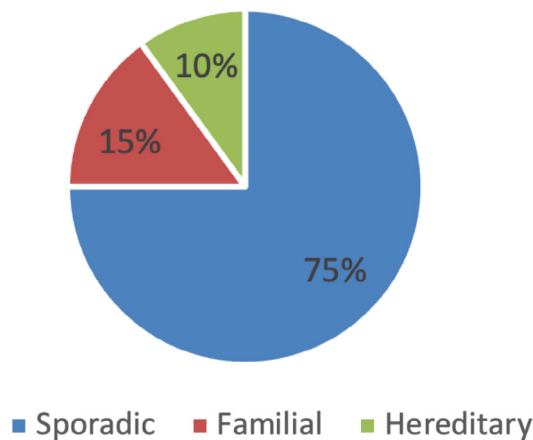


Fig. 1: Types of pancreatic cancers and their prevalence in high-risk individuals.

Methods: Using a Verasonics research ultrasound system, mpEUS was carried out, allowing for custom image-sequence development via MATLAB. A custom imaging script was developed for automated acquisition and storage of the mpEUS imaging modes simultaneously using a graphical user interface (GUI). A 5-MHz curvilinear endoscopic array was connected to the ultrasound system using a custom adapter for clinical imaging, and a 28-MHz high-frequency linear-array ultrasound probe was used for preclinical imaging of an orthotopic mouse model of pancreatic cancer. Software was developed for shear-wave elastography (SWE), quantitative ultrasound (QUS), and ultrasensitive microvessel imaging (UMI).

Results: mpEUS system development and pre-clinical testing

A streamlined system for efficient mpEUS data collection and processing, either offline or in real time, was developed using benchtop testing and pre-clinical mouse imaging experiments. An example QUS parameter map is shown in Figure 2, which uses a sliding region of interest (ROI) to calculate various QUS parameters using radiofrequency (RF) data derived from the B-mode image.

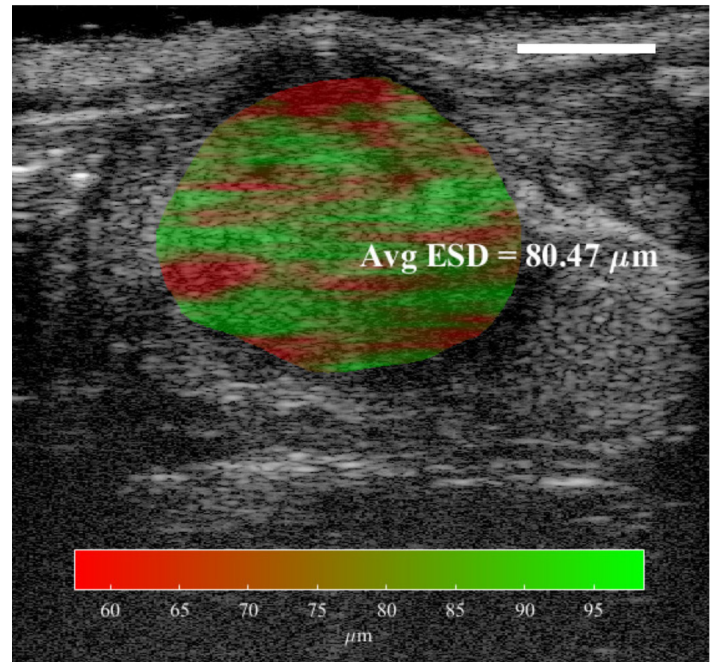


Fig. 2: Example image from an orthotopic mouse model of pancreatic cancer. The B-mode image is overlaid with a quantitative ultrasound parameter map. The scale bar represents 2 mm. ESD: effective scatterer diameter.

Scientific Significance: Expanding not only the QUS imaging toolbox but also utilizing advanced imaging modes such as UMI and SWE, will push the field of EUS biomarker development for pancreatic tissue characterization under normal and abnormal conditions.

Potential Clinical Impact: The enhanced mpEUS imaging protocol will be used to acquire data from 30 patients at high risk for pancreatic cancer and 30 patients with known pancreatic ductal adenocarcinoma (PDAC). The long-term goal is to identify mpEUS imaging biomarkers indicative of early-stage pancreatic cancer. This project will overcome limitations of current EUS screening protocols and provide greater sensitivity to morphologic changes that lead to pancreatic cancer.

Acknowledgments: This work was supported by the NIH (R21-CA296688), and in part by the MSK Cancer Center Support Grant (P30 CA008748).

Clinical Assessment of Radiotherapy-Induced Vaginal Toxicity with Multiparametric Ultrasound Imaging

Tamer Abdelrehim¹, Andrea Arfe², Kaled Alektiar³, and Mark Burgess¹

¹Medical Physics, ²Biostatistics, and ³Radiation Oncology

Motivation: Radiation-induced vaginal toxicity is a common side effect of pelvic radiotherapy, and no clinical tools exist for objective, quantitative evaluation of vaginal health. The goal of this research project is to develop a system and methodology for multiparametric ultrasound (mpUS)-based assessment of vaginal tissue.

Methods: The acquisition and processing software for mpUS imaging was developed using the Verasonics Vantage NXT research ultrasound system (Kirkland, WA, USA) connected to an endocavitary ultrasound probe. Shear-wave elastography (SWE), quantitative ultrasound (QUS), and ultrasensitive microvessel imaging (UMI) were implemented using a multi-purpose tissue phantom, Doppler flow phantom, and shear-wave liver fibrosis phantom. The software was streamlined to acquire all mpUS modes simultaneously and compiled for ease of use using a graphical user interface (GUI).

Preliminary Results: Development of acquisition and processing pipeline for mpUS

A custom mpUS imaging platform was developed using the open programming architecture of the research ultrasound system. For phantom validation and elasticity calibration for SWE, an endocavitary array transducer operating at 7 MHz was used in combination with a CIRS Elasticity Quality Assurance (QA) Phantom (Norfolk, VA, USA), which includes discrete lesions and background of known stiffness (8–80 kPa). The system setup is designed to support the acquisition of radiofrequency (RF) data, shear-wave generation, and tracking pulses for quantitative elasticity measurements (Figures 1 and 2).

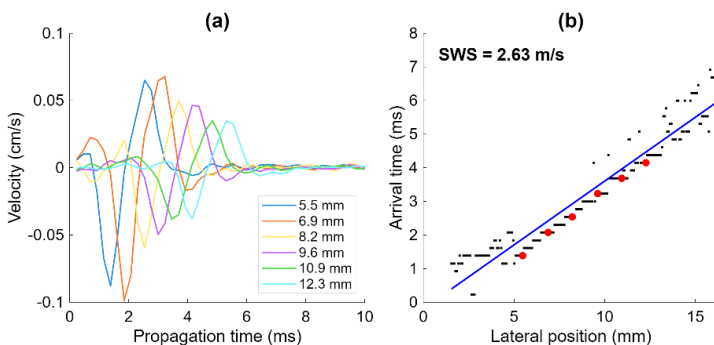


Fig. 1: Measuring the shear-wave speed (SWS) along the tracking of waves in the quality assurance phantom background. a) The shear wave velocity along the propagation time for six selected lateral positions (ranging from 5.5 to 12.3 mm), illustrating the shear wave's temporal evolution. b) Shear wave arrival time (based on displacement and velocity peaks) plotted across lateral positions. The calculated SWS is 2.63 m/s.

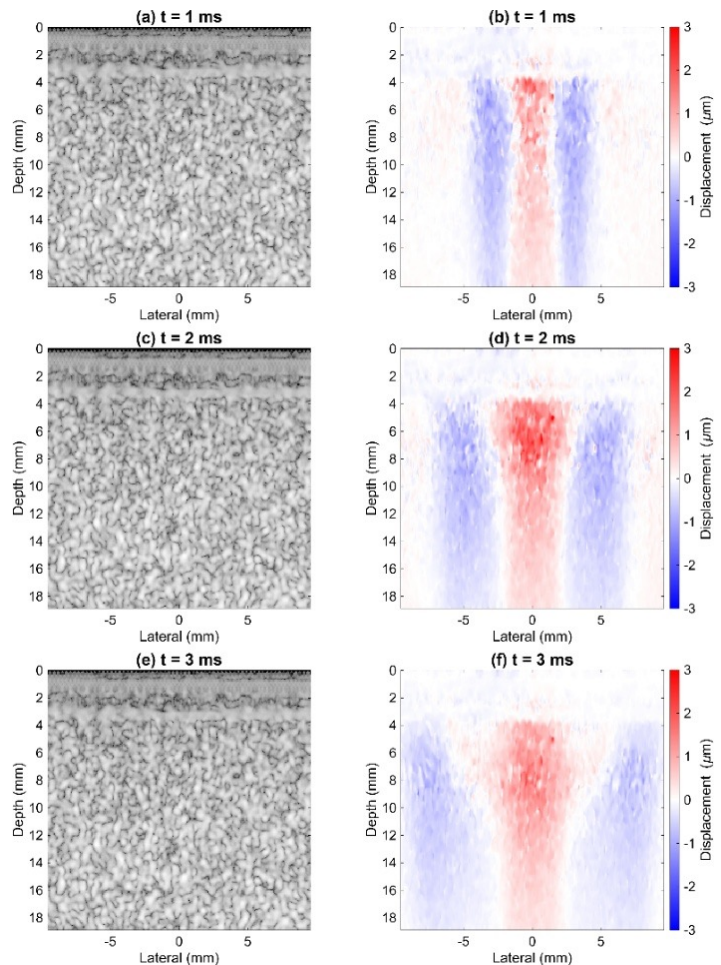


Fig. 2: Shear-wave propagation through the quality assurance phantom at a depth of 5 mm within the phantom background. a, c, and e show the B-mode frames at 1, 2, and 3 ms, respectively, and the corresponding displacement maps are shown in b, d, and f.

Scientific Significance: The combination of different ultrasound modes enables a quantitative assessment of vaginal tissue.

Future Goals and Potential Clinical Impact: A clinical study will be performed with 10 endometrial cancer patients to test the feasibility of mpUS imaging to characterize vaginal tissue response to intravaginal brachytherapy. We believe this study will lead to the development of biomarkers that clinicians can use to prevent and treat radiation therapy-induced vaginal toxicity.

Acknowledgments: This work was supported by the NIH (R21-CA290252), and in part by the MSK Cancer Center Support Grant (P30 CA008748)

Fast Motion-Tolerant Pediatric MRI without Anesthesia using Radial K-space and Deep Learning Reconstruction

Victor Murray¹, Gerald Behr², and Ricardo Otazo¹

¹MRI Physics and ²Radiology

Motivation: MRI would be the ideal imaging modality to evaluate cancer in children if sensitivity to both internal organ motion (e.g., due to breathing) and patient motion could be minimized and thus anesthesia could be avoided.

Methods: The human body is a dynamic entity; however, current pediatric MRI technology has been developed to avoid motion using anesthesia or to reject data acquired with motion, which reduces performance and efficiency. An alternative approach is to exploit the motion information and obtain a short video in a similar manner to taking a live photo with a modern cellphone. The correlations between motion frames can be exploited to reduce k-space sampling requirements for each frame and thus maintain, or even reduce, the scan time compared with conventional static imaging. We recently developed a deep learning-based motion-resolved MRI technique that combines two networks to auto-navigate directly from the acquired k-space data (RANGR) and to reconstruct a short video (Movienet) without increasing scan time, as shown in Fig. 1.

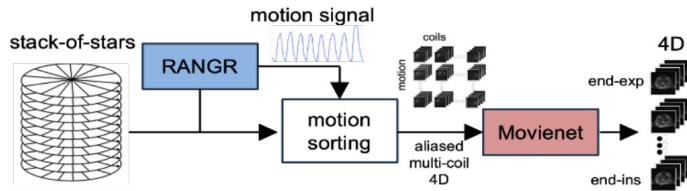


Fig. 1: Accelerated motion-resolved pediatric MRI using radial k-space (stack-of-stars) and deep learning auto-navigation and reconstruction. The RANGR auto-navigation network extracts a respiratory motion signal directly from the acquired data and Movienet reconstruction network computes a motion-resolved four-dimensional MRI from undersampled k-space data. RANGR + Movienet represents a new paradigm that captures motion instead of the conventional approach of rejecting data with motion.

Results: Deep learning-based auto-navigation and reconstruction enables fast pediatric imaging without anesthesia with improved image quality

RANGR + Movienet offers marked image quality improvements in patients scanned with and without anesthesia (Fig. 2) leading to improved lesion detectability and diagnostic efficacy. Cases with anesthesia are still sensitive to breathing motion that was properly compensated for using RANGR + Movienet. The main advantage of using deep learning is to learn directly from the data, resulting in more realistic motion models and more robust auto-navigation. RANGR + Movienet was also able to detect large displacements due to bulk patient motion, offering compensation for both patient and respiratory motion in cases without anesthesia (Fig. 3).

Scientific Significance: The combination of radial k-space and deep learning reconstruction offers an alternative approach to manage both patient and respiratory motion by imaging motion rather than rejecting motion without scan time penalties.

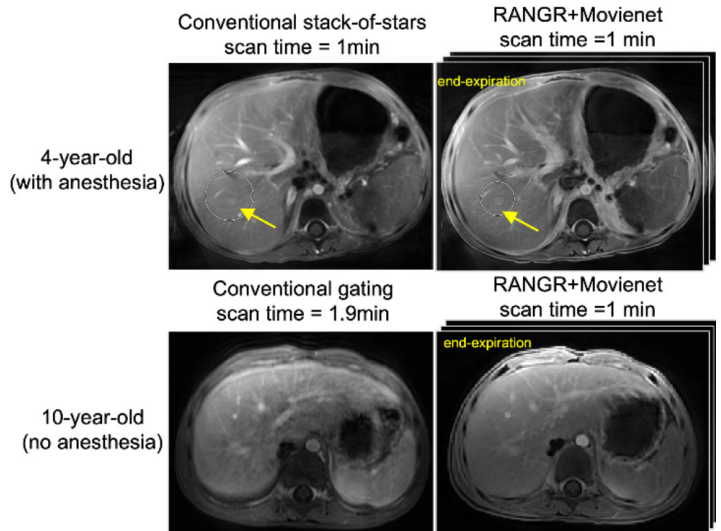


Fig. 2: (Top) RANGR + Movienet improved liver lesion (arrow) detectability compared with conventional stack-of-stars with the same scan time on a 4-year-old patient previously treated for neuroblastoma. (Bottom) The improved motion-robustness of RANGR + Movienet resulted in marked image quality improvement and 2-fold scan time reduction compared with conventional MRI on a 10-year-old patient scanned without anesthesia.

Potential Clinical Impact: The improved motion compensation offered by the combination of RANGR and Movienet can reduce, and in some cases, remove anesthesia, which will improve safety and efficiency and reduce costs.

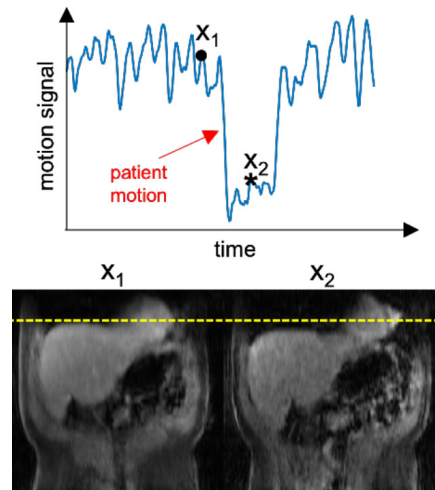


Fig. 3: Motion signal (top) and reconstruction of 2 motion states x_1 and x_2 (bottom) for a pediatric case (8-year-old, no anesthesia) with patient motion and respiratory motion. RANGR + Movienet was able to resolve the large displacement due to patient motion.

Acknowledgments: NIH grant R01-CA255661. This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Quantitative Chemical Exchange Saturation Transfer MR Fingerprinting (CEST-MRF) for Improved Characterization of Brain Metastases

Ouri Cohen¹, Robert J. Young², and Ricardo Otazo¹

¹MRI Physics and ²Radiology

Motivation: Chemical exchange saturation transfer MR fingerprinting (CEST-MRF) is a MR imaging method that provides quantitative molecular tissue parameters, including pH-correlated amide exchange rate and volume fraction that can potentially improve cancer characterization.

Methods: In CEST-MRF the exchange of saturation between protons on proteins and metabolites and the surrounding bulk water is used for high-resolution mapping of biophysical tissue parameters in a short scan time. The CEST-MRF pulse sequence consists of a variable excitation with dynamic scan parameters, which induce variations in the measured signal that depend on the underlying tissue parameters. Deep learning optimization¹ was used to select the dynamic scan parameters to reduce the scan time and improve tissue map accuracy. A physics-trained neural network was used to map the measured signals to the underlying tissue parameters, as shown in Fig. 1. The utility of the method was tested in subjects with brain metastases in comparison to standard-of-care protocols on clinical 3T MRI scanners².

Scientific Significance: The CEST-MRF pulse sequence enables fast and quantitative mapping of molecular tissue parameters in clinically relevant scan times.

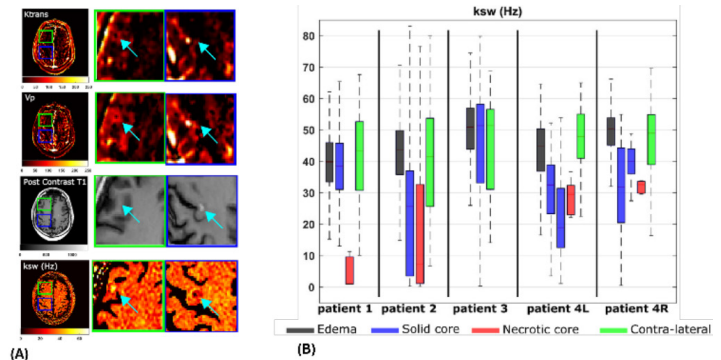


Fig. 2: (A) Standard-of-care perfusion maps: Ktrans (row 1), volume perfusion parameter (Vp, row 2) and post-contrast T1 (row 3) images for a subject with metastatic renal cell carcinoma. The ksw map is shown in row 4. Clear differences in the ksw values are notable for the two lesions shown. (B) The ksw values for segmented regions of metastases arising from different primary tumors. Primary tumors were as follows. Patients 1,3: non-small cell lung cancer adenocarcinoma, patients 2,4: melanoma. Two lesions are shown for patient 4.

Potential Clinical Impact: The quantitative CEST-MRF maps can provide improved characterization of brain metastases and may distinguish tumor progression from treatment-related effects.

Acknowledgments:

This work was funded by an NIH grant (R37-CA262662). This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

References:

1. Cohen, O. & Otazo, R. Global Deep Learning Optimization of CEST MR Fingerprinting (CEST-MRF) Acquisition Schedule. *NMR in Biomedicine* **36**, e4954 (2023).
2. Cohen, O. et al. CEST MR fingerprinting (CEST-MRF) for brain tumor quantification using EPI readout and deep learning reconstruction. *Magnetic Resonance in Medicine* **89**, 233–249 (2023).

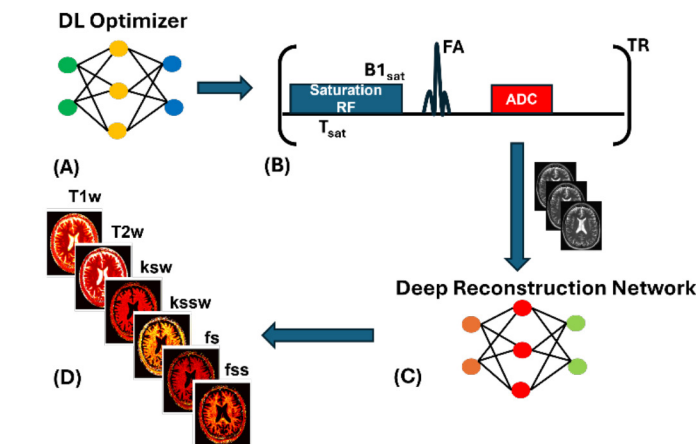


Fig. 1: Overview of the chemical exchange saturation transfer MR fingerprinting (CEST-MRF) method. (A) Deep learning optimization is used to generate the dynamic scan parameters of the CEST-MRF pulse sequence shown in (B). (C) The dynamic images measured are processed by a physics-trained deep reconstruction network to obtain the underlying tissue parameters. (D) The tissue parameters include the water T1 and T2 relaxation (T1w, T2w), amide pool exchange rate and volume fraction (ksw, fs) and semi-solid pool exchange rate and volume fraction (kssw, fss).

Results: In a subject with metastatic renal cell carcinoma, the highlighted previously treated lesions were either invisible (e.g., post-contrast T1) or showed similar contrast on the standard-of-care scans, as shown in Fig. 2A. By contrast, the differential values were visible on the amide exchange rate maps (Fig. 2A). Importantly, the CEST-MRF maps also showed differences between parameter values of metastases arising from different primary tumors in a set of four patients, as shown in Fig. 2B.

Generative AI Reconstruction for Fast and Motion-Compensated Abdominal MRI with 20-second Scan Time

Melanie Schellenberg¹, Richard Do², Oguz Akin², and Ricardo Otazo^{1,2}

¹Department of Medical Physics, and ²Radiology

Motivation: To simultaneously accelerate acquisition and perform volumetric motion correction using generative AI reconstruction without explicit motion navigation for 20-second free-breathing abdominal MRI.

Methods: Using the latest advances in generative AI models, a generative diffusion bridge neural network called “MRI-bridge” was developed to transform the distribution of images corrupted by acceleration and motion to the distribution of high-quality images (1). The diffusion bridge reconstruction learns to reverse the forward diffusion process using a neural network trained with multiple datasets, as shown in Fig. 1. The forward diffusion process gradually mixes a high-quality image x_0 with the corrupted image x_T , and adds Gaussian noise. During *training*, a U-Net model ϵ_θ learns to reverse each step at time t by estimating the score function $\nabla_{x_t} \log p(x_t | x_T) \approx$

$$-\frac{1}{\sigma_t} \epsilon_\theta(x_t, x_T, t).$$

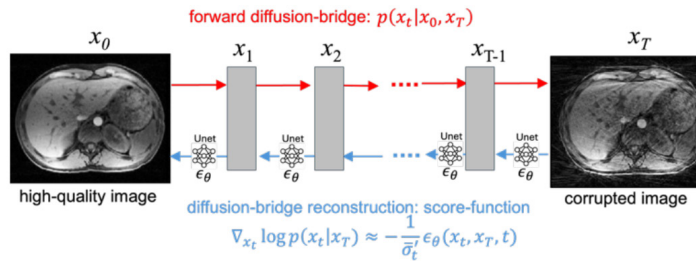


Fig. 1: Generative MRI-bridge technique. The forward process transforms a high-quality image x_0 into a corrupted image x_T (acceleration and motion), using a forward transition probability with a mean value given by a linear combination of x_0 and x_T and a standard deviation that increases with t . The reconstruction process learns to reverse the diffusion process by approximating the score function with a neural network ϵ_θ .

MRI-bridge was implemented to accelerate the T1-weighted stack-of-stars sequence, which is a clinical standard in abdominal MRI. For training, a ~3-min acquisition with 900 spokes was performed on 32 patients with abdominal tumors using different 3T scanners (GE Healthcare). A high-quality image x_0 was obtained using the end-expiration state of XD-GRASP reconstruction. The accelerated image x_T was given by the first 100 spokes, which presents a scan time of ~20 s. After training, MRI-bridge was applied to cases with prospective acceleration. Two new features of generative reconstruction were also evaluated:

- Uncertainty analysis: standard deviation across multiple reconstruction inferences
- SNR enhancement: average across multiple reconstruction inferences

Results: 20 s MRI-bridge scan outperforms clinical 3 min motion-navigated MRI acquisitions.

Given that the standard deviation across multiple reconstruction inferences is low, SNR and image quality in general can be improved by averaging multiple reconstruction inferences, as shown in Fig. 2. This operation

does not increase scan time, and multiple inferences can be parallelized using a GPU.

MRI-bridge with a scan time of only ~20 s presented improved

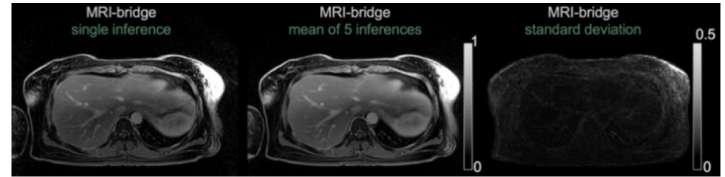


Fig. 2: MRI-bridge using a single inference and averaging 5 inferences, and standard deviation across the 5 inferences.

image quality compared with clinical stack-of-stars and motion-resolved XD-GRASP with significantly longer scan times of ~3 mins (Fig. 3).

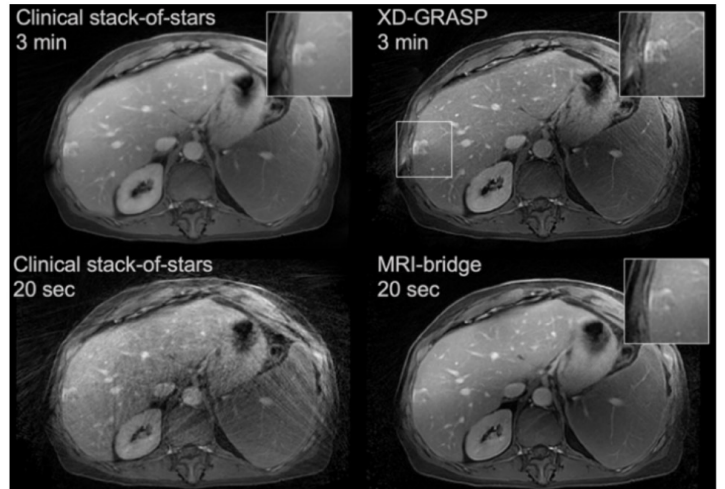


Fig. 3: Free-breathing T1-weighted MRI of a patient with a liver tumor (box) using clinical stack of stars, XD-GRASP and MRI-bridge.

Scientific Significance: Generative diffusion bridge models present a paradigm shift for image reconstruction, where mapping is performed between image distributions rather than the actual images. Multiple inferences can be used to improve SNR and quantify uncertainty.

Potential Clinical Impact: MRI-bridge can enable the quality of motion-navigated imaging with the scan time of breath-holds, without the use of navigators.

Acknowledgments: This project was supported in part by two NIH grants (R01CA255661 and R01CA244532).

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Predictive Informatics



Joseph Deasy



Amita Dave



Harini Veeraraghavan



Aditya Apte



Jung Hun Oh



Rena Elkin



Maria Thor



Jue Jiang



Corey Weistuch



Saad Nadeem



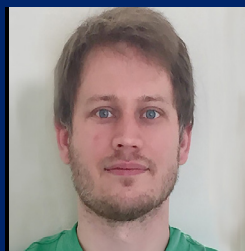
Eve LoCastro



Aditi Iyer



Stephen Petrides



James Matthews Jr



Joseph Marino

Predictive Informatics

The service is led by Joseph O. Deasy, Service Chief, and Amita Dave, Deputy Service Chief, and comprises the following individuals: Harini Veeraraghavan, Jung Hun Oh, Aditya Apte, Saad Nadeem, Maria Thor, Corey Weistuch, Rena Elkin, Ramesh Paudyal, Eve LoCastro, and Aditi Iyer.

The Service for Predictive Informatics develops mathematical models, computational informatics tools, and AI methods to improve the precision of cancer diagnosis and treatment. Research domains, further discussed in this report, include:

Mechanistic Tumor Response Modeling: Cell-population-based models simulate dynamic tumor response to radiotherapy by partitioning cells among metabolically defined compartments and modeling reoxygenation and repopulation as emergent properties of resource-limited microenvironments. Integration of multimodality quantitative imaging, including diffusion-weighted MRI, fluorodeoxyglucose positron emission tomography (FDG PET), and fluoromisonidazole PET (FMISO PET), has enabled patient-specific radiobiological "digital twins" that improve prediction of locoregional recurrence compared with imaging data alone.

AI-Based Image Segmentation and Infrastructure: Deep learning models for automated tumor and normal-tissue segmentation have been deployed clinically in the treatment planning of more than 25,000 patients. Self-supervised pretraining on large, heterogeneous CT datasets enhances generalization to out-of-distribution acquisitions. The pyCERR platform, deployed on the Cancer Genomics Cloud, provides a reproducible infrastructure for cloud-based AI workflow development and multi-institutional validation.

Computational Pathology: The Deep learning-Inferred ImmunoFluorescence (DeepLIIF) platform generates virtual multiplex immunofluorescence from standard hematoxylin and eosin (H&E) and immunohistochemistry (IHC) slides, supporting objective, reproducible cellular phenotyping across more than 20 stain types.

High-Dimensional Data Integration and Predictive Modeling: NetFlow constructs data-driven sample networks from multi-omics data using optimal mass transport and topological data analysis, identifying a lower-risk glioblastoma subtype with significantly improved overall survival in The Cancer Genome Atlas (TCGA) data. BioDeepGWAS, a biologically interpretable deep learning architecture constrained by single-nucleotide polymorphism (SNP)-gene-pathway relationships, can be used to build patient-specific risk models.



**SEEING FARTHER
WITH NEW TOOLS FOR
CANCER RESEARCH**

Supported in part by NIH grants P30 CA008748, R01CA285801, R01CA238392, R01CA258821, U54CA274291, R37CA295658; the Simons Foundation; and the Breast Cancer Research Foundation.

AI Applications for Medical Image Analysis using pyCERR and Cancer Genomics Cloud

Aditya P. Apte¹, Eve LoCastro¹, Aditi Iyer¹, Sharif Elguindi¹, Jue Jiang¹, Jung Hun Oh¹, Harini Veeraraghavan¹, Amita Shukla-Dave¹, and Joseph O. Deasy¹

¹Predictive Informatics

Motivation: To develop a framework for end-to-end analysis of radiological images by pre-configuring software and hardware requirements of AI models. Such a framework facilitates reproducible research and expeditious validation of analyses/AI models on multi-institutional datasets.

Methods: This work introduces a software framework for conducting AI analyses of medical images on Cancer Genomics Cloud (CGC) (Velsera Seven Bridges, Cambridge, MA, USA). The framework allows users to deploy persistent and reproducible AI-based analysis workflows with customized software and hardware dependencies. The primary components of our software framework include the Python-native Computational Environment for Radiological Research (pyCERR) platform for radiological image processing, and CGC for accessing hardware resources and user management. The CGC connects to Genomics Data Commons (GDC), Proteomics Data Commons (PDC), Integrated Cancer Data Commons (ICDC), and Cancer Data Service (CDS) to provide access to curated datasets. The CGC also provides an application programming interface (API) for data transfer to the cloud and to run analyses. GNU General Public License (GNU-GPL) copyrighted pyCERR was ported to Python from MATLAB-based CERR to enable researchers to organize, access, and transform metadata from high-dimensional, multi-modal datasets. This allows researchers to build cloud-compatible workflows for AI modeling in radiation therapy and medical image analysis. An extensible data structure is provided by pyCERR, to accommodate metadata from commonly used medical imaging file formats, and a viewer to allow for multi-modal visualization, as shown in Fig 1. Analysis modules are provided to facilitate AI-based workflows for image segmentation, radiomics, dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) analysis, radiotherapy dose-volume histogram-based features, and normal tissue complication and tumor control models for radiotherapy. Image processing utilities are

provided to help train and perform inference with convolutional neural network-based models for image segmentation, registration and transformation. Radiological image analyses are deployed as applications on CGC with pre-configured software and hardware resources, as shown in Fig 2. These applications can be readily run as tasks via the Representational State Transfer API with support for various programming languages.

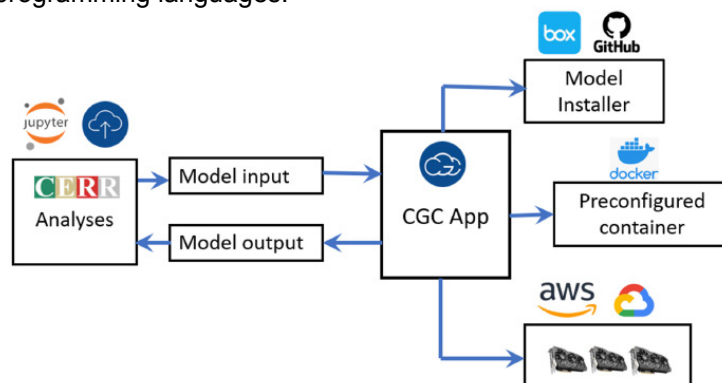


Fig. 2: Components of cloud-based analyses for medical images. CERR: Computational Environment for Radiological Research CGC: Cancer Genomics Cloud (Velsera Seven Bridges, Cambridge, MA, USA).

Results: Open source pyCERR and CGC projects' AI workflows are organized as a sharable project on the CGC platform. Pretrained AI models are provided for segmentation of normal tissues across multiple sites. These can be accessed via the CGC API or via an interactive Jupyter Notebook. The pyCERR package is distributed under an open-source, GNU-GPL at <https://github.com/cerr/pyCERR>.



Scientific Significance: Complete analysis workflows can be readily run on CGC and invoked from local codebases thus simplifying their use.

Potential Clinical Impact: This framework allows for validation and translation of AI models into clinical workflows. For example, image segmentation models clinically deployed at MSK and made available on this platform facilitate their validation and potential use by other groups.

Acknowledgments: This study was supported in part by the MSK Cancer Center Support grant (NIH grant P30 CA008748), The Simons Foundation, the Breast Cancer Research Foundation (grant MATH-23-001), and the NIH ROBIN cooperative group (grant U54CA274291). We also acknowledge in-kind support for cloud computation from Seven Bridges Cancer Research Data Commons Cloud.

References: Apte A, LoCastro E, Iyer A, Elguindi S, Jiang J, Oh JH, Veeraraghavan H, Shukla-Dave A, Deasy JO. Artificial Intelligence Apps for Medical Image Analysis using pyCERR and Cancer Genomics Cloud. *BioRxiv*, 2025. <https://doi.org/10.1101/2025.01.19.633756>.

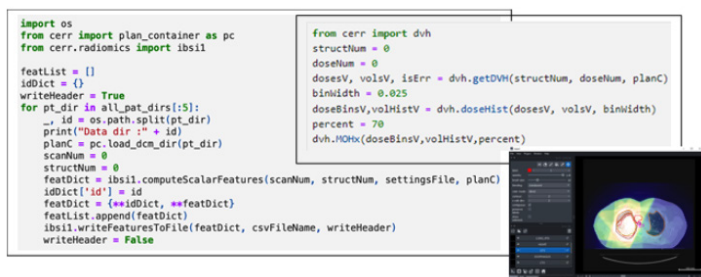


Fig. 1: CT, magnetic resonance (MR), and positron emission tomography (PET) images, along with radiotherapy plans (consisting of dose distributions and segmentation), are visualized in the Napari viewer and Jupyter Notebook. Snapshots and animations can be batch-captured for a cohort of data.

DeepLIIF: An Online Platform for Virtual Multiplex Restaining and Quantification of Clinical Pathology Slides

Joseph Marino¹ and Saad Nadeem¹

¹Predictive Informatics

Motivation: There is a need to develop robust immunohistochemistry (IHC) and hematoxylin and eosin (H&E) quantification algorithms for clinic and translational research.

Methods: Traditional histological H&E and single-plex IHC staining has been adopted in clinics worldwide for cancer diagnosis, prognosis, and treatment recommendation. However, there is significant inter- and intra-observer variability among the pathologists in manually interpreting H&E- and IHC-stained images (e.g., disagreement among pathologists regarding immune cell annotations can be as high as 60%-80%). Recent advances in AI have the potential to remove this observer variability and provide accurate/reproducible interpretation of clinical H&E and IHC pathology slides. However, due to the inherent subjectivity of the visual assessment, single-pathologist annotations, to train state-of-the-art AI algorithms, are highly discordant, leading to not only labeling noise but also disagreement over what should be used as the “ground truth” for AI training and performance evaluation; consensus annotations from multiple pathologists, though more reliable, are time- and cost-prohibitive. Thus, there is an urgent unmet clinical need to develop accurate, reproducible cellular phenotyping AI models with objective “ground truths” that can drive direct clinical interpretation as well as various downstream analyses (e.g., clinical outcome prediction). In this project, we will further develop and refine our clinically-deployed virtual staining Deep Learning Inferred Immunofluorescence (DeepLIIF) platform to support objective, accurate, and reproducible cellular phenotyping on H&E and IHC images for biological exploration and clinical/translational research. DeepLIIF uses restained and coregistered H&E/IHC and multiplex immunofluorescence (mplIF)-stained images for the same tissue section to enable precise/ground truth cellular annotations; mplIF staining allows for examination of panels of several markers individually or simultaneously as a composite (for the same tissue slide) while permitting stain standardization, objective scoring, and cut-offs for all the markers.

We have developed an IHC quantification algorithm that currently supports more than 20 stains across surgical pathology, hematopathology, and cytology. DeepLIIF has been deployed in the clinic with EPIC integration and has an anticipated workload of more than 100,000 whole-slide images per year at MSK alone.

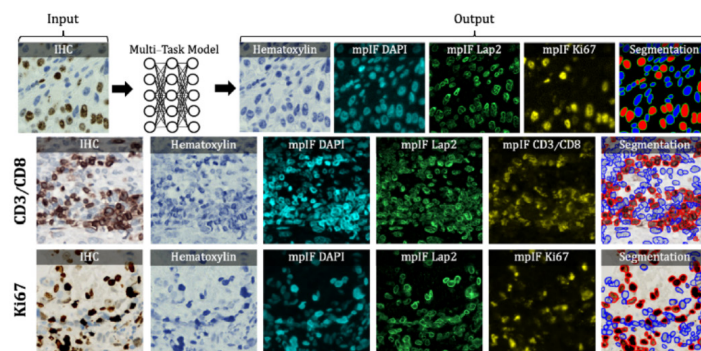


Fig. 2: Deep Learning Inferred immunofluorescence (DeepLIIF) pipeline for generating virtual multiplex immunofluorescence (mplIF) stains from standard clinical pathology slides. DAPI: 4',6-diamidino-2-phenylindole IHC: immunohistochemistry

Scientific Significance: This work could transform diagnostic pathology and unlock new frontiers in companion diagnostics.

Potential Clinical Impact: This work can allow for robust biomarker quantification at scale for clinical and translational research.

Acknowledgments:

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- Department of Pathology and Laboratory Medicine
- Technology Development Fund
- Amazon Web Services

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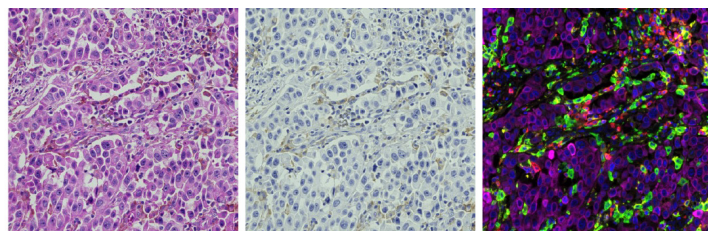


Fig. 1: Corresponding (from left to right) hematoxylin and eosin, immunohistochemistry, and multiplex immunofluorescence for the same tissue section.

Evaluating Deep Learning-based Reconstruction for Diffusion-Weighted MR Imaging: Initial Experience in Head and Neck Region

Ramesh Paudyal¹, Akash Shah², Jaemin Shin⁵, Suchandrima Banerjee⁵, Ashok Shaha³, Richard J Wong³, Lawrence H Schwartz², Nancy Lee⁴, Vaios Hatzoglou², and Amita Shukla-Dave¹
¹Predictive Informatics, ²Radiology, ³Surgery, ⁴Radiation Oncology, and ⁵General Electric HealthCare

Motivation: To evaluate the impact of deep learning reconstruction (DLR) on image quality and quantitative accuracy in diffusion-weighted (DW) MRI-derived apparent diffusion coefficient (ADC) metrics by varying acquisition settings, including the number of excitation (NEX).

Methods: DW MRI-derived ADC is calculated by a monoexponential model of the image signal decay with at least two different b-values. ADC is a surrogate marker for tumor cellularity. However, the use of high b-values can lead to a lower signal-to-noise ratio (SNR), resulting in increased image noise and potentially less reliable ADC measurements.

ADC measurement accuracy in head and neck (HN) imaging is often achieved by involuntary motion affecting the DW signal; thus, deep learning reconstruction (DLR) has emerged as a promising technique to reduce motion artifacts, improve image quality, and automate lesion analysis, thereby enhancing diagnostic reliability and quantitative measurement of biomarkers. Integrating DL into MRI workflows can enable the production of high-quality images, as shown in Fig. 1. It also enables shorter scan times and improves diagnostic accuracy in HN imaging

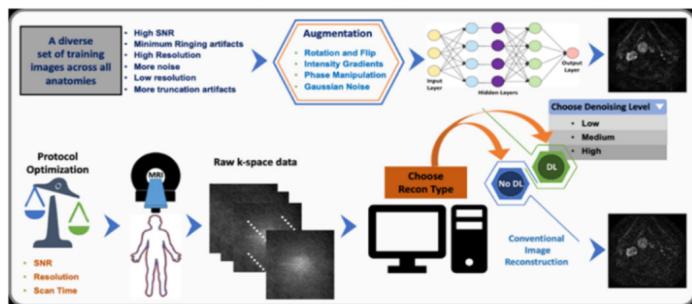


Fig. 1: Workflow diagram demonstrating the seamless integration of deep learning (DL) techniques into the MRI image reconstruction pipeline.

protocols. Recent AI/DL advancements in MR image reconstruction focus on overcoming the traditional trade-offs among resolution, SNR, and scan time. In addition, DL reconstruction for DW-MRI offers high-, medium-, and low-level settings to adjust denoising, allowing the user to balance between noise reduction and image sharpness across the b-values.

Results: The results of our recent study demonstrated that DLR reconstruction significantly improved image sharpness and overall image quality with a minimum NEX while reducing ringing artifacts and shortening scan time, as shown in Fig. 2. A high DL (75% denoising level) setting provided the greatest noise suppression, resulting in a 45% increase in SNR compared with images reconstructed without DL. ADC values calculated with and without DL showed a mean difference of up to 3.92%.

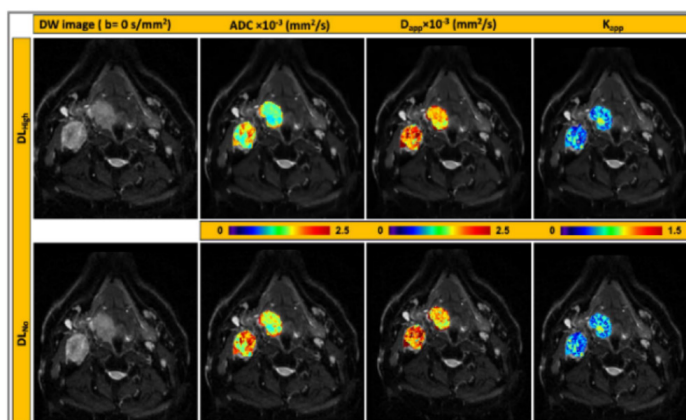


Fig. 2: Representative diffusion-weighted (DW) images from a patient with primary and neck nodal metastasis. Images reconstructed with deep learning reconstruction (DLHigh) and without (DLNo) for select b-values ($b = 0$ and $b = 2000$). Apparent diffusion coefficient (ADC), true diffusion coefficient (D_{app}) and kurtosis coefficient (K_{app}) maps overlaid on $b = 0$ images. High denotes a 75% level of denoising in the image.

Scientific Significance: Integrating DL into MRI workflows offers the potential to produce high-quality images with shorter scan times and improved diagnostic accuracy. DL-based MR image reconstruction eliminates traditional trade-offs among spatial resolution, SNR, and scan efficiency, enabling faster, more precise imaging that can enhance clinical decision-making and patient outcomes.

Potential Clinical Impact: Deep learning-based MRI reconstruction can significantly reduce scan times while enhancing image quality and diagnostic accuracy. This advancement supports faster, more efficient imaging workflows and improves patient care through earlier and more precise diagnoses.

Acknowledgments:

The study is supported by a GEHC grant (2025-2026) and in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Hypoxia-Directed Treatment of Human Papillomavirus-Related Oropharyngeal Carcinoma

Nancy Y Lee¹, Heiko Schöder², Milan Grkovski³, Ramesh Paudyal³, Jung Hun Oh³, Vaios Hatzoglou², Bill H Diplas¹, James Han¹, Can Wu³, Amita Shukla-Dave^{2,3}, John L Humm³, and Nadeem Riaz¹
¹Radiation Oncology, ²Radiology and ³Department of Medical Physics

Motivation: A collaborative research focus of Medical Physics, Radiation Oncology, and Radiology is identifying imaging biomarkers that classify tumors by radio-resistance or sensitivity. This collaboration establishes a hypoxia-specific positron emission tomography (PET) (¹⁸F-fluoromisonidazole [¹⁸F-FMISO]) imaging biomarker for patients with human papillomavirus-positive oropharyngeal carcinoma (HPV+ OPC) (Fig. 1)¹. Patients are administered an ¹⁸F-FMISO radiotracer, followed by a PET scan ~150 min post-injection. A positive ¹⁸F-FMISO image indicates persistent tumor hypoxia, a well-known cause of radiation resistance, whereas a negative scan suggests tumor re-oxygenation and radiosensitivity. Patients are stratified to standard-of-care (SOC) 70 Gy or 30 Gy dose de-escalation based on a positive or negative ¹⁸F-FMISO scan. Results have demonstrated equivalent treatment outcomes with a substantial reduction in radiation-related morbidity.

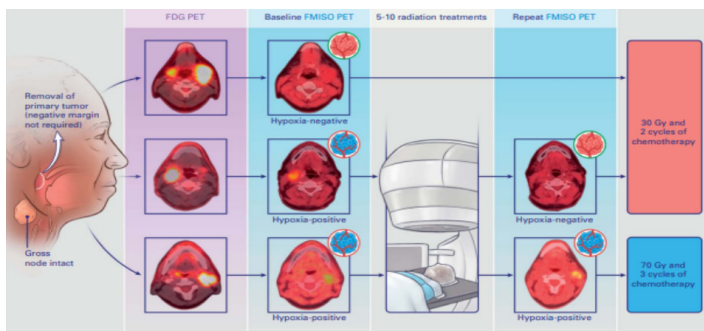


Fig. 1: A phase II clinical trial of personalized radiotherapy for oropharyngeal cancer. Protocol schema illustrating typical positive and negative fluoromisonidazole (FMISO) positron emission tomography (PET) images pre-treatment and at repeated inter-treatment time points, along with which patients received 30 Gy or 70 Gy.

Methods: Patients with HPV+ OPC undergo MRI and are administered an ¹⁸F-FMISO radiotracer in the early-to-mid phase of chemoradiation treatment. When using conventional ¹⁸F-radiotracers, the short 110-minute half-life results in increasing signal loss, resulting in noisy images, which leads to uncertainty in image interpretation. The new total-body PET scanners, Siemens Biograph Vision Quadra (Erlangen, Germany), provide an order-of-magnitude higher sensitivity, allowing imaging for up to an additional three half-lives at a time when the signal-to-background ratio is greater. Tumor hypoxia, caused by imbalanced oxygen supply and demand, drives radiotherapy resistance and poor outcomes. Oxygen-enhanced MRI (OE-MRI) non-invasively monitors hypoxia, supporting personalized adaptive radiotherapy. **Advances in PET and MRI explore mid-treatment imaging biomarkers to track response whereas OE-MRI offers non-radioactive surrogate markers of tumor hypoxia.**

Results: The JCO study (Lee et al.¹) reports 128 patients treated with 30 Gy and 24 with 70 Gy. The two-year locoregional control was 94.7% (95% CI, 89.8–97.7), meeting our primary objective. With a median follow-up time of 38.3 months (range, 22.1–58.4), the two-year progression-free

survival (PFS) and overall survival (OS) rates were 94% and 100%, respectively, for the 30-Gy cohort. The 70-Gy cohort had similar two-year PFS and OS rates, at 96% and 96%, respectively. Acute grade 3–4 adverse events were more common in the 70 Gy versus 30 Gy cohort (58.3% vs. 32%; $P = .02$). Late grade 3–4 adverse events occurred only in the 70 Gy cohort, in which 4.5% experienced late dysphagia.

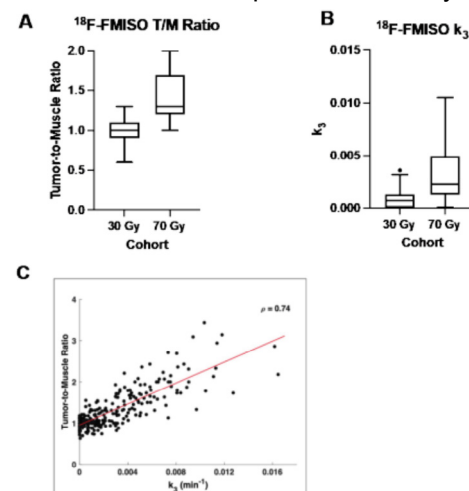


Fig. 2: Quantitative fluoromisonidazole (FMISO) evaluation of patients. Comparison of qualitative-quantitative visual assessment vs. automated computational analysis of FMISO positron emission tomography (PET) scans. a) Boxplot of tumor-to-muscle (T/M) ratio for the 30 Gy vs. 70 Gy cohorts. b) Boxplot of baseline k_3 (computed) for the 30 Gy vs. 70 Gy cohorts, identifying a similar pattern as the manually determined T/M ratio (compared with a). c) Scatterplot of T/M (background) ratio vs. k_3 for all patients, identifying a strong correlation between the T/M ratio and compartmental-analysis-derived k_3 metric.

Scientific Significance: The use of ¹⁸F-FMISO PET imaging mid-chemoradiation enables stratification of HPV+ OPC patients by tumor hypoxia status. This allows for personalized radiation dosing — patients with re-oxygenated tumors receive a reduced dose (30 Gy) with equivalent outcomes and lower treatment-related morbidity. This approach highlights the value of imaging biomarkers in guiding adaptive therapy and improving patient care (Fig.2).

Potential Clinical Impact: This study has shown, for one disease site (HPV+ OPC), the ability to classify patients by tumor radiosensitivity based on tumor hypoxia status using a PET-based biomarker. This technique may have applicability for dose stratification in non-head-and-neck tumors, such as non-small cell lung carcinoma, and offers an opportunity to identify MRI-based surrogate metrics that define tumor radiosensitivity and predict treatment outcomes.

Acknowledgments: This work is supported by Dr. Nancy Lee's grant (2R01CA238392-06). This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Deep Learning Predicts Patient-Specific Risk of Radiation-Induced Erectile Dysfunction in Prostate Cancer Using Genome-Wide Association Studies

Jung Hun Oh¹ and Joseph O. Deasy¹

¹Predictive Informatics

Motivation: Radiation-induced erectile dysfunction (RIED) is a frequent and unpredictable complication of prostate cancer radiotherapy. To improve patient-specific risk prediction, we developed a novel deep learning model that integrates genome-wide genetic variants and clinical data, incorporating known biological components into the analysis.

Methods: The genome-wide association studies (GWAS) cohort (N = 387) was stratified into training, validation, and test sets (0.7:0.1:0.2 ratio) while strictly preserving the RIED rate in each subset. Data preparation involved conducting principal component analysis on the training set's imputed genotype data. We then used univariate logistic regression, adjusting for the first five principal components, to compute association p-values between RIED and individual single nucleotide polymorphisms (SNPs) in the training data. To reduce redundancy and identify crucial genetic input, linkage disequilibrium clumping was performed using PLINK. This procedure yielded a set of lead 810 SNPs that served as the primary input for our deep learning model.

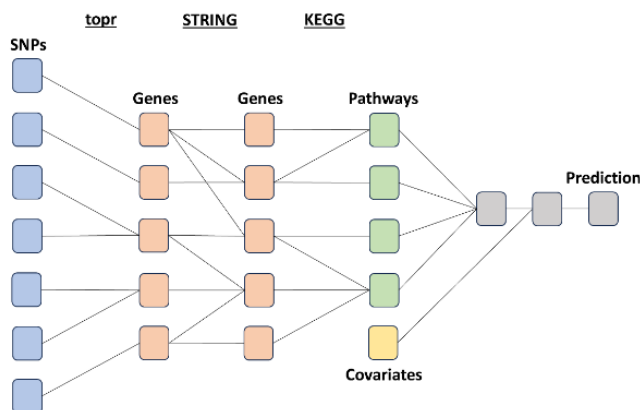


Fig. 1: A simplified schematic of the biologically informed deep learning architecture. Gene-gene interactions are limited to the same pathway. single nucleotide polymorphisms: SNPs

We utilized a novel, biologically interpretable architecture, BioDeepGWAS, shown in Fig. 1. Unlike traditional "black-box" models, biologically informed deep learning structures layers to mimic known biological components (e.g., SNPs, genes, pathways), ensuring a sparse, interpretable network. The BioDeepGWAS architecture comprises five main layers:

1. Input (SNP) Layer: The clumping-identified lead SNPs.
2. Gene Layer: SNPs were annotated to protein-coding genes via the topR package.
3. Gene-Gene Interaction Layer: Interactions among these genes were mapped using the STRING database.
4. Pathway Layer: Genes were connected to 146 non-disease-specific KEGG pathways, plus a pseudo-node for unassigned genes.
5. Output Layer: This layer integrates the pathway signals with key clinical variables for the final RIED risk prediction. This structure creates a model whose connectivity is based entirely on prior biological knowledge, resulting in an interpretable and powerful predictor.

Results: BioDeepGWAS model's predictive power

The final model applied to the test set yielded an area under the curve (AUC) of 0.75. Fig. 2 demonstrates effective risk stratification, highlighting a strong calibration agreement between observed and predicted incidence curves (chi-squared test $p = 0.9531$). Furthermore, the odds ratio of 11.8 ($p = 0.0002$) between the two highest (groups 5 and 6) and the two lowest risk groups (groups 1 and 2) indicates a good level of discrimination.

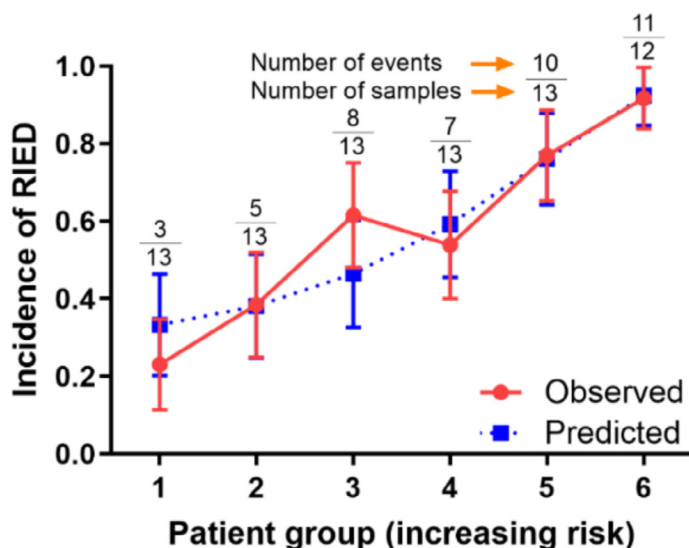


Fig. 2: Comparison of the observed and predicted incidence rates in radiation-induced erectile dysfunction (RIED) risk. The predicted outcomes in the test set were sorted and binned into 6 groups, 1 as the lowest risk group and 6 as the highest risk group.

Scientific Significance: Deep learning can be used for predictive modeling of radiation-induced toxicity in GWAS.

Potential Clinical Impact: The BioDeepGWAS architecture was demonstrated to be an effective deep learning approach to building prediction models for radiation-induced toxicity.

Acknowledgments:

This study was supported in part by the National Cancer Institute (R01CA285801), MSK Cancer Center Support grant (P30CA008748), and Breast Cancer Research Foundation (BCRF-17-193).

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NetFlow: A Framework for Exploring High-Dimensional Biomedical Data

Rena Elkin¹, Jung Hun Oh¹, Anish K. Simhal¹, and Joseph O. Deasy¹

¹Predictive Informatics

Motivation: NetFlow is a comprehensive software tool designed for constructing and intuitively visualizing the organizational structure of observations from high-dimensional data sets. Its purpose is to generate observations and hypotheses regarding patient cancer biology and response to treatment. NetFlow was developed to be applicable to analyzing data sets regardless of the sample size, particularly when the number of samples is much smaller than the number of features.

Methods: Inputs to NetFlow are multi-dimensional bioassays from any modality, and the output is a topology representing the organizational relatedness of the observations. The topology is computed via the novel adaptation of techniques from optimal mass transport, diffusion maps, lineage tracing, and Topological Data Analysis. More specifically, the first step in the NetFlow pipeline is to compute distances between samples based on their feature profiles for a specified metric. The metric influences which characteristics are reflected in the resulting organizational structure and should therefore be chosen accordingly. Next, a kernel function is used to construct the similarity structure from the distances. Kernels inform on geometric structure and help with signal denoising. Normalizing the similarity structure by the sample density yields the diffusion operator. This forms the basis of numerous multi-scale and scale-free techniques, such as diffusion maps. While any distance matrix can serve as input for computing the Pseudo-Organizational StructurE (POSE), we recommend diffusion-based distances for their advantageous geometric and denoising properties. The POSE is constructed in two main steps. First, we infer the branched backbone topology using lineage-tracing-inspired reasoning. Rather than implying a pseudo-temporal ordering, we interpret higher similarity as a greater likelihood of shared characteristics, biomarkers, or subtypes. This yields a pseudo-organizational ordering (or simply, pseudo-ordering) which we computed via the diffusion pseudotime (DPT) algorithm. Second, a purely tree-like backbone enforces a connected and clear ordering but is too restrictive for our setting where the objective is to capture relational structure among samples.

Results: We analyzed triple-negative breast cancer data including tumor-infiltrating lymphocytes, molecular features extracted from histology images, CIBERSORT scores, and gene expression profiles. Figure 1A shows the resulting POSE of NetFlow for each biomarker. Figure 1B shows the Kaplan-Meier curves, indicating the significant survival difference between two groups identified by the POSE.

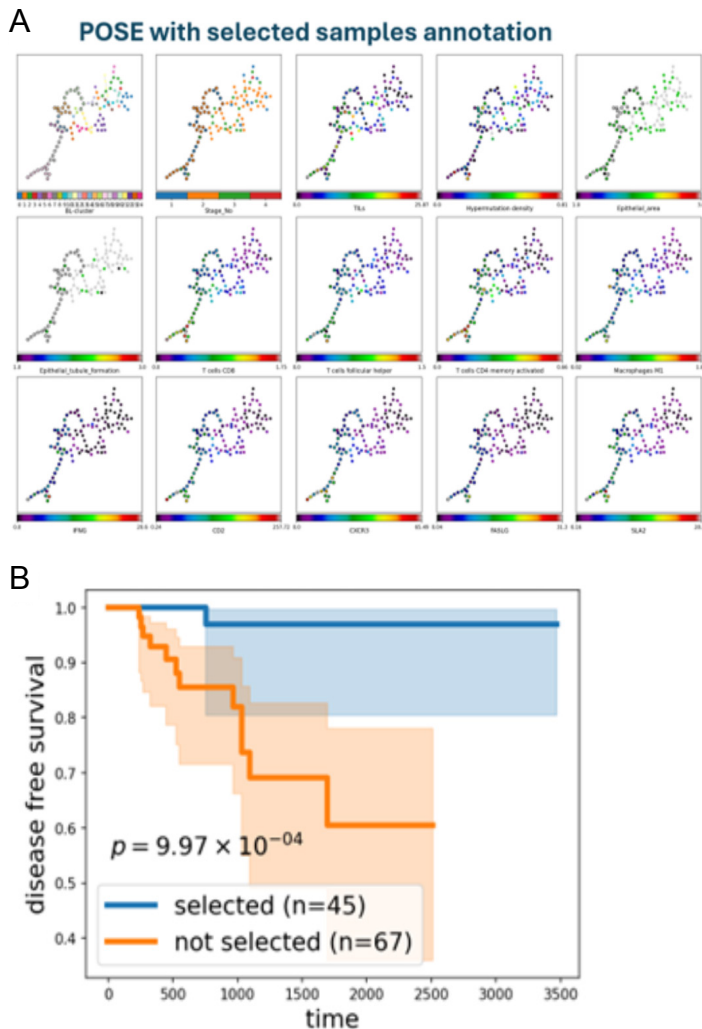


Fig. 1: NetFlow example using all publicly available The Cancer Genome Atlas (TCGA) triple-negative breast cancer (TNBC) cases (N = 112). AI/deep-learning tools were used to extract pathology slide data. Immune-related transcriptomic features were extracted using the CIBERSORT algorithm and combined with other immune-related genes and network-connected genes. (A) The POSE results and (B) The resultant Kaplan-Meier curves for subjects/samples as either selected (dark circles) or not, showing the significant survival difference between the two groups. POSE: Pseudo-Organizational StructurE.

Scientific Significance: This approach applies a mathematical framework, optimal mass transport, to cancer data analysis.

Potential Clinical Impact: NetFlow is applicable to any biomedical data for topological representation, risk stratification, and biomarker discovery.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Elkin R, Oh JH, Simhal AK, Deasy JO. NetFlow: A Framework to Explore Topological Representations of High-Dimensional Biomedical Data. bioRxiv 2025.10.24.683878

Towards Building Generalizable and Trustworthy AI Models for Tumors Segmentation Across Imaging Variations

Aneesh Rangnekar¹, Jue Jiang¹, and Harini Veeraraghavan¹
¹Predictive Informatics

Motivation: Deep learning models exhibit poor generalization when applied on out-of-distribution (OOD) data. The goal of this work is to leverage medical image foundational models to enhance generalizability and combine post hoc interpretability methods to contextualize model performance.

Methods: A medical image foundational model called “self-distilled masked image transformer” (SMIT) was pretrained on 10,412 unlabeled 3D CT imaging datasets sourced from the public The Cancer Imaging Archive and institutional datasets. The model combines a pretrained encoder to extract features with a 3D convolutional UNet decoder for segmentation. It was finetuned to segment lung cancers using a public dataset comprising 377 3D CT images and evaluated on 17,512 cases comprising (a) 352 ID cases from public and institutional cases to assess model generalization under imaging acquisition variations, and (b) 1,400 cases to automatically detect OOD instances to contextualize model predictions using four publicly available datasets consisting of non-lung cancer diseases, including more challenging cases occurring in the lung (COVID-19 and pulmonary embolism) and far-OOD cases occurring outside the lung (kidney cancers and healthy abdominal CTs).

Result (1): Pretrained models enhance generalization to unseen data variations

Impact of pretraining using the numerous, loosely curated dataset comprising various diseases called “wild-pretraining” was compared against self-pretraining, where the model was subject to pretraining using only the lung cancer training dataset, and scratch training, where no pretraining was used. Pretraining utilizes unlabeled datasets and learns useful feature representations using various pretext tasks. Two representative examples, which demonstrate more accurate performance using wild-pretraining compared to other methods are shown in Fig.1.

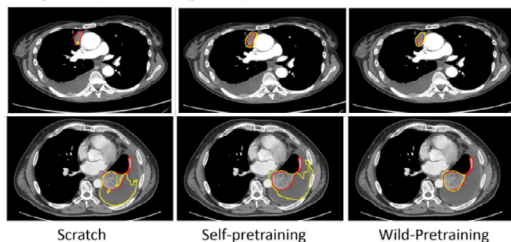


Fig. 1: Lung tumor segmentation on chest CT images under different pretraining strategies. Yellow contours show segmentations and red contours show clinical delineations. Scratch: no pretraining, self-pretraining: pretrained only on lung cancer dataset, and Wild-pretraining: pretrained on large heterogeneous unlabeled CT datasets. Wild-pretraining produced segmentations closer to the delineations.

Next, we analyzed why wild-pretraining enhances generalization by computing feature reuse using centered kernel analysis under various imaging conditions. As shown in Fig. 2, wild-pretrained model resulted in higher feature reuse in the low- and mid-level feature layers, with network specialization occurring close to output layers following fine-tuning for imaging variations.

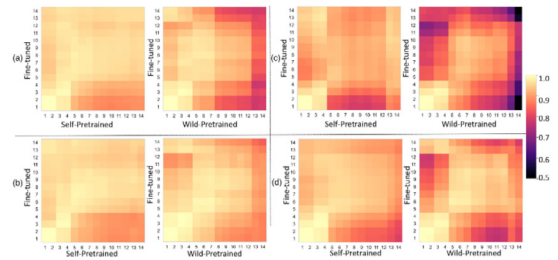


Fig. 2: Centered kernel alignment (CKA) showed higher feature reuse for the wild-pretrained model for low- and mid-level features and task-specific specialization close to output for (a) contrast, (b) non-contrast CT, (c) body and (d) lung reconstruction kernel images. Higher similarity indicates greater feature reuse across layers.

Result (2): Pretrained model combined with random forest can predict OOD

The encoder features of the tumor segmentation model was global average pooled and used within a random forest classifier (RF-Deep) with outlier exposure by providing few representative OOD examples to detect OOD cases. An example of OOD instances detected by RF-Deep and standard pixel-level uncertainty assessment using MaxLogit is shown in Fig. 3, where MaxLogit fails to correctly identify the case with COVID-19 inflammation that is detected by RF-Deep.

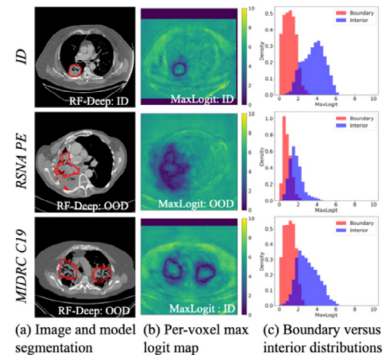


Fig. 3: In-distribution (ID) and out-of-distribution (OOD) detection using RF-Deep (random forest classifier using encoder features) compared with MaxLogit pixel-level uncertainty. The COVID-19 inflammation case is misclassified as ID by MaxLogit but correctly identified as OOD by RF-Deep. RSNA PE: Radiological Society of North America Pulmonary Embolism dataset.

Scientific Significance: Robust and generalizable performance on variety of datasets with contextualized model predictions for safe implementation of AI models.

Potential Clinical Impact: This study shows that safe and trustworthy models can be created for tumor segmentation in image-guided treatments.

Acknowledgments:

• NIH R01CA258821 and NIH/NCI P30 CA008748

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Reducing Masticatory Muscle Doses and Patient-Reported Trismus via Implemented AI Auto-Segmentation-Enabled Dose/Volume Mitigation

Maria Thor¹, Aditi Iyer¹, Aditya Apte¹, Michalis Aristophanous¹, Sharif Elguindi¹, Jean M. Moran¹, Nancy Y. Lee², and Joseph O. Deasy¹

¹Department of Medical Physics and ²Radiation Oncology

Motivation: Mouth-opening inability, trismus, is monitored after radiotherapy (RT) for head-and-neck cancer (HNC), but methods to minimize its risk are scarce. Consequently, post-RT trismus limits patients' daily life. This work implemented mean dose (D_{mean}) guidelines to AI auto-segmented masticatory muscles and studied the impact on radiation-induced trismus.

Methods: The masseters/medial pterygoids D_{mean} guidelines (< 42 Gy / < 68 Gy) were implemented in 2021¹. Included HNC patients had been consecutively treated six months pre/post-implementation (N = 115/110). Patient-reported trismus was defined as $\geq$ moderate $\leq$ one-year post-RT via the Gothenburg Trismus Questionnaire². The mastication-muscle-specific D_{mean} was compared between cohorts (Wilcoxon rank-sum test; significance: two-sided p-value < 0.05; pre-implementation cohort muscles were auto-segmented retrospectively using the clinical AI algorithm). Post-implementation for trismus items with $\geq 15\%$ prevalence, D_{mean} -response relationships were derived for the masseter and the medial pterygoid, utilizing 1000-sample bootstrapping-based logistic regression; discrimination (area under the receiver operating characteristic curve [AUC], and p-values) and calibration (Hosmer-Lemeshow test [pHL] p-values) were assessed as the median value across samples.

Results: Most patients had oropharyngeal tumors (pre/post-implementation: 50% / 56%) and were treated to a median of 60 Gy at 1.8-2.0 Gy. The masseter contralateral (masseter_{contra}) D_{mean} was significantly higher pre- vs. post-implementation (median: 14 Gy vs. 10 Gy; p = 0.01; **Fig. 1**). Post-implementation, the masseter_{contra} and masseter ipsilateral (masseter_{ipsi}) D_{mean} guideline adherence was 96% and 78%, respectively, and was 99% and 93% for the medial pterygoid_{contra} and medial pterygoid_{ipsi}. Trismus was more prevalent when the D_{mean} guideline was not adhered to (masseter; median across items: 33% vs. 9% otherwise).

Significant D_{mean} -response relationships were derived for all 15 / 21 items with $\geq 15\%$ prevalence (eating, jaw, pain, quality-of-life, teeth-tongue: 3, 6, 2, 2, 2 items, respectively), and masseters_{ipsi} provided the stronger relationship (median: AUC = 0.74, pHL = 0.57) vs. the medial pterygoid_{contra}, medial pterygoid_{ipsi}, and masseter_{contra} (median: AUC = 0.67-0.71, pHL = 0.62-0.65; **Fig. 2**).

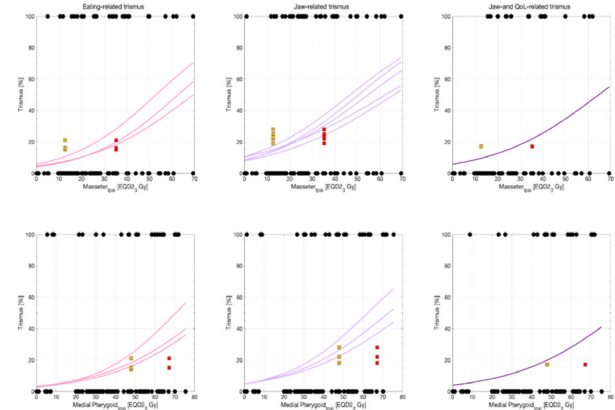


Fig. 2: Post-implementation cohort trismus mean dose (D_{mean})-response relationships for the ipsilateral masticatory muscle representations (ipsilateral masseter, masseter_{ipsi}: upper panel; ipsilateral medial pterygoid (medial pterygoid_{ipsi}): lower panel) for the nine trismus items with $\geq$ moderate symptom degree with an area under the receiver operating characteristic curve ≥ 0.70 (**Left:** eating items; **Middle:** jaw-related items; **Right:** jaw and quality of life (QoL) items). Black dots denote patient-specific observed trismus; red/orange squares indicate the population observed trismus for each item at the D_{mean} guideline (masseter: < 42 Gy / 18 Gy (< 35.3 Gy / 12.7 EQD₂ Gy); medial pterygoid: < 68 Gy / 53 Gy (< 67.2 Gy / 47.9 EQD₂ Gy))

Scientific Significance: Based on clinically AI auto-segmented masticatory muscles and patient-reported trismus for a large cohort (N > 200) treated with radiotherapy (RT) for HNC at a tertiary cancer center, this study has demonstrated that: 1) associated D_{mean} guidelines can be implemented, 2) masticatory muscle doses can thereby be significantly reduced, and 3) when the D_{mean} guidelines are adhered to, trismus is effectively mitigated.

Potential Clinical Impact: This study demonstrates that our implemented AI auto-segmented mastication muscles and associated D_{mean} guidelines are effective in reducing dose to the masticatory system, and the impact of quality-of-life-limiting trismus. Further masticatory dose mitigation is likely possible and should help diminish this burdensome radiation-induced adverse effect.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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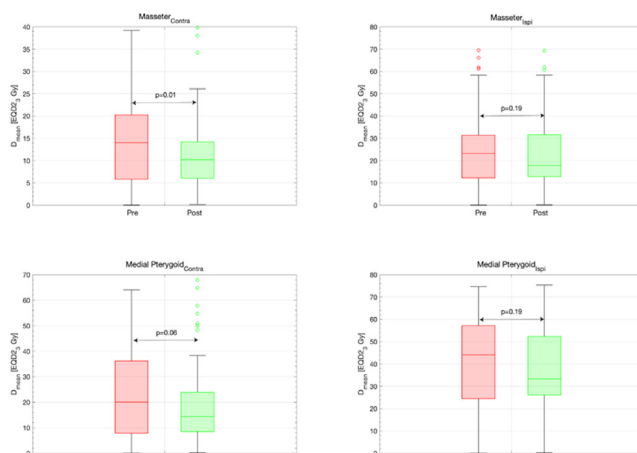


Fig. 1: The four-masticatory muscle-specific mean dose (D_{mean}) comparisons between the pre- (red) and the post-implementation cohorts (green). The population median D_{mean} values for each strata are provided next to each box; the p-value arises from a Wilcoxon rank-sum test.

Bridging mpMRI and Histopathology for Tumor Microenvironment Insights in a Preclinical PDAC Model

Ramesh Paudyal¹, James Russell¹, H. Carl Lekaye¹, Joseph O. Deasy¹, John L. Humm¹, Muhammad Awais¹, Saad Nadeem¹, and Amita Shukla-Dave^{1,2}

¹Department of Medical Physics and ²Radiology

Motivation: To evaluate early changes in multiparametric magnetic resonance imaging (mpMRI)-derived quantitative imaging biomarkers (QIBs) for assessing the tumor microenvironment (TME) in a preclinical pancreatic ductal adenocarcinoma (PDAC) model treated with radiotherapy, and to correlate these QIBs with a histopathology marker, and hematoxylin and eosin (H&E) staining.

Methods: PDAC is characterized by a dense stroma that limits drug delivery and promotes resistance¹. Multiparametric MRI (mpMRI), diffusion-weighted (DW) and dynamic contrast-enhanced (DCE) MRI, evaluates tumor cellularity and vascular permeability². Hoechst 33342 and H&E provide detailed insights into perfusion and tissue morphology. Combining histopathology with mpMRI-derived QIBs improves understanding of therapy-induced changes in the TME³. In this study, subcutaneous PDAC tumors were established in athymic mice (n = 12) using KPC 4662 cells. mpMRI (T2w, DW, DCE) was performed 10-12 days post-inoculation on a 7T system. Apparent diffusion coefficient (ADC) and volume transfer constant (K^{trans}) values were derived from DW and DCE data using monoexponential and extended Tofts models, respectively. Pre- and post-10 Gy treatment QIBs values were compared using the Wilcoxon signed-rank-test. The total tumor cell percentage (%) was quantified from H&E-stained sections using Deep LIIF⁴, and associations with QIBs were evaluated using Spearman correlation.

Results: Representative mpMRI images, derived parametric maps, and corresponding histopathology from a PDAC model shown in Fig. 1. Mean pre- and post-Tx ADC and K^{trans} values differed significantly ($P < 0.01$), with changes of 20.50% and 20.41%, respectively, in the preclinical PDAC model. The median tumor cell percentage was 24% (range: 15%-53%), revealing substantial heterogeneity in tumor cells (Fig. 2). Post-Tx mean ADC and relative changes in v_e ($r\Delta v_e$) showed strong negative Spearman correlations with total

tumor cell percentage ($\rho = -0.77$, $p < 0.014$ for ADC and $\rho = -0.77$, $p = 0.009$ for $r\Delta v_e$), suggesting underlying cellular and stromal composition within the PDAC TME.

Scientific Significance: mpMRI-derived QIBs with DeepLIIF-based quantitative assessment of total tumor cells (%) from H&E, this study establishes a multimodal framework for characterizing the TME in a preclinical PDAC model. This approach provides mechanistic insight into tumor cellular and stromal composition and lays the groundwork for the early assessment of treatment-induced TME changes.

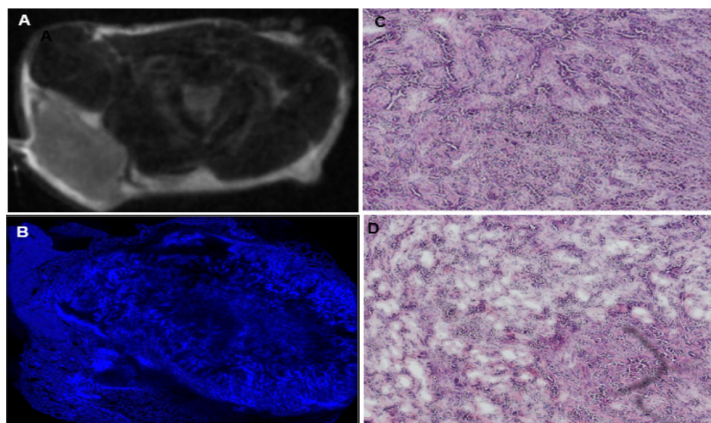


Fig. 2: (A): Representative T2-weighted image and (B): Hoechst 33342 staining, with closely matched histology images from a pancreatic ductal adenocarcinoma tumor in an athymic mice, highlights regions of low or absent perfusion within tumor tissue. (C-D): hematoxylin and eosin-stained sections show nuclei in blue purple; eosin stains cytoplasm and extra-cellular matrix in pink. Stromal content was subjectively scored based on visual assessment: Score 1: < 50% stroma in the slice; Score 2: 51%-100% stroma in the slice. Scale bar = 200 μ m.

Potential Clinical Impact: Understanding the TME is crucial for developing novel therapeutics because it reveals interactions among cancer, stromal, and immune cells that drive growth, therapeutic resistance, and metastasis. These insights can guide targeted therapies and personalized treatment strategies.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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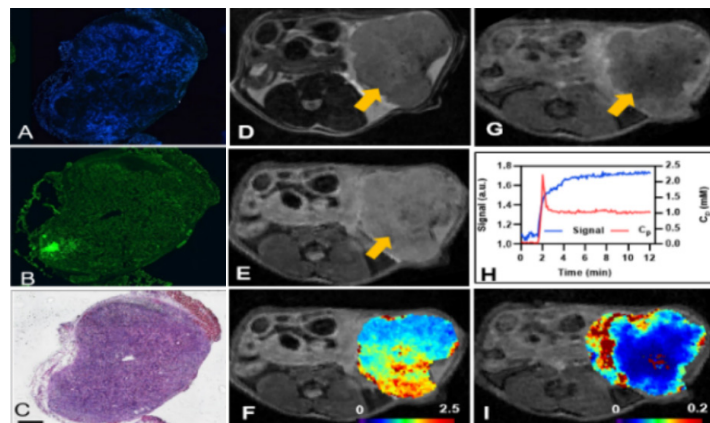


Fig. 1: Representative histology and multiparametric MRI of a KPC4662 pancreatic ductal adenocarcinoma tumor. Perfused vessels (A), collagen-rich stroma (B), and hematoxylin and eosin staining (C). Diffusion-weighted imaging (D) and post-contrast T1-weighted images reflect the tumor microenvironment at $b = 0$ s/mm² and the 30th phase (E). Apparent diffusion coefficient maps highlight increased diffusivity in low-cellularity regions (F), and volume transfer constant (K^{trans}) maps indicate elevated peripheral vascular permeability (I). Scale bar = 200 μ m.

Toward Harmonized AI-Based Quantitative CT: A Voxel-Printed, Patient-Specific Phantom for Cross-Platform Harmonization

Usman Mahmood¹, Aditya Apte¹, Sean Trahan¹, Johannes Hertrich¹, Jason Ocana¹, Anqi Fu¹, Andrew Jackson¹, Yusuf Erdi¹, Daniel Lafontaine¹, Joseph O. Deasy¹, and Amita Shukla-Dave^{1,2}

¹Department of Medical Physics, and ²Department of Radiology

Motivation: AI-based CT analysis performance varies with acquisition conditions. Identifying when models underperform due to changes in scanner protocols is essential to safeguard patient safety. Phantoms offer a solution, but current designs lack anatomical realism. We developed a 3D voxel-printed, patient-specific phantom to enable standardized, clinically relevant evaluation of AI workflows.

Methods: The phantom design originated from a high-resolution chest CT scan. Lung vasculature was isolated using a ray tracing segmentation algorithm that preserved branching topology and vessel caliber. The phantom was fabricated using polyjet 3D printing on a Stratasys J850 system. This voxel-based technique enables precise control of X-ray attenuation at sub-voxel resolution ($42 \times 84 \times 30 \mu\text{m}$) by depositing Radiomatrix, a material engineered to replicate tissue-equivalent densities across a wide range (100 to 1000 HU). Five replicate scans were acquired on a GE HD750 CT using a routine chest protocol. Phantom fidelity was assessed against the original patient CT using Multi-Scale Structural Similarity Index (MS-SSIM), shape metrics, and 104 radiomic features (PyRadiomics). Finally, TotalSegmentator AI was applied to scans at 100 kV and 120 kV to measure segmentation variability under identical anatomy.

Results: The patient-specific phantom showed high fidelity to clinical anatomy (MS-SSIM = 0.97). Despite identical anatomy, AI-based segmentation performance varied across protocol (Dice = 0.905), exposing protocol-driven variability in AI inference and underscoring the phantom's role in stress-testing model robustness.

Scientific Significance: This study introduces a voxel-printed phantom that replicates complex thoracic anatomy and radiomic features with sub-voxel precision. It provides a reproducible platform for evaluating AI performance under variable imaging conditions, addressing a critical gap in harmonization and quality control.

Potential Clinical Impact: Standardized assessment of AI and radiomics across scanners and protocols promotes multi-center consistency, streamlines regulatory validation, and enhances trust in AI-based clinical decisions.

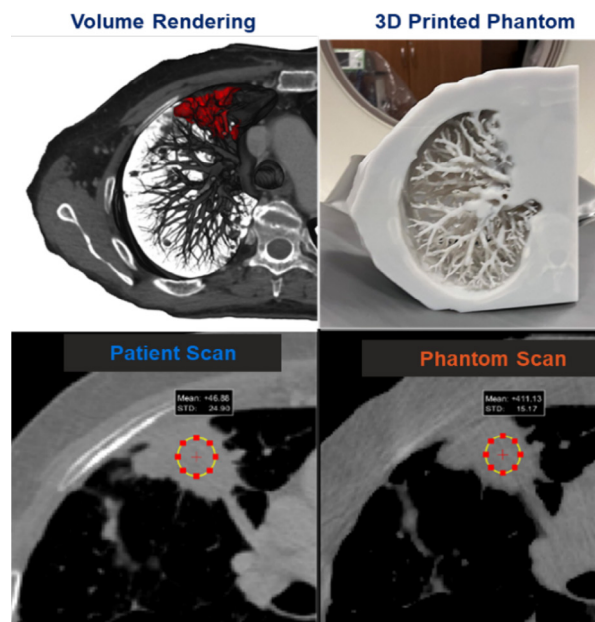


Fig 1: Patient-specific phantom creation using voxel printing. (A) Volume rendering of the patient computed tomography. (B) Three-dimensional (3D)-printed phantom. (C, D) Comparison of matched regions of interest in patient and phantom scans demonstrates preserved anatomy and contrast.

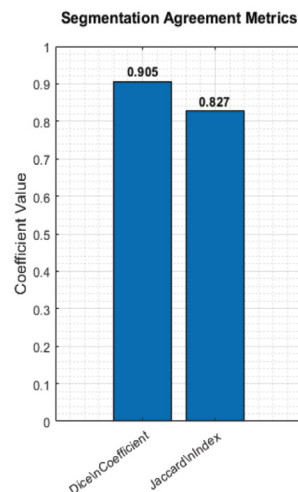


Fig. 2: Dice coefficient and Jaccard index for AI segmentation of lung vasculature from two CT scans of the same phantom. Differences indicate protocol-dependent performance.

Acknowledgments: MSK Biomedical engineering, Samuel Hellman, and Stratasys. This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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The Mathematical Oncology Initiative: Developing Novel Tools for Cancer Research

Joseph O. Deasy¹, Larry Norton², Jung Hun Oh¹, Rena Elkin¹, Anish Simhal¹, and Corey Weistuch¹

¹Department of Medical Physics and ²Department of Medicine

Motivation: A central challenge in cancer research is determining how biological samples relate to one another when each is characterized by multiple measurements. Standard distance metrics (e.g., Euclidean distance) often fail to distinguish meaningful biological or physical variation from noise. Machine learning and AI methods often require more data than are available. Our program addresses this fundamental obstacle in data science by leveraging optimal mass transport (OMT) theory and the Wasserstein distance as principled tools for quantifying sample relatedness without parameter fitting.

Methods: We developed and applied a suite of computational approaches based on OMT to quantify similarity between biological samples across multiple data modalities, including gene expression and imaging. These methods are naturally suited to heterogeneous, multi-omic data and graph-based representations of biological systems. By treating molecular measurements as probability distributions over interaction networks, OMT-based approaches provide mathematically grounded metrics for comparing complex biological states.

Results: We have demonstrated that OMT distances can reveal structure invisible to standard similarity metrics. For example, pediatric sarcoma subtypes formed distinct clusters using the OMT applied to gene expression data. We also developed **awCluster**, which represents patient samples as distributions over gene interaction networks and computes pairwise Wasserstein distances for hierarchical clustering. Applied to breast cancer datasets from METABRIC and TCGA, this method identified a subgroup with significantly worse survival and a distinct immune microenvironment composition compared with known molecular subtypes [1]. We have also applied Wasserstein distances to radiomic features of lung cancer cases to quantify tumor imaging similarity [2]. Using Ollivier-Ricci curvature (ORC), defined through Wasserstein distances on biological networks, we further identified network features associated with therapy response and potential therapeutic targets across multiple cancers. To facilitate broader use of these methods, we released an open-source software package for computing ORC [3]. Lastly, leveraging the connection between OMT and fluid mechanics, we developed unbalanced regularized OMT (**urOMT**) to model contrast agent transport in dynamic contrast-enhanced MRI (DCE-MRI). This framework estimates cross-voxel flow magnitudes and directions, producing tumor-specific transport maps that capture spatial dynamics beyond standard pharmacokinetic models.

Scientific Significance: This body of work establishes optimal mass transport (OMT) as a unifying mathematical framework for analyzing heterogeneous biomedical data. By replacing ad hoc similarity metrics with geometry-aware distances grounded in physical transport principles, OMT enables robust comparison of biological samples without extensive parameter tuning or large training datasets. Furthermore, this approach naturally integrates graph-

constrained multi-omic measurements within a single mathematical framework, providing a new set of tools for characterizing multimodal biological heterogeneity (Fig. 1).

Potential Clinical Impact: These methods have improved patient stratification, identified high-risk subgroups, and revealed potential therapeutic vulnerabilities. Ultimately, the next phase of our research aims to experimentally validate and potentially translate these findings to the clinic.

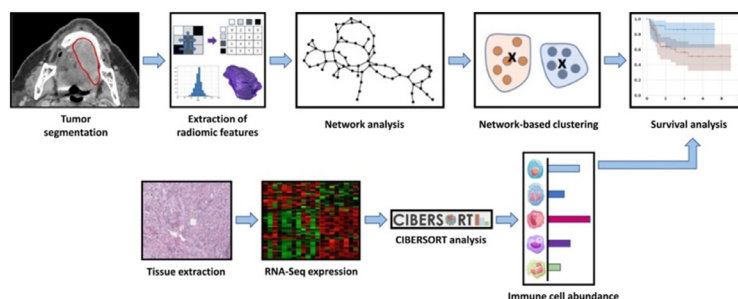


Fig. 1: Schematic of our multi-omic network analysis pipeline. Curvature provides a network-aware method to identify new gene targets, evaluate sample similarity, and stratify patients using only a limited number of samples.

Acknowledgments:

The Mathematical Oncology Initiative (MOI) has been continuously supported by the Simons Foundation and the Breast Cancer Research Foundation since 2017. This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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NetFlow Maps Multi-Modal Sample Relational Landscapes for Rapid Discovery

Rena Elkin¹ and Joseph O. Deasy¹

¹Predictive Informatics

Motivation: Cancer datasets are increasingly high-dimensional and multi-modal, and this complexity often limits discovery of biologically meaningful patterns. To improve interpretability of how samples are organized relative to one another, we developed NetFlow, a computational framework that builds data-driven, reproducible sample networks that reflect global continua and local similarity structure, coupled with interactive visualization and drill-down capabilities to refine subtypes and foster hypothesis generation for discovery and translation.

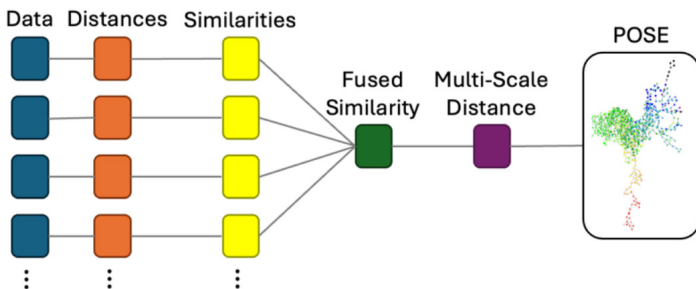


Fig. 1: A simplified schematic of the NetFlow pipeline. POSE: Pseudo-Organizational Structure

Methods: Multi-omics profiles of The Cancer Genome Atlas (TCGA) glioblastoma multiforme (GBM) cohort (N = 213) included messenger RNA (mRNA) expression, DNA methylation, and microRNA (miRNA) expression. Data preparation involved the removal of outliers, imputation for missing data, and normalization. The preprocessed multi-omics data were provided as input for NetFlow analysis.

The NetFlow pipeline (shown in Fig. 1) computes pairwise sample distances for each input data modality, which are then transformed into similarities and integrated to create a single fused similarity structure. Normalizing the fused similarity by sample density yields the diffusion operator used to compute multi-scale distances, from which the Pseudo-Organizational Structure (termed POSE) sample network is computed. Multi-scale distances incorporate the geometry of the underlying space, making them particularly useful for teasing out higher-order relationships. The resultant POSE is a network in which samples are nodes and their relationships are edges.

Biomedical data often fall along a continuum and contain heterogeneity within and across subgroups, presenting challenges for clustering and manifold embedding algorithms, which seek to maximize splits to identify clusters. NetFlow was therefore designed to simultaneously capture global progression along biological continua and local clustering using lineage-tracing-inspired, data-driven pseudo-ordering and local similarity networks.

Results: Interpretability of NetFlow POSE visualizations

The multi-omics fused POSE (Fig. 2a) revealed a lower-risk subtype (BL-cluster 17) in GBM (Fig. 2b) with significantly greater overall survival (log-rank test, $P = 1.19 \times 10^{-5}$). Top features significantly associated with the lower-risk subtype, such as mRNA expression of *EMP3* (Mann-Whitney U test with Benjamini-Hochberg false discovery rate correction, $P = 5.77 \times 10^{-9}$; Fig. 2c), recapitulate known GBM biology. Elevated *EMP3* levels have been linked to glioma progression and immune modulation, and its downregulation in BL-cluster 17 aligns with its favorable prognosis. Furthermore, the POSE's network representation provided finer resolution and visual clarity.

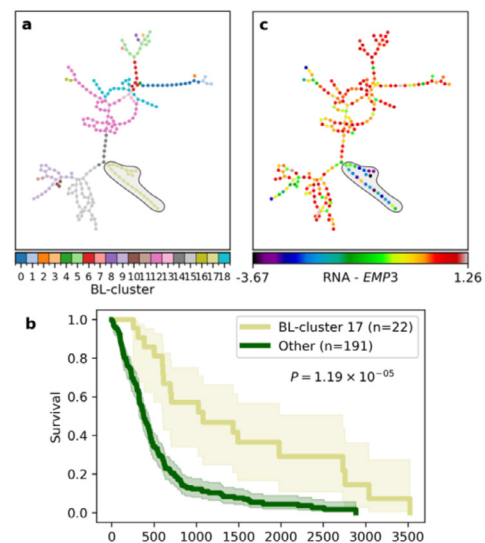


Fig. 2: (a) Multi-omics glioblastoma multiforme Pseudo-Organizational Structure (POSE) colored by cluster, accentuating the lower-risk subtype (BL-cluster 17). BL clustering entailed partitioning the POSE pseudo-ordering branches by their intersection with Louvain clusters. (b) Kaplan-Meier survival analysis comparing BL-cluster 17 with the rest of the cohort (log-rank test; P value shown). (c) The POSE colored by messenger RNA (mRNA) expression of *EMP3*.

Scientific Significance: NetFlow is a user-friendly exploratory tool that can be used to generate and test hypotheses for biological discovery.

Potential Clinical Impact: NetFlow was demonstrated to refine biologically relevant subtypes and uncover genotype-phenotype associations, with the potential to reveal clinically actionable insights.

Acknowledgments:

This study was supported in part by the MSK Cancer Center Support grant (P30CA008748), the Simons Foundation, the Breast Cancer Research Foundation (MATH-23-001) and the NIH ROBIN Cooperative Group (U54 CA274291).

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Spironolactone Drives Synthetic Lethality with Proton Irradiation Not Photon Irradiation, Through Transcription–Replication Conflicts and Checkpoint State Collapse

Hadi Askarifiroozjaei¹, Jung Hun Oh¹, Rena Elkin¹, Haibo Lin², Charles B. Simone², Adriana Haimovitz-Friedman¹, and Joseph O. Deasy¹
¹Memorial Sloan Kettering Cancer Center and ²New York Proton Center

Motivation: Proton therapy and conventional X-ray (photon) radiotherapy differ not only in how they deposit physical dose but also in the qualitative nature of the DNA damage they produce. Protons generate damage that is comparatively clustered along particle tracks. This difference may engage distinct molecular pathways and impose qualitatively different cell-cycle checkpoint programs, with proton irradiation placing greater reliance on homologous recombination and enforcing a more durable arrest at the gap-2/mitosis (G2/M) boundary. Despite the growing clinical adoption of proton therapy, the downstream biological consequences of these differences—and their implications for drug combination strategies—remain incompletely characterized.

Methods: Our research program applies single-cell transcriptomic profiling and differential gene co-expression network analysis to map the cell-state landscapes induced by photon versus proton irradiation at matched physical doses. A central hypothesis of this work is that a modality-dependent checkpoint architecture predicts differential therapeutic vulnerability; drugs targeting pathways preferentially engaged by a radiation type act as more effective modality-specific radiosensitizer. This hypothesis was tested by examining spironolactone, an FDA-approved aldosterone antagonist with documented off-target activity.

Results: This systems-level approach has revealed that the two modalities organize fundamentally different checkpoint architectures. Photon-irradiated cells appear to engage coordinated replication-coupled repair programs involving the proliferating cell nuclear antigen–minichromosome maintenance–cell division cycle 6 (PCNA–MCM–CDC6) axis alongside epidermal growth factor receptor (EGFR)-associated transcriptional activity. Proton-irradiated cells (8 Gy), by contrast, more robustly assemble a cohesive ATR–CHK1–WEE1–CDK1 checkpoint state with enhanced gene (RAD51–BRCA1) coupling and what appears to be a SMAD3-centered stress-integration hub linking transforming growth factor- β (TGF- β) and nuclear factor kappa B (NF- κ B) signaling to cell survival and arrest maintenance. It is unclear whether these network differences represent strictly deterministic effects of modality or result from probabilistic enrichment of particular cell states, and this question remains an area of ongoing investigation.

Preliminary co-expression network analyses suggest that adding spironolactone to proton-irradiated cells produces a cell-cycle network topology strikingly similar to that observed with photon irradiation alone, loosening the proton-characteristic mitotic surveillance architecture and re-engaging the replication module while concomitantly disrupting the survival signaling coordinated by the putative SMAD3 hub. We interpret this as evidence that the drug forces proton-damaged cells into a replication-coupled configuration for which the physically complex, clustered proton lesions are poorly suited, producing persistent replication fork congestion

and escalating replication stress rather than efficient repair. Critically, cell survival experiments (Figure 1) indicate that this interaction is substantially stronger for proton than for photon irradiation, consistent with the modality-specificity hypothesis.

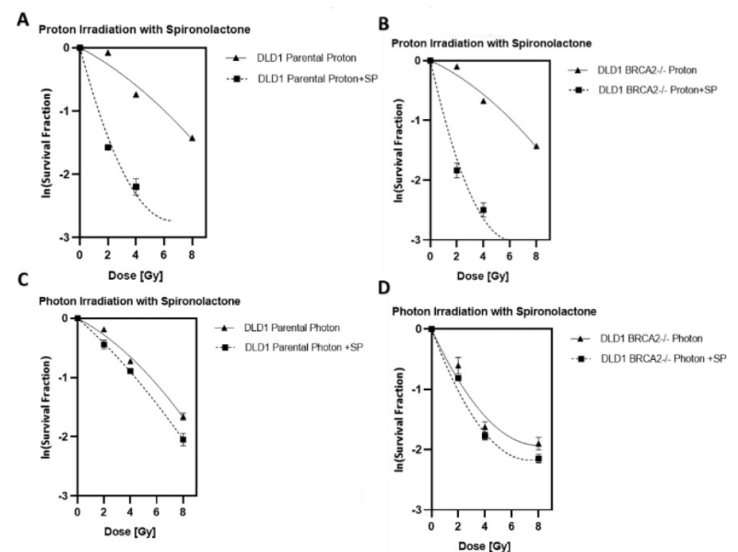


Fig. 1: Radiosensitization by Spironolactone in combination with proton irradiation. DLD1 Parental and DLD1 BRCA2^{-/-} cells were irradiated with 2, 4, or 8 Gy using proton beams (A, B) or photon beams (C, D), followed by treatment with Spironolactone (20 μ M).

Scientific Significance: At clinically relevant concentrations, spironolactone promotes proteasome-dependent degradation of XPB (ERCC3) (1), a core helicase subunit of the transcription and nucleotide excision repair factor TFIIH. XPB degradation disrupts both NF- κ B- and AP-1-dependent transcription through mechanisms independent of mineralocorticoid receptor. Because the proton-specific checkpoint architecture appears to depend critically on these signaling pathways, spironolactone represents a candidate modality-matched radiosensitizer.

Potential Clinical Impact: These findings uncover an unexpected synthetic lethal interaction between proton therapy and the FDA-approved drug spironolactone and provide a strong rationale for translational evaluation of this combination. The markedly enhanced radiosensitizing effect of spironolactone under proton irradiation highlights its promising therapeutic potential.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Mechanistic Simulation of Tumor Response for Radiotherapy

Jeho Jeong¹, Eric Aliotta¹, and Joseph Deasy²

¹Division of Radiotherapy Physics and ²Predictive Informatics

Motivation: To develop biologically-grounded mechanistic models that accurately predict tumor response to radiotherapy and enable patient-specific treatment personalization.

Methods: The simulation framework assumes that oxygen and glucose supply within a tumor sub-volume remains approximately constant during treatment, creating a resource-limited microenvironment.¹ Tumor cells are partitioned into proliferating (P), intermediate (I), and hypoxic/starving (H) compartments, defined by metabolic state (Fig. 1). Radiation-induced cell killing follows the linear-quadratic model, with radiosensitivity modulated by oxygen enhancement ratios. As damaged proliferating cells die and clear, resources become available, allowing intermediate and hypoxic cells to transition into more oxygenated states, naturally representing reoxygenation dynamics (Fig. 1). Later extensions incorporated cell-cycle-dependent radiosensitivity² and integration with quantitative imaging biomarkers for patient-specific modeling.⁵

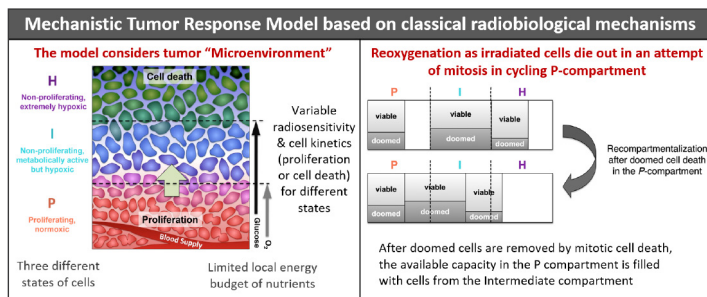


Fig. 1: Brief description of the mechanistic tumor response model: (left) resource-limited tumor microenvironment with three sub-populations of cells; (right) reoxygenation dynamics after cell death.

Results: The model was applied to 38 early-stage lung cancer cohorts ($n = 2701$) treated with various treatment schedules, from conventional radiotherapy to single-fraction stereotactic body radiotherapy (SBRT).² When outcomes were analyzed using a model-derived equivalent dose in 2-Gy fractions, all fractionation schedules collapsed onto a single dose-response curve ($TD_{50} = 62.1$ Gy; $\gamma_{50} = 1.5$), with best-fit parameters of $\alpha = 0.305$ Gy⁻¹, $\alpha/\beta = 2.8$ Gy, and oxygen enhancement ratio = 1.7 (Fig. 2A). These findings were confirmed using an independent validation dataset (23 cohorts, $n = 1628$). For carbon ion radiotherapy (CIRT), modeling predicted radiosensitivity parameters consistent with high-linear energy transfer radiobiology, and the CIRT outcomes fit well into a single dose response curve along with photon data (Fig. 2A). The derived relative biological effectiveness decreased from about 2.1 (18 fractions) to around 1.5 (single fraction).³ Simulation studies of fractionation strategies identified a “primer shot” schedule, consisting of an initial fraction followed by a reoxygenation interval, which can reduce the predicted local failure by 4.6%–7.4% (Fig. 2B).⁴ Most recently, integration with multimodal imaging enabled patient-specific radiobiological digital twins for 72 oropharyngeal cancer patients, improving prediction of tumor response and locoregional recurrence (AUC 0.83 vs. 0.77).⁵ An example of the results is shown in Fig. 2C-E.

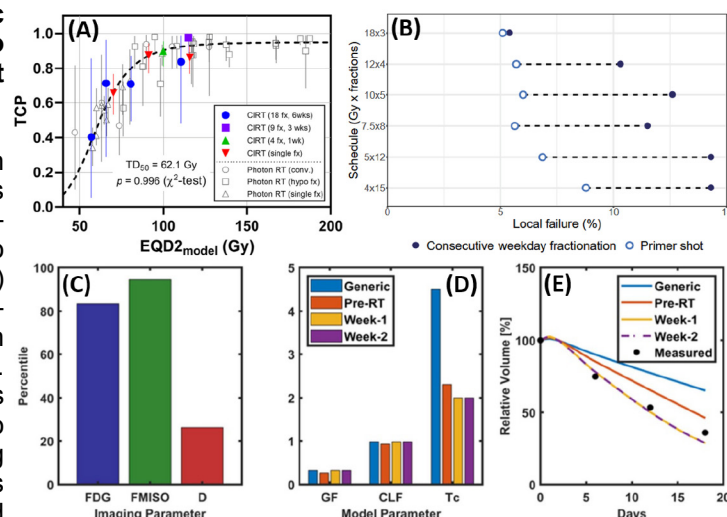


Fig. 2: (A) The dose-response relationship of early-stage lung cancer treated with photon and carbon radiotherapy in various fractionation schedules; (B) primer shot prediction with reduced local failure rate; (C)-(E) examples of personalized digital twin modeling with imaging parameters: (C) percentiles of the study population from pretreatment imaging, (D) model input parameters, and (E) the resultant volume regression trends predicted by each model, alongside the actual relative volumes measured at each week.

Scientific Significance: This work establishes a mechanistic simulation framework which captures key radiobiological processes governing tumor response to radiation, providing a unified explanation for treatment outcomes across diverse fractionation regimens and modalities. By integrating multimodality imaging with biologically-grounded modeling, the framework enables the creation of patient-specific radiobiological digital twins capable of predicting tumor response early during therapy.

Potential Clinical Impact: Such tools have the potential to support adaptive radiotherapy, optimized fractionation strategies, and personalized treatment planning, ultimately improving tumor control and minimizing treatment toxicity.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Division of Radiotherapy Physics



Division of Radiotherapy Physics

The Radiotherapy Physics (RTP) Division of Medical Physics supports the advancement and delivery of care for Radiation Oncology patients. External beam therapy at 2 locations in Manhattan (Main Campus and the Koch Center) and 6 locations in the Regional Network (Basking Ridge, Monmouth, Westchester, Bergen, Nassau, and Commack). Our Brachytherapy program treats at Main Campus and 3 of our Regional Campuses. Members of the division are medical dosimetrists, planner physicists, staff clinical physicists, faculty physicists, and treatment planning coordinators. Individuals in dosimetry and physicist roles are either board certified or in the process of obtaining board certification. In addition, physicists have a New York State license.

A hallmark of our program is our thorough implementation of the OneMSK philosophy across different technology types and regions of the body. Advanced care techniques are delivered throughout our network such as our real-time monitoring program using surface-guided imaging for patients treated for breast cancer and the in-house developed MV/kV program for patients treated to the spine and prostate. Our Manhattan campus has a limited number of additional techniques such as specialized imaging and treatment equipment for small lesions in the brain, total body irradiation, total skin electron therapy. Our Koch system has the MR L system, which offers superior real-time imaging.

Our Brachytherapy program at Main Campus supports a wide range of treatment types, including intracavitary (also delivered at 3 locations in our Regional Network), interstitial, surface implants, and intraoperative radiation therapy.

Individuals have specialized expertise and contribute to general and specialized activities. For example, individuals may have treatment-site specific expertise that aligns with

patients' treatment sites as well as technological expertise. Other teams include the Radiation Dosimetry Core (focusing on network-wide safety and quality, all simulation and linear accelerator equipment throughout the network, and specialized protocols), the Treatment Planning Core (focusing on safety and quality related to the treatment planning systems), the Quality Improvement Section (focusing on the improvements to the process of care), and the MR-guided Radiation Therapy Core (supporting an ever-expanding use of the MR simulation and MR Linac treatment programs).

The Division continually seeks to maintain alignment with MSK institutional values in how we deliver care to our patients. As demonstrated through numerous examples in this report, the Radiotherapy Physics Division actively innovates to improve patient care, often through collaborations with those in other areas of the Departments of Medical Physics and Radiation Oncology. For example, upon seeing a growing need for software solutions to support robust volumetric treatment planning for patients receiving reirradiation, the Radiotherapy Dose Accumulation Routine (RADAR) software was developed and clinically implemented.

In addition to clinical care and development, many dosimetrists and physicists contribute to the educational activities involved in the Therapeutics Medical Physics Radiotherapy Program led by Dr. Megan Hyun and the medical dosimetrist intern training program led by Camille Law. These training programs are essential for building a skilled workforce in medical physics and medical dosimetry.

We are constantly energized by opportunities to advance care in new areas or with better solutions to existing areas such as in adaptive therapy, re-irradiation, use of automation, and other areas for the future.



AI Brain Mets Detection and Longitudinal Lesion Tracking

Dylan Hsu¹, Ase Ballangrud-Popovic¹, Joseph Deasy², Laura Cerviño¹, Jean Moran¹, Luke Pike³, Rob Young⁴, Nate Swinburne⁴, and Michalis Aristophanous¹

¹Division of Radiotherapy Physics, ²Predictive Informatics, ³Radiation Oncology, and ⁴Radiology

Motivation: Brain metastases (BM) are the most common type of brain tumors. In recent years, stereotactic radiosurgery (SRS) has become the standard in the management of BM, with patients returning for multiple courses. As survival has improved, imaging follow up scans have increased. This has made it difficult to track individual lesions accurately to evaluate response. Physicians lack the tools that integrate all imaging and treatment information to assist them in making optimal clinical decisions.

Methods: A critical requirement for tracking lesions over time is to first identify them. We have developed a tumor volume auto-segmentation method based on a deep learning approach that can be used to define individual BM.¹ The method, based on a V-Net 3D convolution neural network (CNN), takes contrast-enhanced T1-weighted MRI and CT images as input and runs them through the network. The algorithm was trained using 1,345 BM (402 patients) gross tumor volumes (GTVs), defined by a radiation oncologist, and taken as the ground truth. With the auto-segmentation algorithm in place, software termed METRO: Metastases Tracking on Repeated Observations, was developed to define and track lesions on serial MRI images.² METRO collects the radiotherapy plan information and diagnostic images. The MRIs are selected, and through a novel iterative process, they are registered to each other with a 2 mm accuracy. The auto-segmentation algorithm is then run to provide candidate tumor volumes, which are then linked together longitudinally to create a plot with the lesion volume and diameter at every imaging visit. Information for each lesion is then assembled on a report and presented to the physicians for evaluation (Figure 1). The results of METRO were compared with expert measurements of lesion volume and diameters.³

segmentations and model performance for different lesion sizes are shown in Figure 2. METRO results were correlated with expert manual measurements of lesion diameter ($R^2 = 0.76$, p -value = 0.0001), and METRO had a sensitivity of 0.72 and a specificity of 0.95 in identifying lesions that responded to SRS.

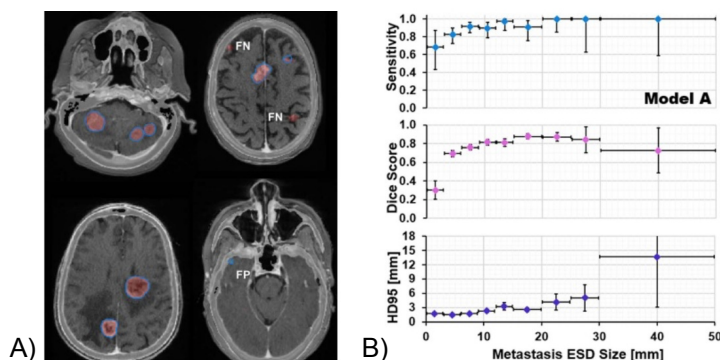


Fig. 2: A) Example lesion segmentations and B) segmentation performance on the right (various metrics against lesion size). ESD: equivalent spherical diameter

Scientific Significance: AI-assisted auto-segmentation and lesion tracking through METRO can greatly assist in streamlining BM detection and contouring for SRS treatment and response evaluation.

Potential Clinical Impact: This work can lead to efficiencies and greatly improved management of patients with BM. Our long-term goal is to leverage AI to predict BM disease progression and risk of toxicity and ultimately assist the clinical team to make personalized treatment decisions for each patient.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748). Eve LoCastro, Aditya Apte, Aditi Iyer, and Jason Hu for their contributions to operationalizing METRO, and all Radiation Oncology Central Nervous System-specializing physicians for their continuous input and interest.

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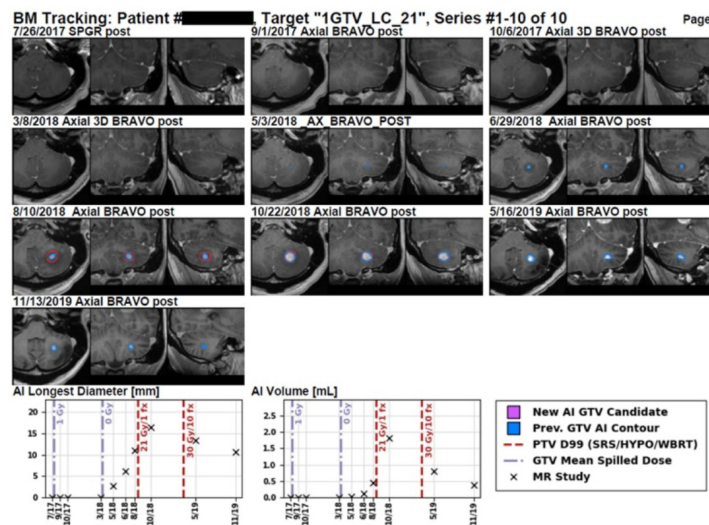


Fig. 1: An example report generated by the Metastases Tracking on Repeated Observations software (termed METRO). BM: brain metastases; GTV: gross tumor volume

Results: The BM auto-segmentation algorithm achieved a detection sensitivity of 90% with 2.4 $\pm$ 0.5 false positives per patient on an independent cohort of 102 patients. Example

AI-Empowered Intrafractional Motion Management with On-Treatment Images

Xiuxiu He¹, Weixing Cai¹, Feifei Li¹, Qiyong Fan¹, John J. Cuaron², Marsha Reyngold², Laura Cerviño¹, Jean M. Moran¹, Pengpeng Zhang³, Xiang Li¹, and Tianfang Li¹

¹Division of Radiotherapy Physics, ²Department of Radiation Oncology, and ³Medical Physics Computer Service

Motivation: Slight geometric inaccuracies in radiation delivery, especially with ablative doses and steep dose gradients, could lead to significant risks of normal tissue toxicity and reduced local control. Intrafractional motion monitoring using on-treatment X-ray imaging has advantages in showing internal motion compared with external markers; however, the accuracy is limited by contrast, which is due to the interference of overlaid structures along the beam path.

Methods: We reconceptualized motion detection by replacing the traditional step, directly registering the on-treatment kilovoltage (kV) projection to the reference digitally reconstructed radiograph (DRR), with a two-stage strategy: first, decompose the kV image using AI, then register the decomposed image to the DRR. Accordingly, we designed a suite of physics-informed AI methods which (1) selectively preserve and amplify the anatomy of interest and (2) suppress distracting structures.

The paradigm shift instigated three key algorithmic advancements:

(i) a bespoke multi-channel, multi-domain loss function optimized for kV image decomposition¹,

$$\alpha mse(Y, Y_{dec}) + \beta Corr(Y, Y_{dec}) + \gamma Corr((X - Y_{dec}), (Y_{All} - Y)) + \delta mse(f(Y), f(Y_{dec}))$$

(ii) integration of patient-specific prior knowledge via Multi-Head Cross Attention module²,

$$\alpha(I_{kv\ feature}, I_{p\ feature}) \leftarrow softmax\left(\frac{I_{p\ feature} \cdot I_{kv\ feature}}{\sqrt{d_k}}\right)$$

(iii) a texture-guided, objective attention mechanism.³

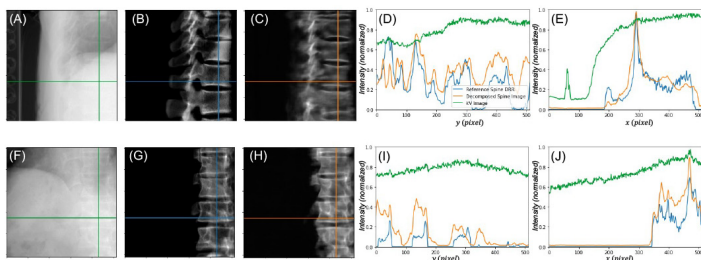


Fig. 1: Kilovoltage (kV) images (A and F), the reference spine digitally reconstructed radiographs (DRRs) (B and G), the decomposed images (C and H), and line profiles (D, E, I, and J).

Results: (I) **Paraspinal stereotactic body radiation therapy (SBRT)** delivers an intense dose with a steep dose gradient in close proximity to the spinal cord. A residual network (ResNet)-based generative adversarial network (ResNetGAN) model¹ was developed and showed effectiveness (shown in Fig. 1) in retaining and enhancing the spine component from the on-treatment images. The decomposed spine component from the on-treatment images, matched with the DRR, had submillimeter accuracy; the accuracy improvement was robust. With the incorporation of patient-specific prior knowledge via the Multi-Head Cross Attention mechanism², the decomposed spine-only X-ray significantly reduced the maximum errors and achieved higher peak signal-to-noise ratio (PSNR) and structural similarity index measure (SSIM).

(II) **Ablative pancreatic radiotherapy** has shown excellent clinical outcomes, with a significantly improved two-year survival rate. The current Varian intrafraction motion review (IMR) system provides only a tool for visually verifying stent motion, lacking quantitative information. For mitigation, a deep learning-based stent automatic recognition (displayed in Fig. 2) was developed from clinical IMR images for quantitative intrafraction motion management in pancreatic radiotherapy and achieved Dice similarity coefficient and 95th percentile Hausdorff distance values of 0.96 ± 0.01 mm and 1.01 ± 0.55 mm, respectively.

Scientific Significance: Our novel image-decomposition technique accurately and efficiently enhanced 2D kV image contrast by removing irrelevant content, thereby establishing a new paradigm in AI-driven image processing.

Potential Clinical Impact: AI-driven on-treatment imaging enables us to visualize the anatomy being irradiated as we treat, in ever-greater detail and with sub-millimeter precision, thereby facilitating more effective intrafraction motion management.

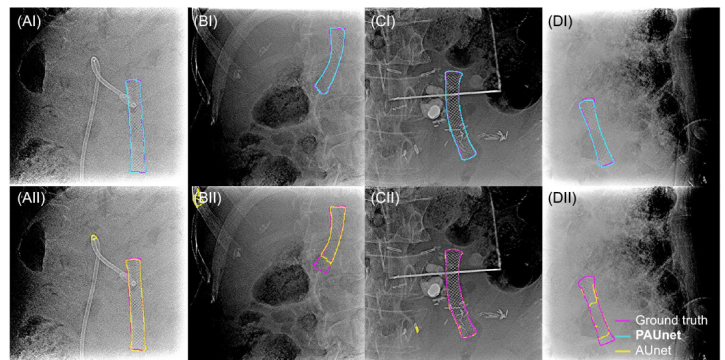


Fig. 2: Visualization of the ground truth contour and the auto-segmented stent contour using the trained patient-specific perceptual attention U-Net (PAU-Net)³ using a texture-guided, objective attention mechanism, compared with the conventional attention U-Net (AU-Net).

Acknowledgments: This work is supported in part by the research grant from Varian Medical Systems and in part by the MSK Cancer Center Support Grant/Core Grant (P30 CA008748).

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Development of an AI-Based Incident Analysis and Learning System to Improve Patient Safety and Treatment Quality

Abbas J. Jinia¹, Katherine Chapman¹, Shi Liu¹, Cesar Della Bianca¹, Elizabeth Hipp¹, Eric Lin¹, Robin Moulder², Dhvani Parikh³, Jason Cordero³, Mary Gil³, John Ford⁴, Anyi Li⁵, and Jean M. Moran¹
¹Division of Radiotherapy Physics, ²Division of Quality and Safety, ³Department of Radiation Oncology, ⁴Department of Nursing, and ⁵Medical Physics Computer Service

Motivation: Patient safety and treatment quality are crucial in healthcare, requiring a feedback loop of incident reporting and detailed analysis to develop targeted mitigation strategies^{1,2}. However, manually analyzing large volumes of incident reports is a challenge. Recent advancements in AI offer an opportunity to develop AI-based incident analysis and learning systems (referred to as AI-ILS), which can efficiently process large volumes of incidents to identify trends and guide the development of appropriate mitigation strategies.

Methods: The AI-ILS comprises traditional language models (LMs), and the more recent large language models (LLMs). The LMs are used for preprocessing tasks, such as de-identifying sensitive patient and hospital data, and expanding standard medical abbreviations and institution- and department-specific short forms. These preprocessing steps were carefully designed to ensure data security and consistency, enabling cross-institutional data sharing for collaborative learning.

An open-source LLM, Llama 3, with eight billion parameters, which is instructionally aligned, was fine-tuned to perform Human Factors Analysis and Classification System (HFACS) categorization. HFACS is a multi-tier, hierarchical framework used to identify contributing factors to human error. The fine-tuning of the LLM was performed using a set of 1,524 mock incident reports, carefully curated by medical professionals involved in patient care for radiation therapy. The fine-tuning process resulted in four adapters, each corresponding to the four tiers of the HFACS framework.

To evaluate the end-to-end performance of the AI-ILS, 350 incidents were randomly extracted from the institution's Reporting to Improve Safety and Quality (RISQ) database. Experienced medical professionals reviewed the AI-ILS classifications to assess accuracy.

Results: Table 1 summarizes the performance metrics of the Llama 3 model before and after fine-tuning, using the validation dataset. The results show that the base model's performance was close to random guessing without fine-tuning. However, after fine-tuning, the model's performance improved significantly, demonstrating effective learning of the AI model from mock incidents.

The model's performance was evaluated on 350 real-world incidents, from which eight were excluded due to the patients contribution to the incidents rather than professional error. Expert reviewers strongly agreed with the AI-ILS classifications in 79% of cases and showed partial agreement in 10% of cases, which was influenced by their prior clinical experiences. In the remaining cases, reviewers disagreed with the AI-ILS classifications, primarily due to nuanced clinical judgments that the AI-ILS system did not capture.

Table 1: Performance metrics for the Llama 3 instruct model before and after fine-tuning.

HFACS Tiers	Before fine-tuning		After fine-tuning	
	Accuracy	AUROC	Accuracy	AUROC
Unsafe Acts	54.24%	0.50	77.97%	0.91
Preconditions for Unsafe Acts	60.94%	0.48	87.50%	0.97
Unsafe Supervision	48.11%	0.54	78.30%	0.90
Organizational Influences	48.05%	0.50	75.32%	0.90

Scientific Significance: This work presents a novel AI-based incident analysis pipeline that leverages AI for HFACS analysis. Notably, this is the first system to apply AI to HFACS analysis in radiation oncology, and it has been successfully tested on a large dataset of 350 incidents.

Potential Clinical Impact: Currently, the resultant AI-ILS is being used to process incidents specific to re-irradiation. It can be applied to efficiently analyze aggregated data and to optimally allocate resources to improve existing workflows and mitigate different types of errors.

Acknowledgments: Department of Digital Informatics & Technology Solutions: High Performance Computing Group. This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Optimizing Diffusion-Weighted Imaging Acquisitions for Head and Neck Radiotherapy

Eric Aliotta¹, Ramesh Paudyal², Amita Shukla-Dave², Laura Cervino¹, Ricardo Otazo³, and Victoria Yu¹

¹Division of Radiotherapy Physics, ²Predictive Informatics, and ³MRI Physics

Motivation: To develop diffusion-weighted imaging (DWI) acquisitions with sufficient geometric fidelity to broaden clinical translation into radiotherapy treatment planning.

Methods: DWI is a quantitative magnetic resonance imaging (MRI) technique which characterizes the Brownian motion of water molecules and is sensitive to the elevated cell densities observed in tumors. DWI has numerous applications in head and neck radiotherapy, including target definition, response prediction, and longitudinal treatment response monitoring. Unfortunately, current techniques rely on single-shot echo planar imaging (ssEPI), which suffers from low spatial resolution and severe geometric distortions, limiting their use in radiotherapy applications. The purpose of this study was to quantify the geometric fidelity and efficiency of alternative DWI pulse sequences, including multi-shot EPI (msEPI), single-shot turbo-spin-echo (ssTSE), and multi-shot periodically rotated overlapping parallel lines with enhanced reconstruction (PROPELLER) readouts.

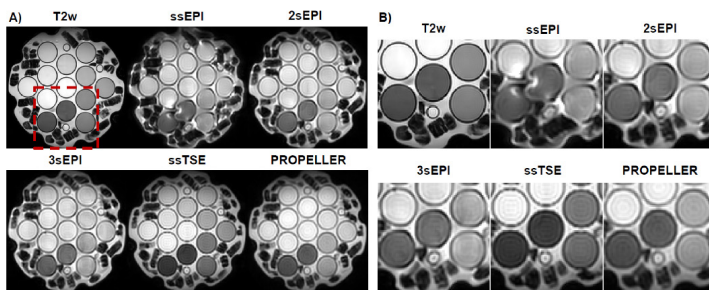


Fig. 1: Diffusion phantom images acquired with each protocol ($b = 0$ images shown) as well as a non-diffusion-weighted image T2-weighted (T2w) turbo spin echo sequence. Localized distortions were clearly visible in the single-shot echo planar imaging (ssEPI) image (likely arising from an inadvertent air pocket), which were reduced considerably with 2-shot EPI (2sEPI), further reduced with 3sEPI, and effectively eliminated with single-shot turbo-spin-echo (ssTSE) and periodically rotated overlapping parallel lines with enhanced reconstruction (PROPELLER).

Results: Alternative methods all significantly reduced distortions compared with ssEPI in both phantom (Fig. 1) and in vivo (Fig. 2) studies (ssEPI: mean distortion = 3.06 ± 1.25 mm, 2sEPI: 2.62 ± 0.99 mm, 3sEPI: 2.21 ± 0.98 mm, ssTSE: 1.78 ± 0.94 mm, and PROPELLER: 1.49 ± 0.63 mm [all $P < 1 \times 10^{-3}$ vs. ssEPI]). A clear trade-off with acquisition efficiency was observed, as signal-to-noise ratio (SNR) efficiency was inversely correlated with distortion (ssEPI: 21.9 ± 7.9 , 2sEPI: 15.1 ± 5.0 , 3sEPI: 12.1 ± 4.5 , ssTSE: 6.0 ± 1.6 , and PROPELLER: 5.7 ± 1.9).

Apparent diffusion coefficient (ADC) quantification was similar for all techniques in phantoms but was reduced by approximately 12% in vivo for ssTSE and PROPELLER, likely due to lower SNR. Multi-shot EPI with 3 shots (3sEPI) appears to represent an appealing middle ground for radiotherapy with low distortions and reasonable efficiency.

Scientific Significance: High-fidelity DWI may enable new opportunities for quantitative imaging applications in radiotherapy treatment planning. For example, cell density information afforded by DWI may provide insights into tumor heterogeneity, which can be targeted with local dose escalation and/or de-escalation. By improving the geometric fidelity of DWI measurements, we aim to collect data to inform such innovative directions.

Potential Clinical Impact: Highly localized tissue characteristics and radiation-induced changes, which may be washed out by distortions using ssEPI but be visible using more advanced acquisition techniques, may enable more personalized radiotherapy.

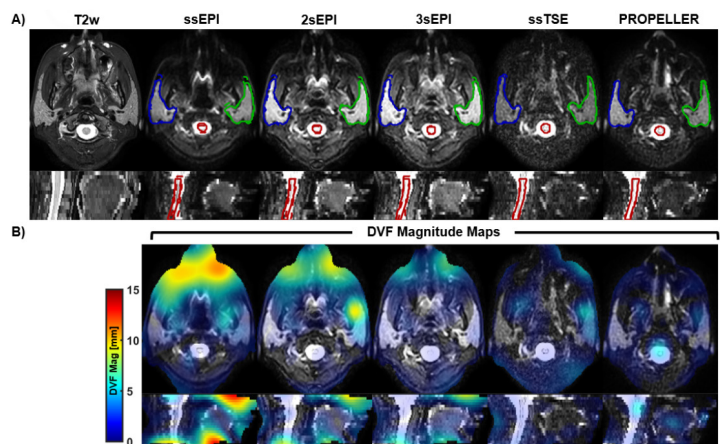


Fig. 2: Images acquired with each diffusion-weighted imaging (DWI) protocol ($b = 0$ shown) are compared with a non-DWI T2-weighted (T2w) sequence (A). Displacement vector field (DVF) maps, computed from deformable registration between each DWI scan and the T2w reference, are overlaid (B). Distortions were clearly visible in the nasal cavity and inferior spinal cord for single-shot echo planar imaging (ssEPI), which were reduced with 2-shot EPI (2sEPI), further reduced with 3sEPI, and largely eliminated with single-shot turbo-spin-echo (ssTSE) and periodically rotated overlapping parallel lines with enhanced reconstruction (PROPELLER).

Acknowledgments: We appreciate our collaborators Nancy Lee (Radiation Oncology) and Alex Dresner (Philips Healthcare). This project has been conducted under a research agreement with Philips. This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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DART - Automated Planning of Stereotactic Spine Re-irradiation Using Cumulative Dose Limits

Sebastian Meyer¹, Lei Zhang¹, Yilin Liu¹, LiCheng Kuo¹, Yu-Chi Hu¹, Yoshiya Yamada², Masoud Zarepisheh¹, Pengpeng Zhang¹, and Laura Cervino¹

¹Department of Medical Physics and ²Radiation Oncology

Motivation: To develop an automated re-irradiation planning framework based on cumulative doses from multiple treatments.

Methods: Re-irradiation refers to a radiotherapy course that treats a previously irradiated volume or in which the cumulative dose to organs at risk (OARs) raises toxicity concerns. Re-irradiation planning remains a complex process that faces three significant challenges: 1) radiobiological dose summation using equivalent dose in 2 Gy fractions (EQD2) is necessary to account for the differences in fractionation schemes between prior radiation therapy (RT) and re-irradiation when computing cumulative doses, 2) the substantial anatomical changes between treatment courses typically require deformable image registration (DIR), which can introduce uncertainties, and 3) expert consensus guidelines and knowledge of cumulative tissue tolerance and recovery are limited. Although re-irradiation has become more prevalent, few studies have investigated dedicated approaches to optimize re-irradiation by accounting for the spatial dose distribution of the previous RT. Existing solutions rely on rigid registration or the maximum OAR dose and are not streamlined for clinical application or are implemented only in research software. This work introduces the Dose Accumulation-based Re-irradiation Tool (DART), a fully automated planning framework that combines deformable dose mapping with a clinically viable planning strategy integrated within a commercial TPS. The goal was to improve the target coverage to maximize the therapeutic ratio while accounting for the spatial dose distribution of the prior RT and ensuring that plans meet cumulative OAR dose limits. We performed a retrospective study of 14 patients who received spine SBRT re-irradiation near a previously irradiated treatment site. A fully automated workflow was implemented in DART within Eclipse using a combination of a dose accumulation script and a proprietary automated optimization algorithm. First, we converted the prior treatment dose to EQD2 and mapped it to the current anatomy, utilizing DIR. Next, the intersection of EQD2 isodose lines with relevant OARs defines a series of optimization structures. During plan optimization, the residual allowable dose at a specified tissue tolerance was treated as a hard constraint.

Results: All DART plans met institutional physical and cumulative constraints and passed plan checks by medical physicists. DART demonstrated significant improvements in target coverage over clinical plans, with an average increase in PTV D_{99%} and V_{100%} of 2.3 Gy [range -0.3–7.7 Gy] and 3.4% [range -0.4%–7.6%] ($p < 0.01$, paired t -test), respectively (Fig. 2). Moreover, high-dose spillage ($> 105\%$) outside the PTV was reduced by up to 7 cm³. The homogeneity index for DART plans was improved by 19% ($p < 0.001$).

Scientific Significance: DART provides a powerful framework for more tailored re-irradiation plans by accounting for dose distributions from the previous treatments (Fig. 1). In future work, we intend to investigate potential modifications to the ECHO template (e.g., the objectives and plan normalization). Tailoring the template for re-irradiation applications could further improve target coverage.

In addition, we aim to extend our dose smearing approach to account for the spatial variation of DIR uncertainty, i.e., using a spatially-dependent smearing radius. Moreover, we need to consider that DIR uncertainty is not isotropic.

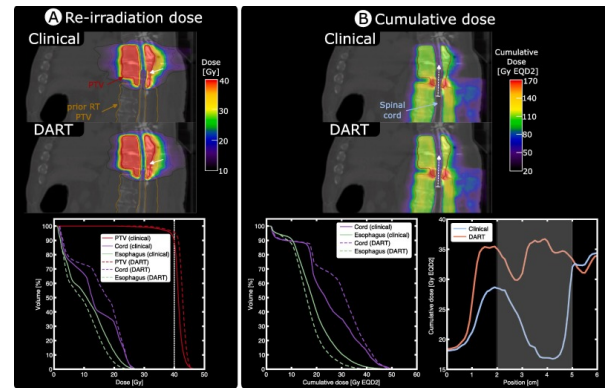


Fig. 1: Dose distributions for an example case. Comparison of the clinical and Dose Accumulation-based Re-irradiation Tool (DART) plan for a T7-T9 treatment with prior radiation therapy at the T10-T12 vertebrae. (A) Physical dose distribution and corresponding planning target volume dose-volume histogram (DVH) of the re-irradiation plans. (B) Cumulative dose distributions in equivalent dose in 2 Gy fractions (EQD2) and corresponding DVHs for relevant organs at risk. Dashed white arrow: line profile along the spinal cord on top of the dose distribution.

Potential Clinical Impact: The superior plan quality could improve the therapeutic ratio for re-irradiation patients. Spinal malignancies are a key indication for re-irradiation, as ~ 40% of cancer patients develop spinal metastases. Re-irradiation in the spine can be particularly challenging, given the tissue tolerance of critical organs in the proximal region, such as the spinal cord and esophagus. At MSK, we treated around 1,500 spine SBRT plans in 2021, conservatively estimating that more than 30% were in a re-irradiation setting.

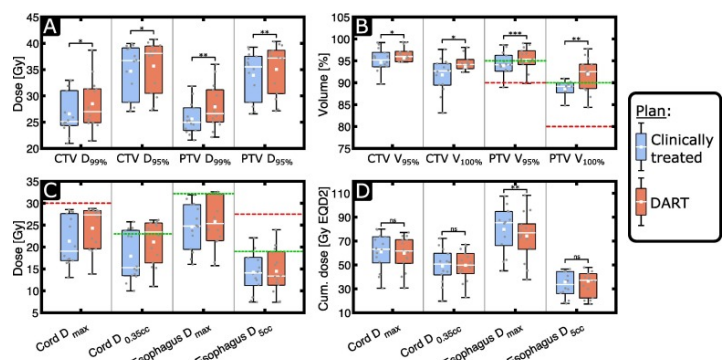


Fig. 2: Dose metric comparison for the patient cohort. Re-irradiation plan (A and B) target coverage and (C) critical structure dose. Dotted green and dashed red lines are ideal and acceptable criteria, respectively, per institutional policies. Results of the paired t -test are indicated by ns, * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.

Acknowledgments: The authors thank Gourav Jhanwar for helping with implementing the ECHO template. This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Clinical Implementation of a Knowledge-based Decision Support System for Breast Treatment Plan Auditing

Shi Liu¹, Katherine Chapman¹, Jean M. Moran¹, and Cesar Della-Biancia¹
¹Division of Radiotherapy Physics

Motivation: Implement the Isolation Forest (iForest) algorithm to breast volumetric modulated arc therapy (VMAT) plan auditing.

Methods: Two senior physicists have been performing an annual time-intensive manual treatment plan audit across our campuses, with the aim of further standardizing our planning procedures, updating policies and guidelines, and providing training opportunities of all staff members. Because the iForest algorithm was previously validated and proven to be a promising tool for improving auditing efficiency¹, we are motivated to implement it in various disease sites to facilitate manual auditing and with the aim to identify additional areas in need of quality improvement (QI).

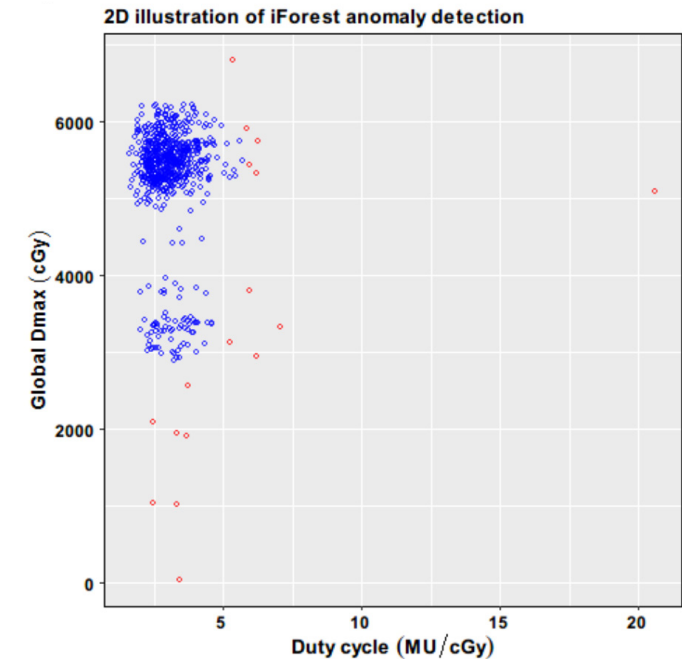


Fig. 1: Results of two-dimensional (2D) Isolation Forest (iForest) anomaly detection analysis of volumetric modulated arc therapy breast plans.

Results: Figure 1 illustrates the anomaly detection result in two dimensions when two plan parameters, i.e. duty cycle and global dose maximum (Dmax), are chosen. Each dot represents one volumetric modulated arc therapy (VMAT) breast plan. With 300 Isolation Trees (iTrees) developed in iForest, the top 23 plans represented by red dots are isolated as a result of ranking anomaly scores from highest to lowest. The average path lengths of the “anomalous” plans (red) and “normal” plans (black) converge to 31.52

and 7.65 respectively, which indicates anomalies have noticeably shorter paths. The reported method enables rapid detection of treatment plan anomalies, providing effective decision support for our manual plan auditing process. Auditing results indicated consistent adherence to the established departmental VMAT breast procedures. The findings are summarized in Table 1. Some of the flagged plans displayed a higher level of complexity, which requires detailed scrutiny.

Forest plan audit findings	% of plans (n = 23)
Organ-at-risk (OAR) contours accuracy	100%
Optimal beam arrangements	96%
Good dose distributions	91%
Optimization priority values higher than usual	44%
Large number of optimization objectives (> 100)	26%
Higher level of plan complexity (bilateral breast)	26%

Table 1: Isolation Forest (iForest) breast volumetric modulated arc therapy plan auditing findings categories with their corresponding statistics

Scientific Significance: A novel knowledge-based machine learning algorithm has been implemented to improve clinical workflow.

Potential Clinical Impact: Isolation Forest (iForest) effectively detects anomalous plans and strengthens our cross-campus manual plan auditing procedure by adding decision support and further improve standardization. Due to its efficiency, this automated method is currently used to establish a standard plan auditing procedure, enabling more frequent assessments.

Acknowledgments:

This work was supported in part by the Quality Improvement (QI) team. We thank Drs. Sean Berry, Julian Bertini, and Deshan Yang for their support. This work was also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Material Decomposition Accuracy and Low Iodine Concentration Detectability of Dual-Energy CT Utilizing Twin-Spiral Technology

Hsiang-Chi Kuo¹, Maria F. Chan¹, Usman Mahmood², Seng Boh Lim¹, Michalis Aristophanous¹, Laura Cerviño¹, Jean Moran¹, and Xiang Li¹

¹Division of Radiotherapy Physics and ²Molecular Imaging and Therapy Physics

Motivation: To evaluate the material decomposition accuracy in spectral images, and to determine the limit of low iodine concentration in twin-spiral dual-energy (DE) scanners.

Methods: (1) Material decomposition accuracy: A commercial iodine phantom featuring a circular inner ring (small size, denoted as S) and an elliptical outer ring (large size, denoted as L) containing iodine concentrations of 0.5, 1, 2, 5, 10, and 15 mg/mL was scanned using various scanners with head and neck and brain protocols at 100 kV / (Sn) 140 kV and 80 kV / (Sn) 140 kV, respectively. To evaluate the feasibility of using virtual non-contrast (VNC) images for dose calculations, a CT density phantom (CTDP) was scanned to produce a range of spectral images, including mixed-energy images (MEI) (composed of 60% low-kV images and 40% high-kV images) and virtual monochromatic images (VMIs) at energies of 50, 70, 75, 80, 120, and 190 keV. (2) Limit of low iodine concentration: The limit of quantification (LOQ) for iodine maps was tested in a 3D-printed phantom with vessel diameters of 15, 10, 5, and 2 mm, using fat and liver as background materials, and featuring seven iodine solutions ranging from 0.25 mg/mL to 20 mg/mL.

Results: (1) **Material decomposition accuracy:** When comparing the Hounsfield unit (HU) accuracy of various materials in the CTDP phantom to the treatment planning system (TPS) (Fig. 1A), results were within 50 HU for mixed-energy and 75 keV images, and within 100 HU for 70 keV and 80 keV images. The HU accuracy of VNC images remained within 20 HU for both S and L iodine phantoms, irrespective of beam hardening corrections (Fig. 1B). Due to DE overestimating the contrast material (CM) in higher-density bone materials (CB2-50 and inner bone), the HU exhibited inaccuracies exceeding 100 HU (Fig. 1C).

(2) **Limit of low iodine concentration:** The LOQ was 0.5 to 1 mg / mL for vessels ≥ 10 mm, and 0.5 to 5 mg/mL for vessels ≤ 5 mm, as shown in Fig. 2. Spearman analysis demonstrated that the correlation of LOQ to the scanned conditions was as follows: filter (CC = 0.235, $p < 0.01$), diameter (CC = 0.225, $p < 0.01$), scanner (CC = -0.196, $p = 0.01$), and protocol (CC = -0.086, $p = 0.27$). LOQ was improved in CT scans with a tin filter. This is likely due to the improved energy separation provided by the tin filter or the low-energy selection of kilovolt peak.

Scientific Significance: Material decomposition accuracy was satisfactory. Iodine mapping quantifies concentrations from 0.5 mg/mL to 1.0 mg/mL in scanners with a filter, which provides improved energy separation. LOQ increases with smaller target sizes.

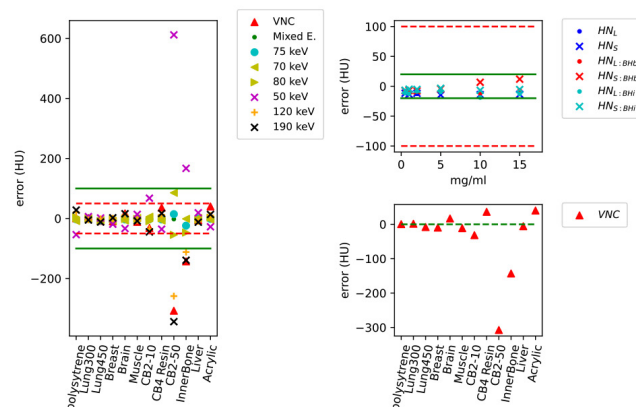


Fig. 1: Hounsfield unit (HU) calculation accuracy: (A) HU accuracy of materials in CT density phantom (CTDP) from different spectral images compared with the HU curve of planning system; (B) HU accuracy of iodine with or without the beam hardening correction; and (C) materials in virtual non-contrast (VNC) images. keV = kilo-electron volt; BHB and BHI denote beam hardening correction for bone and for iodine, respectively.

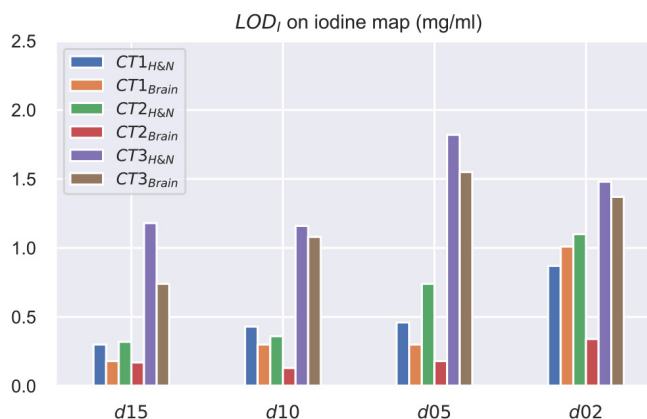


Fig. 2: Bar chart illustrating the limit of quantification (LOQ) for the iodine samples on iodine images. Samples CT1 & CT2 were acquired with a tin (wSn) filter. "d" denotes vessel diameter.

Potential Clinical Impact: The change in HU (Δ HU) of the original images, along with precise iodine quantification, may serve as significant biomarkers for informed clinical decision-making.

Acknowledgments: Jason Ocana from the Biomedical Engineering shop provided assistance in building a customized 3D-printed iodine phantom. This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Adaptive Lung Radiotherapy Planning with Expedited Constrained Hierarchical Optimization (ECHO) - Empowered Knowledge-based Models on Ethos (E3)

LiCheng Kuo¹, Ellen D. Yorke¹, Michelle Savacool¹, Albert Kuo¹, Laura I. Cerviño¹, Masoud Zarepisheh¹, Andreas Rimner², Pengpeng Zhang¹, Joseph O. Deasy¹, Jean M. Moran¹, and Seng Boh Lim¹

¹Department of Medical Physics and ²Radiation Oncology

Motivation: The goal of the study is to investigate the benefits of adapting the optimization capabilities of ECHO within the Ethos system by incorporating a knowledge-based planning (KBP) model pretrained on ECHO-generated Pareto optimal plans for online adaptive radiotherapy (oART) planning of conventionally fractionated lung treatments.

Methods: Rapid innovations in hardware and software have brought commercial online adaptive radiotherapy (oART) systems into clinical use. A key challenge in oART is generating high-quality treatment plans that account for daily anatomical changes within the limited time available during patient setup. The Ethos Adaptive RT platform uses an intelligent optimization engine (IOE) to create plans from user-defined templates designed to emulate experienced planners. Pogue et al. showed that Ethos can produce plan quality comparable to manual and knowledge-based planning (KBP) approaches for locally advanced lung cancer [1]. However, the impact of incorporating KBP models into Ethos planning has not been investigated.

RapidPlan, a KBP tool in the Eclipse treatment planning system, can generate consistently high-quality plans efficiently. As with most AI-based models, performance depends strongly on training data quality and may require iterative refinement [2]. Frequent changes in clinical constraints, treatment techniques, and protocols can also make model maintenance challenging.

At MSK, we developed the fully automated intensity-modulated treatment planning system ECHO. ECHO eliminates the trial-and-error planning process by automatically generating Pareto-optimal plans with improved speed and efficiency [3]. Its integration with RapidPlan for prostate bed irradiation has been explored previously by our group [4]. However, the current Ethos oART workflow remains a closed system that does not allow third-party software during initial or adaptive replanning.

Results: Seventy-six treatment plans for conventionally fractionated lung treatment (2 Gy × 30 fractions) were generated using our in-house ECHO system. Sixty-six plans were randomly selected to train a commercial KBP model, and the remaining 10 cases were used for validation. For each validation case, four to five adaptive plans with different beam geometries were generated for the ring gantry delivery system, with and without the trained KBP model. Plan quality was evaluated using clinical dose metrics for target coverage and organ-at-risk (OAR) sparing, and metric ratios were calculated to assess the impact of the KBP model.

Planning target volume coverage and OAR dose metrics from all plans met all department guidelines. Compared with plans without the KBP model, the mean ratios of target metrics ranged from 0.974 to 1.003 with statistically insignificant deviations ($p > 0.01$). Esophagus mean dose, heart mean dose, and V30Gy were significantly lower with KBP ($p < 0.0001$, $p = 0.0004$, and $p = 0.0003$, respectively).

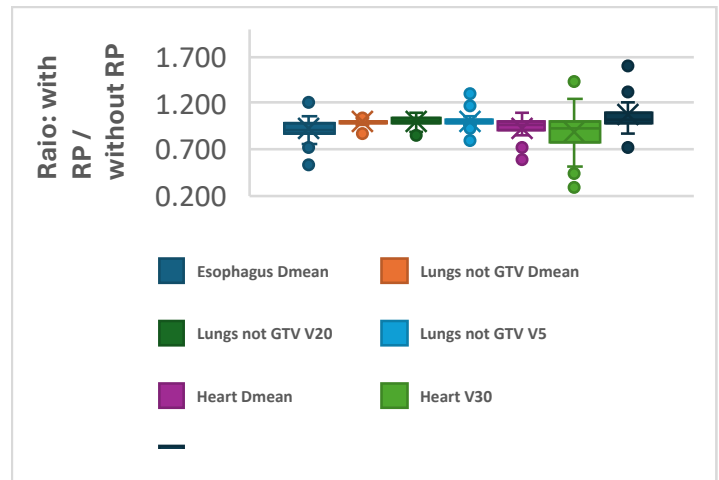


Fig. 1: Ratios of dosimetric metrics of Ethos plans with and without RapidPlan (RP) model for different organs at risk. P values are above each metrics. GTV: gross tumor volume

Lungs (excluding gross tumor volume) showed minimal deviations in mean dose and V20Gy/V5Gy. Spinal cord maximum dose was slightly higher (1.068 ± 0.018), but statistically insignificant ($p = 0.018$) and remained within department guidelines.

Scientific Significance: We successfully adapted ECHO's optimization capabilities for delivery in the Ethos system by incorporating a pretrained KBP model based on ECHO-generated Pareto-optimal plans for conventionally fractionated lung radiotherapy. ECHO generates high-quality training plans efficiently, allowing models to be updated when new clinical constraints arise and producing optimal planning goals for daily anatomy changes during initial and online oART.

Potential Clinical Impact: This method will be validated on more preclinical cases before real clinical oART of conventionally fractionated lung radiotherapy is rolled out, and more KBP models based on ECHO plans will be trained for other oART treatment sites. For example, the scope will be expanded to other lung fractionations, including SBRT.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Super-Resolution Cone-Beam CT (CBCT) on a New Generation Flat Panel Imager on a C-arm Gantry Linear Accelerator

LiCheng Kuo¹, Feifei Li¹, Yabo Fu¹, Hao Zhang², Laura Cerviño¹, Jean M. Moran¹, Xiang Li¹, and Tianfang Li¹

¹Division of Radiotherapy Physics and ²Formerly Department of Medical Physics

Motivation: Modern radiotherapy relies on image guidance for accurate treatment delivery, with kilovoltage (kV) cone-beam CT (CBCT) providing real-time 3D anatomical visualization and reducing dose to nearby organs. However, CBCT image quality, particularly spatial resolution, often remains inferior to that of diagnostic CT. Although Varian Medical Systems’ new kV imaging panel offers improved resolution and smaller pixel pitch, clinically practical CBCT frame rates still require binning, which substantially reduces resolution and limits use of the panel’s full capability.

Methods: This feasibility study investigates the use of pix2pix [1], a deep-learning super-resolution (DLSR) technique, to develop a model that explores the maximum potential of the new kV imaging panel. The study focuses on evaluating the impact of DLSR on the spatial resolution of reconstructed CBCT images and exploring potential clinical applications.

Results: Seventy-two sets of paired lateral radiographic (LR) and super-resolution (SR) projections were obtained from a Rando head phantom and a thorax phantom at every 5° gantry angle for model training, yielding 144 paired images in total. LR acquisition parameters for the head and thorax phantoms followed the corresponding TrueBeam CBCT scan protocols. For SR projections, image quality was improved by using three times the milliampere-seconds (mAs) of LR projections together with a smaller focal spot.

Scan mode	Tube Energy	Panel Position	Low Resolution (Bin2x8HighGainContinuous) 1424 x 268, Large Focal Spot		Super-Resolution (Bin1x1) 2848 x 2144, Small Focal Spot	
			mA	mS	mA	mS
Head	100	Full	15	20	15	60
Thorax	125	Half	15	20	15	60

Table 1: Projection acquisition parameters at low- and high-resolutions.

The LR projections were upsampled to match the SR dimensions using bicubic extrapolation, then padded to a uniform size of 2944 × 2176 pixels for pix2pix training. A pre-trained pix2pix model was used. The loss function was defined as mean squared error (MSE) + β × total variation (TV), where MSE was computed between the 2 × 8 binned up-scaled LR image and the 2 × 8 binned predicted high-resolution (HR) image. β was set to 1 × 10⁻⁹. Training was performed for 4000 epochs using random 512 × 512 pixel crops, a learning rate of 0.0002, and instance normalization. The Catphan 604 phantom (Phantom Laboratory) was subjected to scanning using the head CBCT protocol to validate the performance of the model. A total of 501 LR projections obtained from this protocol were transformed into SR projections. Subsequently, CBCT reconstruction was performed on both the LR projections and the predicted SR projections using the Feldkamp-Davis-Kress algorithm implemented in the TIGRE toolkit [2].

Prior to reconstruction, we applied corrections for detector point spread, scatter, and beam hardening on the projections provided in the toolkit. Aside from the detector geometry settings, the reconstructed CBCT geometry remained identical between LR and SR projections. A comparison of image resolution between the CBCT reconstructed from LR projections and the CBCT reconstructed from predicted SR projections, focusing on section 1 of the phantom, is presented in Fig. 1. Notably, the line pair (lp) resolution significantly improved from 5 lp/cm to 8 lp/cm.

Scientific Significance: The developed model represents a promising approach for achieving super-resolution CBCT. It enhances the resolution of the raw data while preserving data fidelity and fully incorporating all necessary corrections.

Potential Clinical Impact: These advancements potentially offer significant advantages for clinical applications, such as improving image-guided radiation therapy setup accuracy for small lung lesions, fine lung substructure alignment, and spine treatments. We will acquire more phantom data with varied scanning protocols to train a more comprehensive model and validate the model with different phantoms and clinical patient CBCTs.

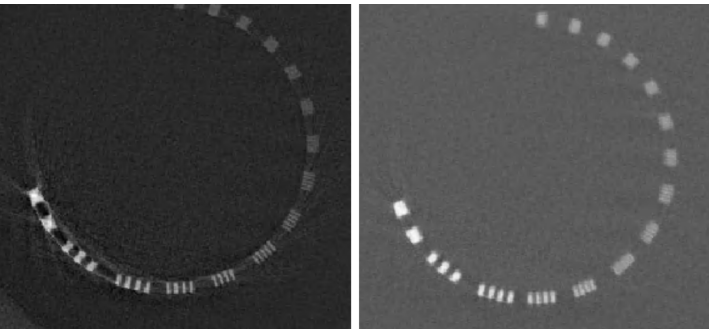


Fig. 1: Line-pair resolution comparison between cone-beam CT (CBCT) of low-resolution projections (Left) and CBCT of predicted super-resolution projections (Right).

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Commissioning Single-Fraction Dorsal Spinal Nerve Ablation Radiosurgery for the Treatment of Chronic Thoracoabdominal Wall Pain

Gary Lim¹, Lei Zhang¹, Stella Xing¹, Shih-Chi Lin¹, Michalis Aristophanous¹, James Mechalakos¹, Gary Kuo¹, L. and Yoshiya Yamada²

¹Division of Radiotherapy Physics and ²Department of Radiation Oncology

Motivation: Through ablating the dorsal spinal nerve root, image-guided stereotactic radiosurgery (SRS) offers new hope as a noninvasive treatment modality for patients with intractable thoracoabdominal wall pain. Here, we present the development and commissioning of this SRS technique on a standard C-arm linear accelerator (Linac).

Methods: An Institutional Review Board-approved phase I protocol will deliver 70-90 Gy in a single fraction to ablate the involved dorsal nerve root ganglion using a 10-megavolt flattening filter-free (10FFF) beam from a Linac with a high-definition multileaf collimator (HD-MLC). A custom small-field model was developed in Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA). The calculated output factor, S_t , and percent depth dose (PDD) were compared with stereotactic diode and CC04 ionization chamber measurements for field sizes (FS) $< 30 \times 30 \text{ mm}^2$ and $\geq 30 \times 30 \text{ mm}^2$, respectively. A commercial Monte Carlo-based independent dose verification system was commissioned for this application. The delivery method used a modification of the University of Alabama at Birmingham virtual cone (VC) technique, which employs arcs with fixed MLC-defined fields. The VC was modified for paraspinal treatments by changing the treatment arrangement, intrafraction monitoring, and dosimetry. The ExacTrac Dynamic system (BrainLab Inc., Germany) was commissioned for intrafraction monitoring with oblique stereoscopic kilovoltage imaging, referred to as ET-kV, using an anthropomorphic spine phantom (ASP) on a motion platform. An end-to-end (E2E) test was delivered with an ASP using MD-V3 Gafchromic™ film.

Results: As shown in Fig. 1, the output factors (S_t) were within 0.5% of measurements for FS $> 5 \times 5 \text{ mm}^2$. The PDDs were within 1.0% at depths of 10 cm and 20 cm for FS between $5 \times 5 \text{ mm}^2$ and $150 \times 150 \text{ mm}^2$. The S_t and PDD values of the independent verification system agreed within 3.0% and 1.0% for $5 \times 5 \text{ mm}^2$ and $10 \times 10 \text{ mm}^2$, respectively. An eight-pair partial-arc arrangement without couch rotation was optimized for the treatment, with a maximum dose ($D_{\max}$) to the spinal cord of 385-546 cGy. The tracking sensitivity of the ET-kV was 0.3 mm and 0.3° . The 2D dose cloud and profile from E2E are shown in Fig. 2. The dosimetric and localization uncertainties were 3.5% and 0.6 mm, respectively. The commissioning results meet the standards recommended by the American Association of Physicists in Medicine Medical Physics Practice Guideline (AAPM-MPPG) 9a, demonstrating a safe and precise treatment delivery process for single-fraction 90 Gy dorsal spinal nerve SRS.

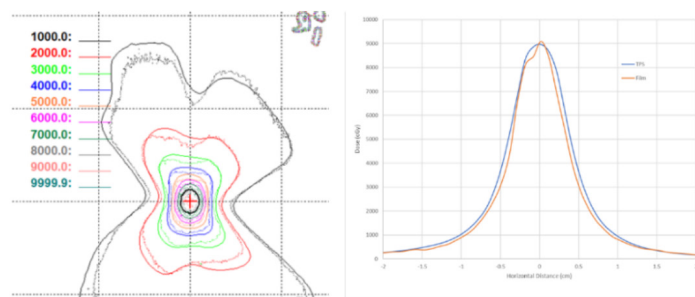


Fig. 2: Results of the end-to-end (E2E) test. Left: 2D dose cloud on the axial plane across the isocenter; Right: horizontal dose profile across isocenter accuracy.

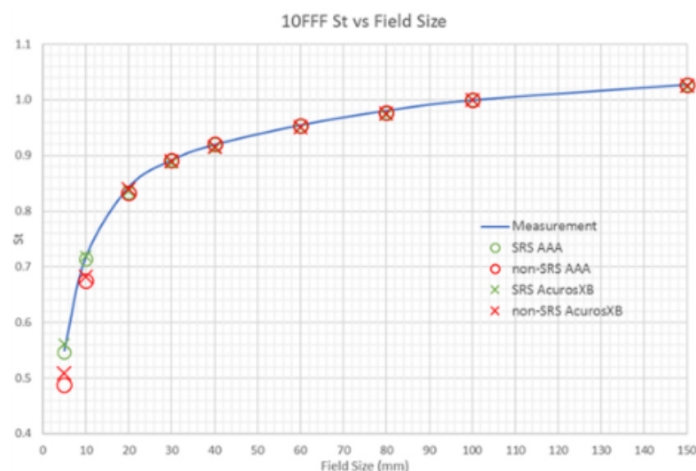


Fig. 1: Output factor (S_t) ratios between calculations (denoted by symbols) and measurements (blue line) at a source-to-surface distance of 100 cm and depth of 10 cm. Red and green symbols represent non-stereotactic radiosurgery (SRS) and SRS custom models, respectively. 10FFF: 10-megavolt flattening filter-free

Scientific Significance: This is the first functional SRS protocol at MSK and one of the first clinical trials worldwide to deliver ultra-high-dose extracranial SRS on a conventional Linac for treating chronic thoracic and abdominal wall pain.

Potential Clinical Impact: This novel SRS technique could potentially become a noninvasive alternative to alleviate chronic pain for patients who are otherwise faced with limited treatment options.

Acknowledgments: This project was partially funded by Varian Medical Systems (Palo Alto, CA). This work was also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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A Potential Pitfall and Clinical Solutions in Surface-Guided Deep Inspiration Breath Hold Radiation Therapy for Left-Sided Breast Cancer

Chuan Zeng¹, Qiyong Fan¹, Xiang Li¹, Yulin Song¹, LiCheng Kuo¹, Michalis Aristophanous¹, Laura Cerviño¹, Linda Hong¹, Simon Powell² and Guang Li¹

¹Division of Radiotherapy Physics and ²Radiation Oncology

Motivation: Modern radiotherapy relies on image guidance for accurate treatment delivery, with kilovoltage (kV) cone-beam CT (CBCT) providing real-time 3D anatomical visualization and reducing dose to nearby organs. However, CBCT image quality, particularly spatial resolution, often remains inferior to that of diagnostic CT. Although Varian Medical Systems' new kV imaging panel offers improved resolution and smaller pixel pitch, clinically practical CBCT frame rates still require binning, which substantially reduces resolution and limits use of the panel's full capability.

Methods: Sixty patients with left-sided breast cancer treated with surface-guided radiation therapy (SGRT) were analyzed: twenty abdominal DIBH (A-DIBH) patients with vertical chest elevation (VCE) ≤ 5 mm were prospectively identified, and 40 control patients were retrospectively and randomly selected for comparison. At simulation, both free-breathing (FB) and DIBH computed tomographic (CT) images were acquired, guided by a motion surrogate placed around the xiphoid process. For SGRT setups, the region of interest (ROI) was defined on the chest surface in CT images, with the surrogate-based setup as a backup. For each patient, the VCE was measured as the average of the FB-to-DIBH elevations at the breast and xiphoid process, together with abdominal elevation (Fig. 1). A-DIBH patients were identified in the control group. Of the twenty A-DIBH patients, ten were treated with volumetrically modulated arc therapy, and the rest with tangent fields. Clinical DIBH plans were recalculated on FB CT datasets to compare maximum dose, top 5% dose, mean dose, and $V_{30\text{ Gy}}$, $V_{20\text{ Gy}}$, and $V_{5\text{ Gy}}$ for the heart and lungs.

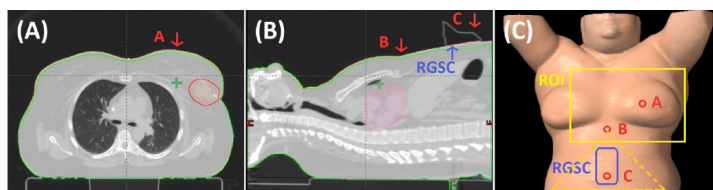


Fig. 1: Vertical body surface elevation at (A) breast, (B) xiphoid process and (C) abdomen. The default chest region of interest (ROI) (solid yellow rectangle) for surface-guided setup in free-breathing (FB) and thoracic deep inspiration breath hold (DIBH) monitoring, and an alternative abdomen ROI (dotted yellow triangle) for abdominal DIBH monitoring, are shown. The vertical chest elevation of the ROI was estimated as the average of those at points A and B. The Respiratory Gating for Scanners (RGSc) block is visible in the sagittal image (light gray; see "RGSC" arrow) with superimposed FB body contour (green).

Results: Patients with abdomen-driven breathing must be identified before treatment delivery, as shown in Fig. 2. Four opportunities to identify A-DIBH patients are presented: (1) during simulation, (2) during planning, (3) during plan check, and (4) on the first treatment day. Heart dose reduction from FB to DIBH is significant ($P < 0.01$) for this cohort.

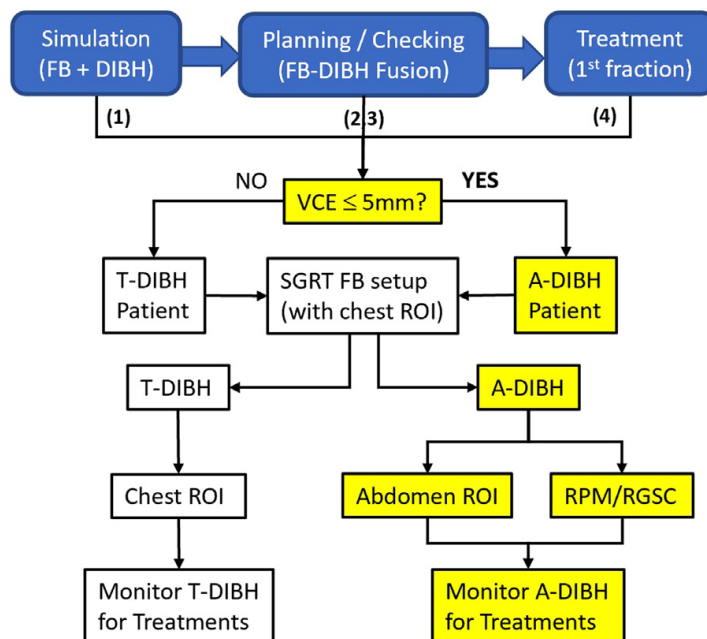


Fig. 2: Proposed clinical workflow for online identification of abdominal deep inspiration breath hold (A-DIBH) patients and adaptation of an alternative region of interest (ROI) for surface-guided radiation therapy setup, or use of real-time positioning management (RPM) / Respiratory Gating for Scanners (RGSc) as the alternative technique. Abbreviations: FB = free-breathing; DIBH = deep inspiration breath hold; VCE = vertical chest elevation.

Scientific Significance: The A-DIBH patient population is significant (15%), and they should be identified in the SGRT workflow and monitored accordingly.

Potential Clinical Impact: Instead of the conventional chest ROI in SGRT, a new abdominal ROI or an abdominal surrogate should be used.

Acknowledgments:

- This work is supported in part by the MSK Support Grant/ Core Grant (P30 CA008748).
- Drs. Bo Zhao, Wei Lu, Ellen Yorke, Feifei Li and Jeonghoon Park from Medical Physics for their help in identifying and collecting patient data from the radiation oncology clinics.

References:

Zeng C, Fan Q, Li X, Song Y, Kuo L, Aristophanous M, Cervino L, Hong L, Powell S, Li G. A potential pitfall and clinical solutions in surface-guided deep inspiration breath hold radiation therapy for left-sided breast cancer. *Advances in Radiation Oncology*. 2023;8(6):101276

Automation in External Beam Radiotherapy Plan Checks to Support Clinical Advancements, Improve Safety Barriers, Reduce Inter-user Variation, and Increase Efficiency

Sean Berry¹, Ying Zhou¹, Jianping Xiong², Jim Mechalakos¹, Cesar Della Bianca¹, Qiyong Fan¹, Jeonghoon Park¹, Ingrid Valencia Lozano¹, Pengpeng Zhang², and Jean Moran¹

¹Division of Radiotherapy Physics and ²Computer Service

Motivation: The physics pretreatment plan check is the most effective individual quality control check for detecting high-severity radiation therapy incidents. The introduction of an automated plan check tool, initially developed at the University of Michigan and later co-developed between our two institutions, has been shown to increase efficiency and decrease errors at both institutions.

Methods: The current phase of development is focused on using automation to ensure the safety of clinical rollouts for new and evolving treatment techniques. It also focuses on incorporating our custom automated checkers within a commercial platform to leverage the resources of a commercial company while retaining the customization necessary for our clinic to continue to innovate. These efforts are organized as follows: (1) **Software Design:** The plan check tool, termed PCT, is a stand-alone application programming interface (API) script that interfaces with the Eclipse treatment planning system (Varian Medical Systems, Palo Alto, CA). As shown in Figure 1, the software analyzes the radiotherapy treatment plan against a list of automated rules and, for each check, returns an output of “pass” (result is consistent with expectations), “flag” (result is inconsistent with expectations), or “report” (information is given to the user for review and decision-making). There is also functionality for manual reminders to be included in the checklist, which the user can acknowledge.

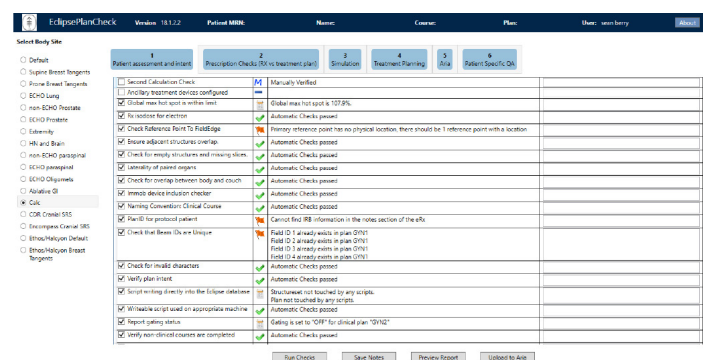


Fig. 1: The interface of the plan check tool.

(2) **Analysis of the software release cycle over the past five years:** An analysis of the number of new and updated automated checkers was performed to document the evolution of the software over the past five years. (3) **Co-development with a commercial partner:** Through a co-development agreement, we are collaborating with the company Radformation to have our custom checks handled through their commercial interface.

Results: As shown in Figure 2, the number of automated checkers increased from 78 in 10/2020 to 106 in 09/2024. We then pivoted to a collaboration with a commercial

partner, in which the partner supports the user interface and standard checkers, allowing us to focus on developing checkers that support our clinical innovations. Examples of such innovations include automated breast planning, nerve root ablation, volumetric modulated arc therapy for irradiation of the craniospinal axis, and a new bore-based adaptive radiotherapy linear accelerator (Linac) system.

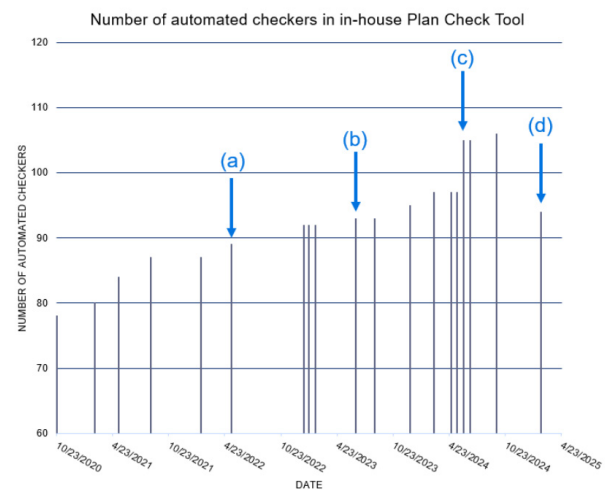


Fig. 2: Support for various clinical initiatives is highlighted: (a) upgrade of Eclipse (Varian Medical Systems, Palo Alto, CA) software version, (b) introduction of automated breast planning, (c) transition to delta couch shift and volumetric modulated arc therapy craniospinal irradiation, and (d) adoption of a commercial tool, where a number of our checkers were retired in favor of their commercial analogues.

Scientific Significance: Our automation has demonstrably increased the effectiveness and efficiency of this vital clinical task and contributed to a paradigm shift in physicists' approach to their work

Potential Clinical Impact: Automation of external beam plan checks, particularly for new and innovative clinical treatments and techniques, reduces inter-user variation and increases efficiency. The integration of a commercial partner's software improves the user experience while retaining our ability to customize.

Acknowledgments:

- University of Michigan collaborators who were involved in initially developing the plan check tool: Kelly Paradis, Xiaoping Chen, Elizabeth Covington, and Katie Woch Naheedy
- Radformation co-development partners: Wayne Keranen, Hope Wright, William Meyers, Elisabeth Van Wie, and Kurt Sysock
- This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Quantitative Intrafractional Motion Monitoring in Paraspinal SBRT using a Proprietary Software Application

Qiyong Fan¹, Hai Pham², Pengpeng Zhang², Lei Zhang¹, Yabo Fu¹, John Cuaron³, Laura Cerviño¹, Jean Moran¹, Xiang Li¹, Tianfang Li¹
¹Division of Radiotherapy Physics, ²Medical Physics Computer Service, and ³Radiation Oncology

Motivation: High-dose spine radiation therapy requires precise motion monitoring to ensure patient safety and treatment quality, yet effective commercial solutions are lacking. We aim to develop proprietary software and a streamlined clinical workflow for seamless implementation across the MSK network.

Methods: (1) **Software Design:** The interface is built for intuitive use, minimizing disruption to the existing treatment workflow (shown in Fig. 1). Once treatment begins, the software automatically captures intrafraction motion review (IMR) images from the treatment machine. It then compares each IMR image to its reference digitally reconstructed radiograph (DRR) to detect vertebral motion in real time.

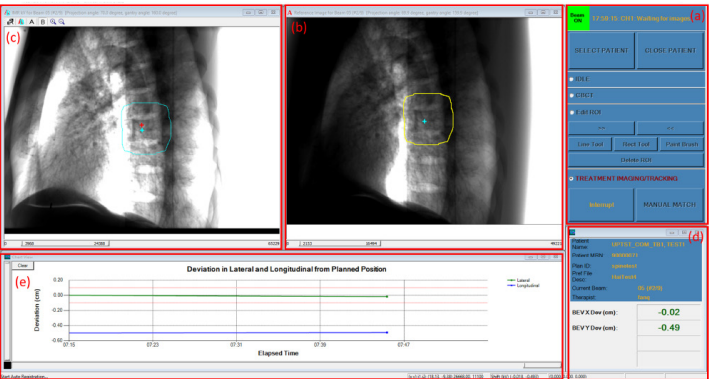


Fig. 1: The interface of the proprietary software consisting of five major panels: (a) workflow panel, (b) reference image panel, (c) intrafraction motion review (IMR) image panel, (d) patient/plan info and tracking results panel, and (e) graphic results panel.

(2) **Clinical Workflow:** After plan approval, planners use an Eclipse (Varian Medical Systems, Palo Alto, CA) plugin to generate the reference DRR and tracking region of interest. During treatment, therapists open the software and patient files, activate tracking mode before beam-on, and monitor motion updates. If motion exceeds thresholds, therapists' re-position the patient. (3) **Patient Studies:** We enrolled 84 paraspinal stereotactic body radiation therapy (SBRT) patients with sites spanning the full vertebral column. Prescription doses ranged from 24 Gy to 30 Gy, delivered in one to five fractions. Each plan used nine intensity-modulated radiation therapy beams. IMR was triggered every 200 to 500 MU per beam.

Results: (1) **Motion Statistics:** Among 1,371 IMR images studied, 36%, 17%, and 7% had motion exceeding 1.0 mm, 1.5 mm, and 2 mm, respectively, in either the X or Y direction. This underlines that accurate and quantitative motion monitoring is critical in paraspinal SBRT. (2) **Tracking Error:** 97% and 95% of the software registrations had a tracking error of $< \pm 0.5$ mm in the X and Y directions (shown in Fig. 2), respectively, indicating the software's high tracking accuracy for complex patient anatomy.

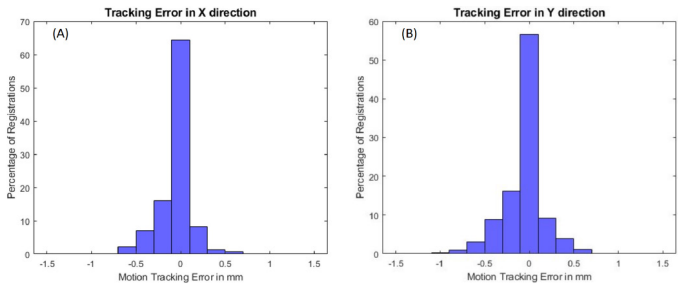


Fig. 2: Distribution of motion-tracking errors in X and Y directions.

(3) Sensitivity and Specificity

Table 1: Software specificity and sensitivity in guiding treatment interruption decisions.

Motion Threshold for Treatment Interruption	1 mm	1.5 mm	2 mm
True Positive	181	85	31
False Positive	37	17	8
False Negative	22	6	2
True Negative	397	529	596
Specificity	91.5%	96.9%	98.7%
Sensitivity	89.2%	93.4%	93.9%

(4) Example Cases with Large Motion Detected

Examples where the software detected large motion shifts are shown in Fig. 3.

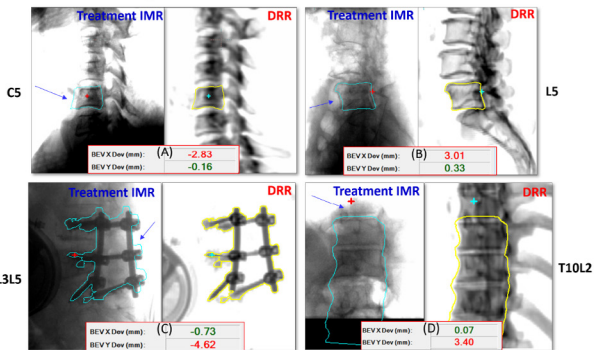


Fig. 3: Example tracking cases for (A) C5, (B) L5, (C) L3-L5 with hardware, and (D) T10-L2. IMR = intrafraction motion review; DRR = digitally reconstructed radiograph.

Scientific Significance: Accurate motion monitoring is critical for safe, high-quality paraspinal SBRT. Our software offers a practical, effective solution.

Potential Clinical Impact: Real-time motion monitoring improves treatment accuracy and outcomes and offers a scalable benefit to a broader patient population.

Acknowledgments: This work is supported in part by (a) a research grant from Varian Medical Systems and (b) the MSK Cancer Center Support Grant (P30 CA008748). We thank the Long Island Therapists and Physicists for their support and feedback.

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Short Arc Dynamic Cone-Beam CT Reconstruction via Spatiotemporal Gaussian Neural Representation for Markerless Prostate Tracking

Yabo Fu¹, Hao Zhang³, Weixing Cai¹, LiCheng Kuo¹, Laura Happersett¹, Pengpeng Zhang², Xiang Li¹, and Tianfang Li¹
¹Division of Radiotherapy Physics, ²Computer Service, and ³Formerly Department of Medical Physics

Motivation: To support adaptive radiotherapy that maintains target coverage while reducing normal tissue toxicities by providing rapid short-arc dynamic cone-beam computed tomography (CBCT) volumetric imaging of the prostate and adjacent organs-at-risk (OARs).

Methods: We propose a differentiable 4D Gaussian representation initialized from the setup CBCT acquired prior to treatment. Each Gaussian point encodes position, covariance, rotation, and density, enabling a compact and dynamic representation of the CBCT scene. A Gaussian deformation network — comprising a HexPlane encoder and a multi-head decoder — predicts spatiotemporal deformations to align rendered projections with measured ones, minimizing a combined L1 and structural similarity index (SSIM) loss. An adaptive control mechanism is used to prune low-contribution Gaussians and densify high-gradient regions, improving representation fidelity.

Figure 1 illustrates the primary components: a modified 3D Gaussian splatting framework tailored for X-ray imaging, and a deformation field network for dynamic modeling. The setup CBCT initializes the 3D Gaussian field, while projection images from both setup and intra-treatment phases are tagged with timestamps to model anatomical motion. The deformation network warps the 3D Gaussians to match each timestamp, producing rendered projections that align with the measured ones. An X-ray rasterization module renders the 3D Gaussians into 2D projections, which are compared with raw images to compute the total loss — a weighted sum of L1 and SSIM. The adaptive Gaussian control module updates point densities and scales based on accumulated gradients and predefined thresholds.

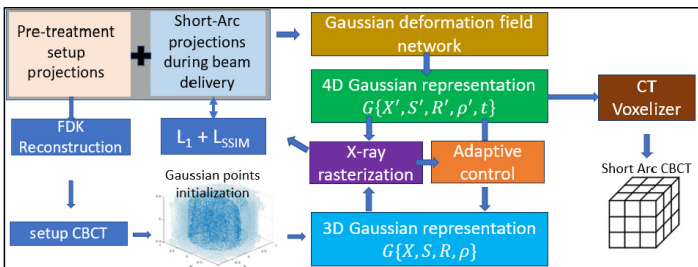


Fig. 1: The proposed dynamic 4D Gaussian representation network. FDK: Feldkamp-Davis-Kress CBCT: Cone Beam Computed Tomography SSIM: Structural Similarity Index

The Gaussian deformation network (shown in Fig. 2) consists of two primary components: a spatiotemporal structure encoder and a multi-head Gaussian deformation decoder. The encoder extracts dynamic motion features from the sequence, whereas the decoder predicts the necessary deformations for the Gaussian points.

The deformation network and the 3D Gaussians are jointly optimized using the same loss function.

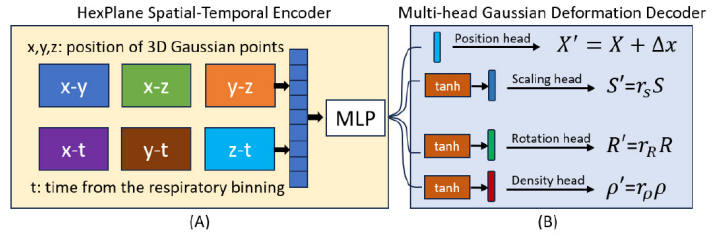


Fig. 2: The Gaussian deformation field network, consisting of the HexPlane spatial-temporal encoder (A) and the multi-head Gaussian deformation decoder (B).

Results: Short-Arc reconstruction with improved image quality was achieved.

Our method enabled high-quality reconstruction derived from only 30° of projection data. Figure 3 compares (A) Feldkamp-Davis-Kress (FDK) reconstruction using 210° projections, (B) our method using 30° projections, and (C) FDK with the same 30° projections. Prostate, spacer, and rectum contours were drawn on (A), and overlaid on (B) and (C). In (B), these structures remain clearly visible and anatomically consistent with (A), unlike (C), which suffers from significant blurring and artifacts.

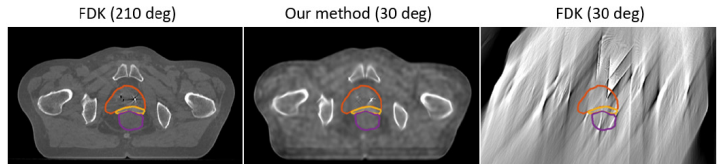


Fig. 3: (A) Feldkamp-Davis-Kress with full 210° projections; (B) our method with 30° short-arc; (C) Feldkamp-Davis-Kress with 30° short-arc. Contours denote the prostate, spacer, and rectum.

Scientific Significance: The proposed method overcomes projection sparsity in short-arc CBCT by learning temporally aware Gaussian deformations that incorporate prior anatomical information.

Potential Clinical Impact: This technique shows promise for markerless prostate and OAR tracking during volumetric modulated arc therapy and for accurate post-treatment dose reconstruction.

Acknowledgments:

- This work is supported in part by the MSK Cancer Center Support Grant/Core Grant (P30 CA008748).
- This work is also supported in part by the research grant from Varian Medical Systems.

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Y Fu, H Zhang, W Cai, H Xie, L Kuo, L Cervino, J Moran, X Li, T Li. Spatiotemporal Gaussian Optimization for 4D Cone Beam CT Reconstruction from Sparse Projections. 2025. arXiv:2501.04140

Single-Fraction Stereotactic Body Radiotherapy for Liver Metastases

Wei Lu¹, Eric Lin¹, Lakshmi Santanam¹, Sharif Elguindi¹, Hasti Hesami¹, Kiran Hudka¹, Wendy Harris¹, Tianfang Li¹, Bo Zhao¹, Xiang Li¹, Paul Romesser², Marsha Reyngold², and Christopher Crane²

¹Division of Radiotherapy Physics and ²Department of Radiation Oncology

Motivation: Single-fraction 35-40 Gy stereotactic body radiotherapy for liver metastases has been shown at other institutions to be safe and well tolerated, with excellent local control and long-term follow-up.

Methods: We collaborated with a peer institution to learn about their single-fraction liver metastases treatment methodology [1] and to then translate it into our institutional workflow for both a conventional C-arm linear accelerator (linac) and a magnetic resonance-guided linear accelerator (MR-Linac), in order to provide this treatment regimen to selected MSK patients.

Patient inclusion and exclusion criteria were defined by the physicians. A workflow from simulation through segmentation and treatment plan design, to pre-treatment imaging and treatment delivery, was established and tested. A planning study was performed to identify the optimal planning technique depending on the location and shape of the target, its proximity to relevant organs at risk (OARs), and the physician's planning priorities.

Results: A workflow (Fig. 1) was established and tested. Patient eligibility was defined as the presence of liver metastases, with a planning target volume (PTV) size of less than 100 cc. The tumor was expected to be at least 1 cm away from any gastrointestinal OARs. Because these patients were treated using deep inspiration breath hold (DIBH), patients were expected to demonstrate the ability to hold their breath for at least 20 s.

The treatment planning study established that 3D dynamic conformal arcs (DCA) are preferred due to reduced planning and treatment time. However, volumetric modulated arc therapy (VMAT) is preferred if critical OARs are within 1 cm of the PTV, the target has an irregular shape, there is relevant prior radiotherapy, or there are multiple targets. A comparison of these two treatment planning techniques is shown in Fig. 2.

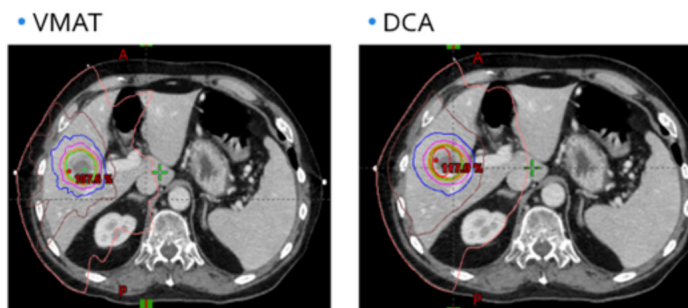


Fig. 2: Comparison of volumetric modulated arc therapy (VMAT) versus dynamic conformal arcs (DCA). Note the higher hot-spot (red isodose line) magnitude observed for DCA and that the hot-spot is not centered within the target (PTV, orange contour).

Because liver metastases are often poorly visualized on non-contrast CT imaging, which is used for pre-treatment patient alignment on a conventional C-arm linac, this workflow and procedure was also applied to a MR-Linac. The MR-Linac provides superior soft-tissue contrast resolution, resulting in reduced positional uncertainty during patient treatment.

Scientific Significance: The publication of our experience and workflows can aid in the translation of this technique, from being offered at an extremely limited number of large academic practices, to being more widely available.

Potential Clinical Impact: The development of this procedure introduces a new treatment paradigm for eligible MSK patients with liver metastases. This treatment technique significantly reduces the number of appointments that patients need to receive world-class healthcare.

Acknowledgments:

- Physics and physician collaborators at UT Southwestern Medical Center in Dallas, TX.
- The Long Island outpatient facility physics and therapy teams who contributed to drafting and testing the patient workflow.
- This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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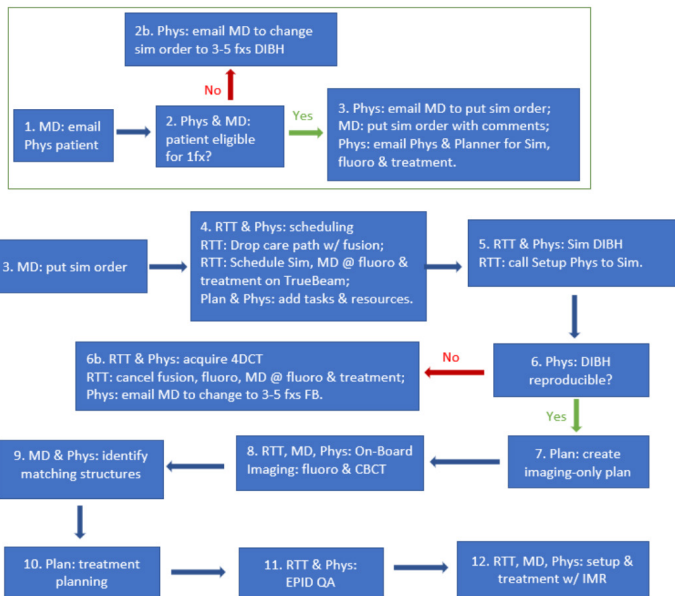


Fig. 1: Defined workflow from patient identification through simulation, planning, setup, and treatment.

Diffusion-based CBCT Image Reconstruction in Radiotherapy

Yabo Fu¹, Weixing Cai¹, LiCheng Kuo¹, Laura Cerviño¹, Jean M. Moran¹, Xiang Li¹, and Tianfang Li¹

¹Division of Radiotherapy Physics

Motivation: The diffusion model holds promise for accurately representing the underlying distribution of a patient's anatomy, enabling highly sparse or short-arc cone-beam CT (CBCT) reconstruction.

Methods: Diffusion-based image priors offer promise for CT reconstruction; however, their application is hindered by slow image reconstruction and hallucination artifacts. This study aims to investigate the potential of a patient-specific diffusion-based image prior for CBCT image reconstruction in a radiotherapy clinical workflow.

We performed both simulation and real-patient CBCT reconstruction studies to investigate the potential of a diffusion model. The patient's axial CT images were used with random shifts to train a patient-specific denoising diffusion probabilistic model (DDPM). Utilizing the trained model as prior knowledge, we applied it in sparse-view CBCT reconstructions with 20 and 90 equiangular projections on treatment day.

Results: For the simulation, our method (Algorithm 2) with $N = 5$ demonstrated superior performance across all evaluation metrics compared with Algorithm 1, irrespective of the parameter settings ($N = 5$ or $N = 20$). These findings underscore the effectiveness of Algorithm 2 in achieving enhanced image quality. To demonstrate the superiority of diffusion-based methods, the traditional conjugate-gradient least square (CGLS) iterative reconstruction results were also provided. For real clinical projection data, the patient was scanned with half-fan geometry (imager offset), with a total of 897 projections acquired across a 360-degree circular trajectory. For sparse-view CBCT image reconstruction testing using the proposed method, we randomly selected 20 and 90

the denoising diffusion implicit model sampling, we proposed a equiangular projections from the 897 projections. Leveraging CG-guided diffusion sampling mechanism shown in Fig. 1. We utilized strided diffusion steps of 30 instead of the conventional 1000 steps. CG iterative reconstruction was selected for its rapid convergence, which effectively complements the strided denoising diffusion steps. To reduce hallucination and expedite the sampling process, the proposed sampling scheme was initialized from step 15 with noise-blended reconstruction images. We utilized FDK for CBCT reconstruction using all available projections, thereby establishing the resultant images as ground truth for our evaluation.

Scientific Significance: This study introduces a patient-specific diffusion prior that effectively constrains sparse-view CBCT reconstruction, improving image fidelity under highly limited projection data.

Potential Clinical Impact: Diffusion model-based image reconstruction is a promising technique with the potential to generate high-quality images from sparse data acquisition. This innovation offers a solution for ultra-fast sparse-view and limited-angle CBCT image reconstruction, enhancing CBCT image quality, including for 4D CBCT, and shortening scanning time to potentially allow single breath-hold (~10 s) CBCT acquisition on a conventional TrueBeam platform. Additionally, it could address the issue of body truncation resulting from short-arc scans due to treatment couch collision, while also significantly reducing patient imaging dose.

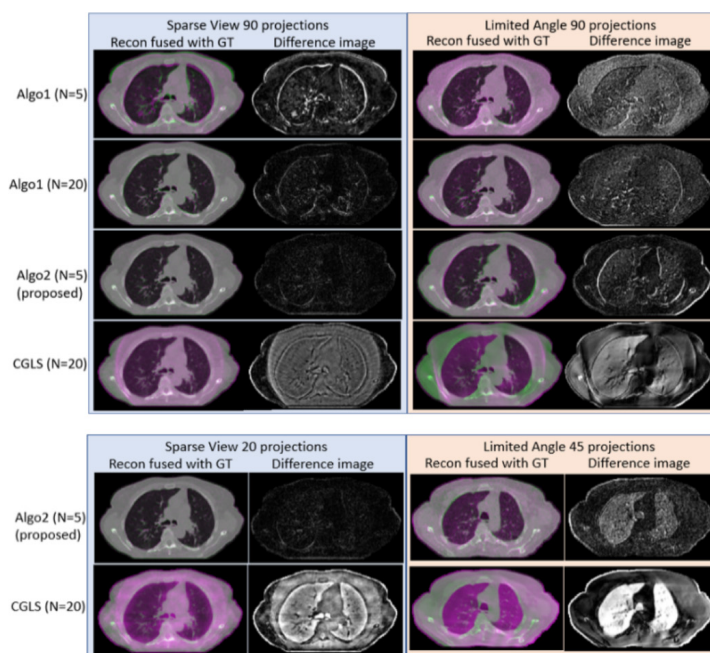


Fig. 1: Simulation study. The reconstructed images were fused with the ground truth (GT) to demonstrate the hallucination artifacts introduced during image reconstruction.

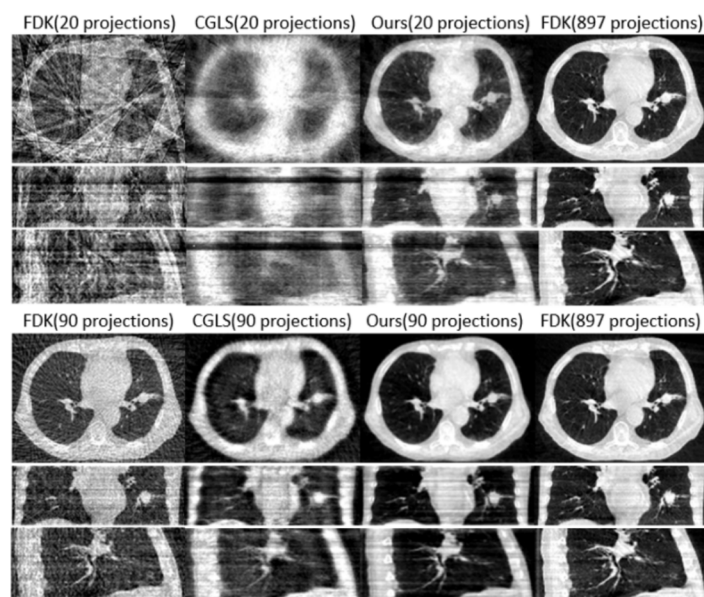


Fig. 2: Cone-beam CT reconstruction with real clinical projections. First to third columns: Feldkamp-Davis-Kress (FDK), conjugate-gradient least squares (CGLS) and our reconstruction. Last column: FDK reconstruction with all 897 projections.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

Establishing a Surface-guided Radiotherapy (SGRT) Program for Radiotherapy in the World's Largest SGRT Institution

Guang Li¹, Wei Lu¹, Yulin Song¹, Chuan Zeng¹, Qiyong Fan¹, Lei Zhang¹, Sang Kyu Lee¹, Songye Chi¹, Linda Hong¹, Michalis Aristophanous¹, Xiang Li¹, and Laura Cerviño¹

¹Division of Radiotherapy Physics

Motivation: To establish a clinical SGRT program at eight MSK campuses, the world's largest SGRT user, with 30+ AlignRT units (Vision RT, London, UK), by developing standardized SGRT procedures and workflows, and investigating new ideas for future SGRT applications.

Clinical SGRT applications have increased at an accelerating pace, reaching an unprecedented level. SGRT has demonstrated faster and more accurate patient setup compared with the tattoo-laser approach and has the potential to be applied across all disease sites. At MSK, 30+ TrueBeam/Ethos/Halcyon Linacs (Varian Medical Systems, Palo Alto, CA) are 100% integrated with SGRT systems, and additional SGRT applications are expected, but will rely on thorough evaluation before clinical implementation.

Methods: For all clinical SGRT studies, 2D kV or cone-beam CT (CBCT) was applied as the ground truth¹⁻⁴, focusing on: (1) **Developing a SGRT commissioning procedure for brain stereotactic radiosurgery (SRS)**¹⁻²: This procedure was developed to meet the high standard of 1.0-mm error tolerance in SRS and was applied at all MSK campuses. (2) **Assessing SGRT accuracy for brain setup**³: By capturing a SGRT verification image right after CBCT setup in 269 SRS patients, the AlignRT six-degree-of-freedom (6DOF) shifts represent the SGRT accuracy. (3) **Minimizing breast deformation using a two-step SGRT setup**³: Alignment of the ipsilateral arm was achieved using SGRT to minimize breast deformation and reproduce local node position (Fig. 1), which is impossible to achieve using any other setup techniques. (4) **Reproducing chest-wall-heart separation using SGRT vs. real-time position management (RPM) to guide deep inspiration breath hold (DIBH)**³: Two cohorts of breast patients' DIBH setups using SGRT or RPM were studied by comparing distances from the tangent field edge to the chest wall and heart. (5) **Assessing SGRT setup accuracy for breast DIBH vs. 2D kV**: Following a two-step breast DIBH SGRT setup procedure, the setup accuracy of SGRT and 2D kV was assessed against CBCT, which uses the skin and bone as landmarks for alignment. (6) **Handling thorax- and abdomen-driven DIBH in breast SGRT setup**³: It was first found that SGRT can only be applied to thorax-driven DIBH, as the simulation CT did not cover the abdomen, which can be monitored with RPM. (7) **Automatic region-of-interest (ROI) drawing for breast SGRT setup**³: Based on breast contour from Eclipse and a convolutional neural network, the automatic ROI model was trained and tested against manual ROI. (8) **Defining a valid ROI for abdominal DIBH SGRT setup**³: Using SGRT to reproduce diaphragm position for abdominal DIBH treatments, we found the best ROI with the highest external-to-internal correlation. (9) **Inferring spinal canal alignment using SGRT in head-and-neck setup**⁴: Using two ROIs (face and chest), SGRT setups were reproduced and verified with lateral photographic images to check anterior and posterior neck alignment. Further, CBCT images of 11 patients were used to assess surface and spine alignment and correlation. **Results:** (1) Based on the AlignRT error from commissioning tests across eight MSK campuses, the 6DOF SGRT motion

tolerance for SRS was determined, e.g., $\Delta\text{Vertical} = 1.5 \text{ mm}$. (2) The SGRT brain setup accuracy was found to be $1.0 \text{ mm} \pm 2.5 \text{ mm}$ and $0.1^\circ \pm 1.4^\circ$, which is useful for conventional brain treatment setup. (3) The uniform two-step breast SGRT setup procedure has been developed for all breast treatments and applied across eight MSK campuses, ensuring high-accuracy treatments. (4) SGRT setup offers consistently small variations in heart-beam distances compared with RPM in DIBH setups. (5) Compared with CBCT, SGRT, and 2D kV setup errors were comparably small; however, skin and bony alignments are inconsistent, so 2D kV should not be omitted. (6) SGRT using the breast ROI cannot set up abdominal DIBH, which can be identified and resolved by using RPM, eliminating the possibility of false DIBH setup for heart sparing. (7) The quality and consistency of auto-ROIs are higher than manual ROIs, based on three experts' blind evaluation, and their Dice similarity coefficient (DSC) is greater than 0.8. (8) A new ROI of non-rib-supported surface can infer diaphragm position from FB to DIBH with a correlation coefficient of 0.75. Therefore, the new ROI is preferable for the abdominal DIBH setup. (9) A two-ROI approach reproduces neck curvature, extending the SGRT ability to reproduce neck deformation and infer spinal canal position with $\text{DSC} = 0.84 \pm 0.04$ and mean distance to agreement = $1.0 \text{ mm} \pm 0.3 \text{ mm}$. This requires a high-precision SGRT setup to ensure the correlation.

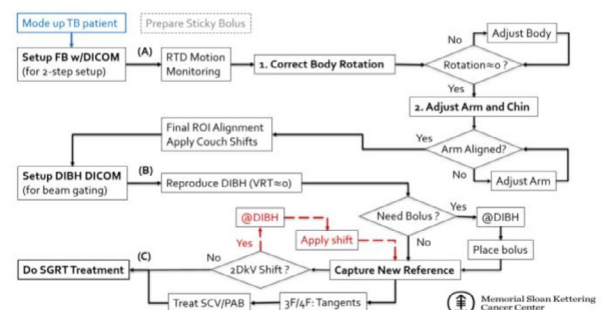


Fig. 1: Clinical two-step breast surface-guided radiotherapy (SGRT) setup and deep inspiration breath hold (DIBH) workflow. TB: TrueBeam (Varian Medical Systems, Palo Alto, CA); FB: free breathing; RTD: real-time delta; ROI: region-of-interest; SCV/PAB: supraclavicular/posterior axillary boost

Scientific Significance: Our studies unveil clinical benefits of SGRT to reproduce body deformation in real time and to infer internal organ alignment for the first time^{1,4}.

Potential Clinical Impact: Reliable and standardized SGRT brain and breast treatments are established, offering ease of use, low maintenance, and potential for other disease sites.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Real-time Catheter Tracking and Target/Organ Segmentation in Prostate High-Dose-Rate (HDR) Brachytherapy

Tonghe Wang¹, Yining Feng², Joel Beaudry¹, David Aramburu Nuñez¹, Marisa Kollmeier³, and Antonio L. Damato¹

¹Division of Radiotherapy Physics, ²Formerly Department of Medical Physics, and ³Radiation Oncology

Motivation: In the current procedure for high-dose-rate (HDR) prostate brachytherapy, physicians insert catheters under ultrasound guidance in the operating room. Catheter placement relies on physician experience, with no feedback on plan quality during implantation. In this study, we explored a novel automatic, real-time catheter tracking and target/organ segmentation method, which can be used with the current plan optimization program to potentially provide instant feedback on plan quality, permitting physicians to optimize needle placement and expedite the subsequent planning process.

Methods: A deep learning neural network was developed to take the last five frames of real-time ultrasound videos and provide the coordinates of all the catheters it detected, as well as the contours of the prostate, rectum and urethra, on the last frame. After the ultrasound probe scanned the entire prostate region, the catheter coordinates on each frame were then fitted to corresponding 3D lines to produce the line functions of each catheter in 3D space, and the segmented contours from each frame were stacked together. A total of 518 patients who underwent prostate HDR brachytherapy as a boost treatment in our clinic were retrospectively investigated, each of whom had ultrasound images acquired, contoured, and digitized for treatment planning after catheter placement. Among them, 482 patients were used for the training cohort, and 36 patients were used for the testing cohort. The median number of catheters per patient was 14.

Results: An exemplary comparison case of the results from the proposed method with the ground truth is shown in Fig. 1. Among the 477 catheters in the testing patients, the proposed method successfully detected 472 catheters, with an accuracy of 99.0%. The average displacement between the detected catheters and the ground truth catheters on 2D US images was 0.63 ± 0.55 mm. The mean Dice score for prostate segmentation was 0.90 ± 0.08 mm. The mean maximum distance of the rectum between ground truth and segmentation was 2.80 ± 1.71 mm across all patients. The mean centerline distance of the urethra between ground truth and segmentation was 0.76 ± 0.56 mm. The mean processing time per frame was 15.54 ± 1.31 ms.

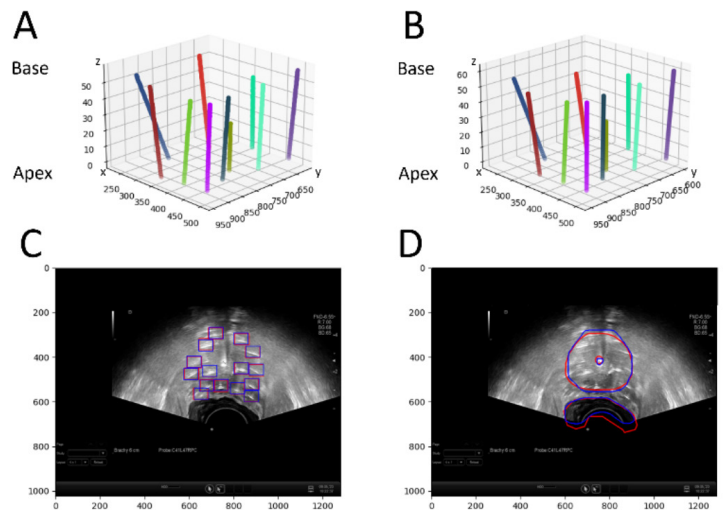


Fig. 1: An exemplary comparison case of the results from the proposed method with the ground truth. A and B: Catheters reconstructed in 3D space from clinical plan and from tracking results of the proposed method. C: Annotated catheters from clinical plan (red boxes) and from tracking results of the proposed method (blue boxes). D: Contours of prostate, rectum, and urethra from clinical plan (red) and from tracking results of the proposed method (blue).

Scientific Significance: Catheters and targets/organ can be tracked in real-time transrectal ultrasound (TRUS).

Potential Clinical Impact: The proposed method can potentially facilitate a real-time, US-based automatic treatment planning program for prostate HDR brachytherapy.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Wang T, Feng Y, Beaudry J, et al. Instant plan quality prediction on transrectal ultrasound for high-dose-rate prostate brachytherapy. *Brachytherapy* 2025;24:171-176.

A Streamlined and Efficient Workflow for Comprehensive 4DCT Imaging QA with Automated Analysis of Spatial Integrity and Image Quality

Yunjie Yang¹, Donghoon Lee¹, and Grace Tang¹
¹Division of Radiotherapy Physics

Motivation: Because a comprehensive 4D computed tomography (4DCT) quality assurance (QA) program can be resource-intensive, an efficient, scalable, and standardized QA protocol is needed.

Methods: An image quality phantom, Catphan®, was placed on the QUASAR™ motion platform (Fig. 1). The acquired image sets were automatically analyzed using a newly designed 4DCT analysis module in TotalQA, which we developed in collaboration with ImageOwl. Four-dimensional CT data were acquired on CT scanners from three major vendors and two different Catphan models. The metrics of interest for 4DCT QA were analyzed for image sets of all motion bins and compared with the stationary reference image set. Three broad categories of imaging tests for 4DCT QA were defined: spatial integrity, HU constancy, and image quality. The sensitometry plugs in the Catphan were used as motion surrogates for evaluating spatial integrity, including the dimensions of the plugs and the observed motion amplitude in the scans. HU values of the sensitometry plugs in different phases were evaluated for consistency. For image quality, spatial resolution, low contrast resolution, and image noise were evaluated.

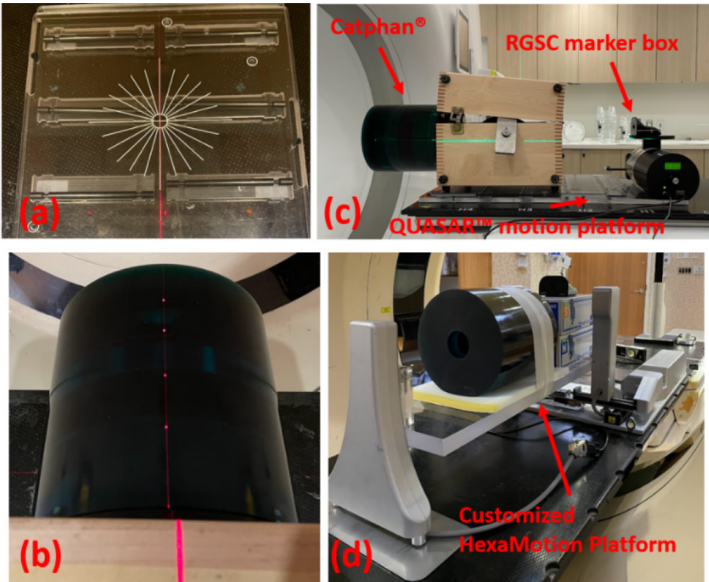


Fig. 1: Experimental setup for the 4DCT QA image acquisition: (a) the QUASAR motion platform was first aligned with the room laser, (b) the Catphan was then aligned with the room laser, (c) an overview of the setup, (d) the customized HexaMotion platform with the Catphan.

Results: Compared with the stationary reference CT, spatial integrity was within ± 1 mm (Fig. 2), and the HU values were within ± 2 HU in 4DCT for all phases. The spatial resolution was consistent although slightly higher noise was observed in the 4DCT images (Table 1). The automated analysis in TotalQA was completed in approximately 20 min per motion trace, improving efficiency by more than 80% compared with the manual workflow. The workflow is agnostic to both the CT scanner vendor and the Catphan model.

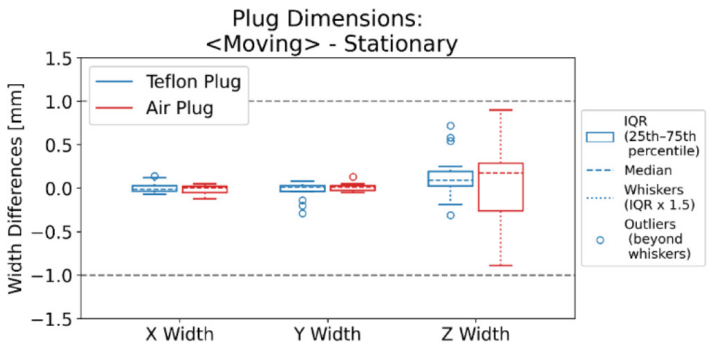


Fig. 2: Differences between the average plug dimensions measured in the moving images (i.e., 4DCT) and those measured in the stationary images. The phantom motion was along the Z direction. IQR: inter-quartile range.

	CT1			CT2			CT3		
	4DCT	Stat.	Avg. CT	4DCT	Stat.	Avg. CT	4DCT	Stat.	Avg. CT
Geom. Dist. [mm]	0.0±0.0	0.0	0.0	0.0±0.0	0.0	0.0	0.0±0.0	0.0	0.2
Spat. Res. [lp/cm]	6.4±0.3	6.5	6.1	6.1±0.2	6.4	5.7	6.3±0.1	6.4	5.9
Contrast	7.7±1.2	5.5	3.0	5.2±0.9	4.0	2.0	4.0±0.1	4.0	1.0
HU constancy [HU]	14.3±2.2	15.8	97.0	35.6±1.7	37.0	71.8	16.0±2.4	7.0	152.2
Uniformity [HU]	3.1±0.9	1.9	3.6	2.6±1.0	2.3	3.8	4.0±1.0	3.8	5.3
Noise [HU]	22.5±0.7	10.9	7.3	14.9±2.8	9.4	4.7	12.4±0.3	12.3	4.7
CNR-Low Contrast	1.9±0.1	3.8	4.8	2.9±0.5	4.4	6.9	3.7±0.1	3.7	7.9

Table 1: Comparison of image quality metrics among the moving (4DCT), stationary (Stat.), and the average CT generated from the 4DCT image sets (Avg. CT). The average values of the image quality metrics are presented alongside with the standard deviation across all binned images for 4DCT. CNR: contrast-to-noise ratio

Scientific Significance: An efficient and standardized QA workflow as proposed here will enable a risk-based quality management program.

Potential Clinical Impact: This work lays the foundation for an improved 4DCT QA procedure that is scalable and standardized across the whole OneMSK network.

- Acknowledgments:**
- Matthew Whitaker (ImageOwl)
 - Wendy Harris, Jeho Jeong, Shih-Chi Lin, Ellen Yorke, Lakshmi Santanam
 - This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Yang Y, Lee D, Whitaker M, et al. A streamlined workflow for comprehensive 4DCT imaging QA with automated analysis of spatial integrity and image quality. *J Appl Clin Med Phys*. (accepted). 2025. doi: 10.1002/acm2.70168

Adaptive Radiotherapy for Head and Neck Cancer with Automated Longitudinal Tracking

Eric Aliotta¹, Philip Lichtenwalner¹, Shira Abraham¹, Peng Zhang¹, Pengpeng Zhang², Yu-Chi Hu², Laura Cervino¹, and Michalis Aristophanous¹

¹Division of Radiotherapy Physics and ²Computer Service

Motivation: To reduce toxicity in head and neck radiotherapy by adapting treatment plans to account for changes in anatomy over time.

Methods: Anatomic changes are common during head and neck radiotherapy due to radiation effects and/or weight loss. Such changes can increase doses to normal tissues (and therefore treatment toxicity) compared to initial treatment plans. In adaptive radiotherapy (ART), treatment plans are updated to account for these anatomic changes and restore, or even improve upon, initial dose distributions (Fig. 1). Despite these advantages, ART is time- and labor-intensive and cannot be performed for all patients. We have implemented an automatic image tracking system (called the Automated Watchdog in Adaptive Radiotherapy Environment: "AWARE") developed in-house to help identify patients who will benefit most from ART.

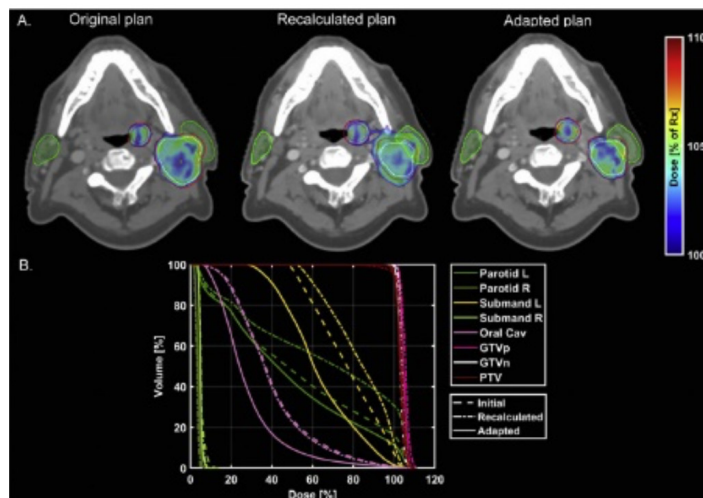


Fig. 1: An example of the original, recalculated and adapted plans, shown as dose maps (A) with the 100% dose color wash turned on and as dose volume histogram (DVH) plots (B).

Results: In a cohort of N = 46 patients, we found significant reductions in mean doses to key oropharyngeal organs with ART, including parotid glands (mean dose difference = -68.2 ± 197.7 cGy, p-value = 0.001), submandibular glands (-219.2 ± 291.2 cGy, p-value < 10^{-5}), and oral cavity (-238.7 ± 206.7 cGy, p-value < 10^{-5}). Systematic volume changes were also observed for tumors and normal tissues using AWARE (Fig. 2). A candidate trigger for adaptation based on parotid volume changes > 7% was identified (Fig. 3).

Scientific Significance: The key areas for improvement in clinical implementation are 1) patient selection to better target our efforts, and 2) improving efficiency of ART to increase access and benefit more patients. In addition to the volume-tracking described in this project, potential improvements in patient selection based on weekly dose assessments are currently under evaluation. Ongoing efforts towards improving efficiency and throughput are also underway based on new treatment technologies (e.g., MR-Linac and Varian Ethos) and treatment planning automation.

Potential Clinical Impact: This study demonstrates that ART can reduce normal tissue doses in head and neck cancer treatment and automated image tracking may be able to identify patients most likely to benefit.

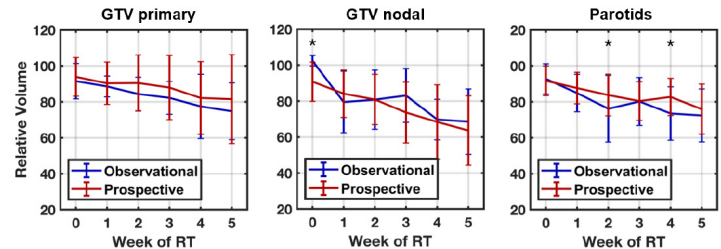


Fig. 2: Changes in gross tumor volume (GTV) and parotid gland volume observed over the course of treatment using the Automated Watchdog in Adaptive Radiotherapy Environment (termed AWARE).

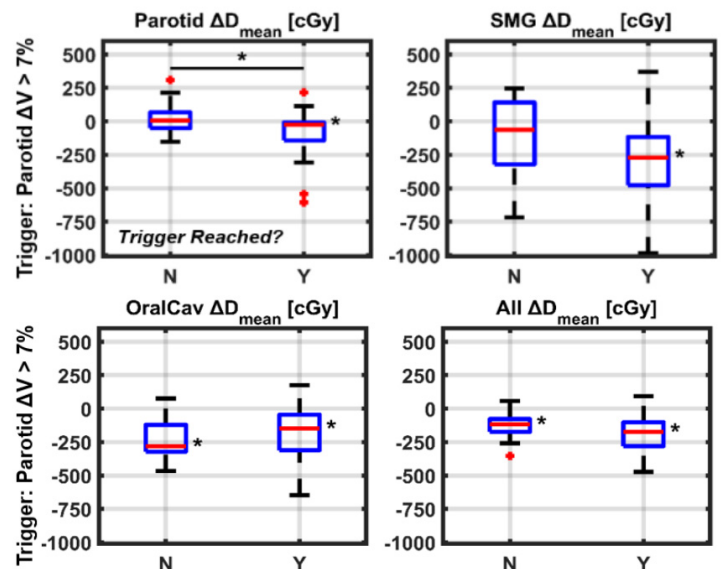


Fig. 3: Differences in mean dose of different organs-at-risk between adaptive and recalculated plans for a proposed trigger: Parotid volume change (ΔV) > 7%. Asterisks to the right of boxes indicate that a given distribution is significantly different from 0. Asterisks and lines above boxes indicate significant differences between the two distributions.

Acknowledgments: We appreciate our collaborators in Radiation Oncology, including Sean McBride, Daphna Gelblum, Nadeem Riaz, Linda Chen, Yao Yu, Kaveh Zakeri, and Nancy Lee. This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Simulation-Free Adaptive MR-Guided Prostate SBRT Using Diagnostic MRI

Nicolas Cote¹, Lian Sun¹, Angela Ng¹, Himanshu Nagar¹, Victoria Brennan¹, Ching-Yun Chan¹, Gabrielle Maggia¹, Paola Godoy Scribes¹, James Mechalakos¹, Eric Aliotta¹, Victoria Yu¹, and Neelam Tyagi¹
¹Division of Radiotherapy Physics

Motivation: Traditional prostate stereotactic body radiation therapy (SBRT) typically involves a dedicated computed tomography (CT) or magnetic resonance (MR) simulation scan and approximately one week of radiotherapy treatment planning before treatment initiation. Using online adaptive radiotherapy to enable daily anatomical and plan adjustments, we assessed the feasibility of substituting diagnostic MRI for simulation images. This simulation-free workflow would reduce the number of patient visits and expedite the timeline from consultation to treatment initiation.

Methods: We implemented population-based relative electron density (RED) overrides to enable dose calculation on diagnostic MR scans within the simulation-free workflow. Derived from retrospective analysis of over 100 prostate patients, such overrides were validated through dosimetric equivalence testing in a validation cohort of 10 patients, in which adaptive plans calculated with patient-specific RED assignments were compared with those using the population-based RED approach. Clinical target volumes (CTVs) and organs-at-risk (OARs) were retrospectively contoured on a separate set of 10 diagnostic whole-pelvis MR images, which served as surrogates for conventional simulation images. Adaptive plans were subsequently generated and compared with the clinically delivered adaptive plans to assess dosimetric equivalence. Fig. 1 shows the current adaptive workflow alongside the simulation-free workflow. A comprehensive Failure Modes and Effects Analysis (FMEA) was conducted to systematically identify and mitigate workflow risks. Prior to clinical implementation, the complete simulation-free workflow was tested under non-treatment conditions in a healthy volunteer and subsequently in a five-patient pilot cohort.

Results: Population-based RED assignments resulted in mean dose differences under 1%. The simulation-free workflow produced dosimetrically-equivalent adaptive plans compared with our standard workflow, producing mean deviations in clinically-relevant dosimetric parameters that were consistently below 2%. The most significant failure modes were identified, and corresponding corrective actions were implemented for patient safety prior to broader clinical implementation. The initial pilot phase, and subsequent clinical integration confirmed the practicality and efficiency of this new approach.

Scientific Significance: The resultant work validates the clinical feasibility and safety of a simulation-free workflow for prostate MR-Linac radiotherapy.

Potential Clinical Impact: The simulation-free workflow accelerates patient treatment initiation by removing the need for a simulation appointment. It also offers a pathway toward same-day consultation-to-treatment delivery scenarios.

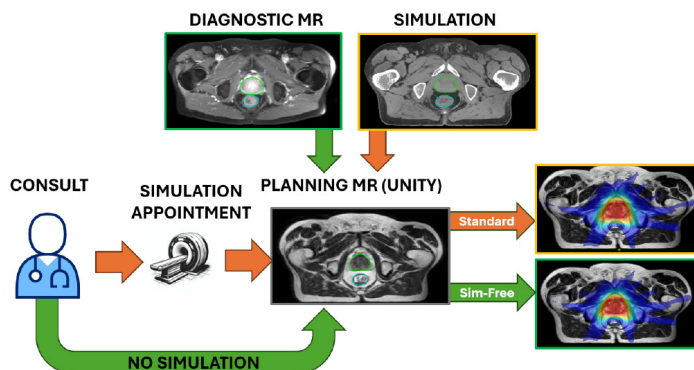


Fig 1: Overview of the simulation-free adaptive workflow for prostate stereotactic body radiation therapy (SBRT) on the magnetic resonance-linear accelerator (MR-Linac). Orange arrows depict the standard workflow, in which patients undergo a simulation appointment, and a reference plan is generated from the simulation images. Green arrows illustrate the simulation-free workflow, in which the simulation appointment is omitted, and the reference plan is generated directly from the patient's diagnostic MR images.

Acknowledgments:

This work was supported in part by the MSK Cancer Center Support Grant P30 CA008748.

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Innovative Treatment for Metastases: Lattice Radiation Therapy

Lei Zhang¹, Maria Chan¹, Yunjie Yang¹, and Atif Khan²

¹Division of Radiotherapy Physics, Department of Medical Physics and ²Department of Radiation Oncology

Motivation: Different from conventional radiotherapy, spatially fractionated radiation therapy (SFRT) delivers highly inhomogeneous dose distributions with alternating high- and low-dose regions within the tumor, which is believed to activate unique radiobiological response and holds new promise for large tumors that are not amenable to conventional radiotherapy. Here, we present our work on implementing the SFRT technique at MSK for the first time to treat extracranial soft tissue metastases.

Methods: Lattice radiation therapy (LRT), the latest form of SFRT, employs modern technological advancements in planning and treatment delivery to achieve spatial modulation in three dimensions. Preclinical and early clinical trials have demonstrated the remarkable effectiveness of LRT in managing certain bulky metastatic and primary tumors, with successes in local control and minimal toxicity. We commissioned LRT using volumetric-modulated arc therapy (VMAT), which can be delivered using a standard C-arm linear accelerator. This technique is being successfully implemented in an Institutional Review Board (IRB)-approved clinical trial.

The LRT plan dose distribution is characterized by a lattice pattern that consists of spherical vertices placed within the gross tumor volume (GTV). The vertices are typically 1-2 cm in diameter, well separated throughout the volume, and serve as the planning targets to deposit ablative “peak” dose levels (20-25 Gy in a single fraction), whereas the dose between vertices is minimized to achieve “valley” dose regions (5-7 Gy), hence the spatial modulation. The high-dose vertices are kept away from any critical organs. The LRT plans were created in the Eclipse treatment planning system (TPS) (Varian Medical Systems, Palo Alto, CA) using VMAT with 4-5 coplanar arcs. Dose calculation is performed using a 6-MV flattening filter-free (FFF) photon AAA beam model. An example LRT plan is shown in Fig. 1, illustrating the distinctive alternating high- and low-dose pattern.

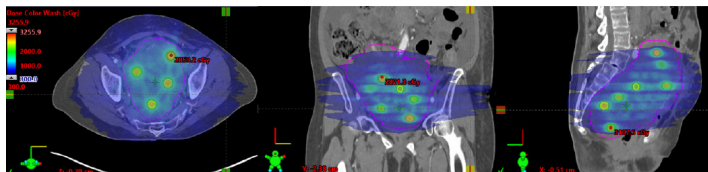


Fig. 1: Dose distributions in a Lattice radiation therapy (LRT) plan, delivering a single fraction of 24 Gy to 20 vertices within the gross tumor volume (GTV).

Results: Dosimetric validation was performed using preclinical LRT plans created in a solid water phantom, as well as the clinical treatment plan for the first patient. Dose calculation was first verified using a Monte-Carlo based calculation engine. Measurements were subsequently performed using three dosimetry systems: 1) Gafchromic

EBT-XD films (Ashland Inc., Bridgewater, NJ) at various depths in a multi-slab solid water phantom, 2) a high-resolution complementary metal-oxide-semiconductor (CMOS) 2D detector array in a tissue-equivalent cylindrical phantom, and 3) electronic portal imaging device (EPID) portal dosimetry.

Dosimetric validation for LRT poses unique challenges due to plan complexity and the demand for high spatial resolution. The results of this work demonstrated consistently high dosimetric accuracy using three measurement methods and independent dose calculations across all preclinical and clinical plans. The results of film dosimetry are shown in Fig. 2, illustrating both the agreement between TPS calculations and measurements in the 2D dose distribution and the distinctive peak-to-valley dose profile achieved.

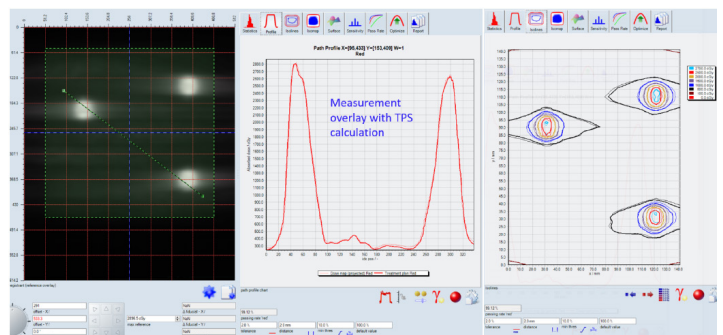


Fig. 2: Profiles and dose overlay of vertices (targets) between film and treatment planning system (TPS) calculations, shown in a screenshot of FilmQA Pro™.

Scientific Significance: We have demonstrated the successful development and commissioning of the first LRT technique at MSK for treating bulky extracranial metastases. Two patients have been treated with this technique to date under an IRB-approved clinical trial.

Potential Clinical Impact: We plan to further improve our technique with automated vertex placement for improved consistency and quality assurance (QA), which will allow this technique to be expanded for use as a standard of care in the future. We expect that our clinical experience with LRT, combined with the findings from the clinical trial, will help the community to uncover the underlying radiobiological mechanism of SFRT.

Acknowledgments: Thanks to Michael Hazoglou, Ase Ballangrud-Popovic, Joshua Feldman, Gary Lim, Jun Lin, Michalis Aristophanous, James Mechalakos, Lakshmi Santanam, Laura Cerviño, Jean Moran, Paul Romesser for supporting this work.

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748) and Varian Medical Systems.

A Novel Quality Assurance Procedure for Trajectory Log Validation Using Phantom-less, Real-Time Latency Corrected EPID Images

Seng Boh Lim¹, Benjamin J. Zwan², Danny Lee², Peter B. Greer^{2,3}, and Dale Michael Lovelock¹
¹Division of Radiotherapy Physics, Department of Medical Physics, Memorial Sloan Kettering Cancer Center,
²CalvaryMater Newcastle Hospital, and ³University of Newcastle

Motivation: The use of trajectory log files for routine patient quality assurance is gaining acceptance. Such use requires validating the trajectory log itself. However, accurately localizing a multileaf collimator (MLC) leaf while it is in motion remains a challenging task. We propose an efficient, phantom-less technique using the electronic portal imaging device (EPID) to verify the dynamic MLC positions with high accuracy.

Methods: Measurements were made on four Varian TrueBeam linear accelerators (Linacs) equipped with Millennium 120 (M120) MLCs. Two machines were equipped with the S1000 EPID, and two were equipped with the S1200 EPID. All EPIDs were geometrically corrected prior to measurements. EPID measurements were acquired in dosimetry mode using a frame grabber card directly linked to the Linac. All leaf position measurements were corrected both temporally and geometrically. The readout latency of each panel, as a function of pixel row, was determined using a 40 × 1.0 cm² sliding window (SW) field moving at 2.5 cm/s orthogonal to the row readout direction (as shown in Fig. 1). The latency of each panel type was determined by averaging the results from the two panels of that same type. Geometric correction was achieved by computing leaf positions with respect to the projected isocenter position as a function of gantry angle. This position was determined by averaging the central axis location of fields acquired at two collimator angles of 90° and 270° (as shown in Fig. 2). The radiological-to-physical leaf-end position was determined by comparing the measured gap with that obtained using a feeler gauge.

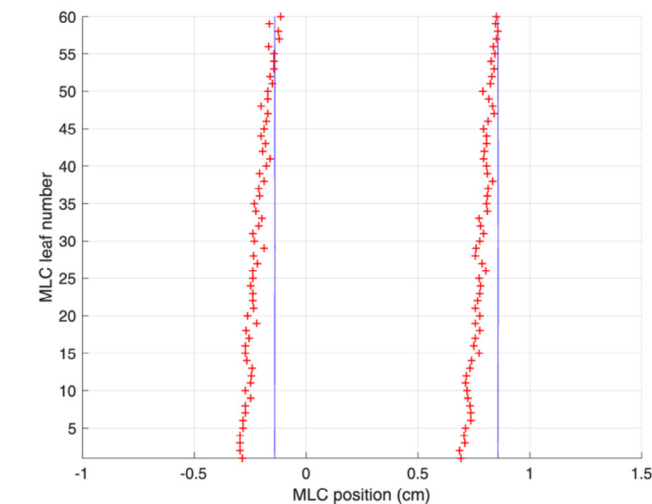


Fig. 1: A snapshot of a SW slit delivery, which shows the false positive error of the uncorrected EPID (red crosses) caused by read-out latency, where the blue line is the expected position. MLC: Multileaf collimator

Results: The radiological-to-physical leaf position difference was found to be 0.1 mm. With geometric and latency corrections applied, the proposed method improved the detection of dynamic MLC leaf positions, reducing error from ≤ 1.0 mm to ≤ 0.2 mm across all leaves (as shown in Table 1).

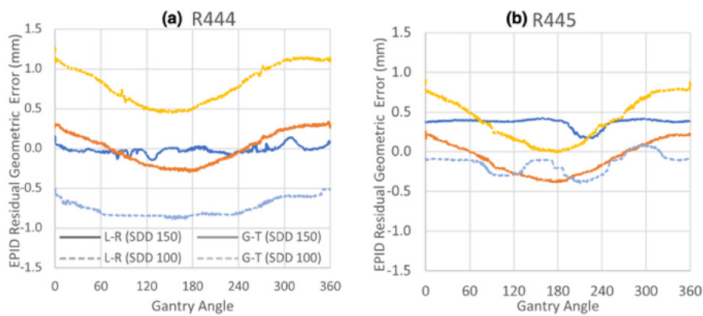


Fig. 2: Residual geometric error of the electronic portal imaging device (EPID) in the gun-target (G-T) and left-right (L-R) directions at source-to-surface distances (SSDs) of 100 cm and 150 cm for two EPID panels: (a) R444 equipped with an aS1200 EPID and (b) R445 equipped with an aS1000 EPID.

Table 1: Summary of the average leaf position error for static and dynamic leaf motion traveling at 2.5 cm/s.

Average leaf error (mm)	A		B	
	Uncorrected	Corrected	Uncorrected	Corrected
Static				
Mean	−0.79	0.08	−0.59	0.28
Range	0.22	0.22	0.34	0.34
Max standard deviation	0.06	0.06	0.06	0.06
Dynamic (0.30 cm/s)				
Mean	−0.92	−0.05	−0.69	0.18
Range	0.32	0.22	0.38	0.29
Max standard deviation	0.16	0.15	0.16	0.16
Dynamic (1.25 cm/s)				
Mean	−0.90	−0.02	−0.70	0.18
Range	0.60	0.21	0.64	0.29
Max standard deviation	0.31	0.18	0.28	0.17
Dynamic (2.5 cm/s)				
Mean	−0.84	0.03	−0.72	0.16
Range	0.98	0.23	0.98	0.28
Max standard deviation	0.54	0.27	0.46	0.17

Scientific Significance: Time delay and panel residual error corrections improve EPID-based MLC position measurement.

Potential Clinical Impact: These improvements provide the accuracy necessary to validate the use of trajectory logs for patient-specific quality assurance.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

References:
Lim, S.B., Zwan, B.J., Lee, D., et al, A novel quality assurance procedure for trajectory log validation using phantom-less real-time latency corrected EPID images. J Appl Clin Med Phys, 22: 176-185. <https://doi.org/10.1002/acm2.13202>

Real-time Markerless Lung Tumor Tracking using Deep Learning-Based Target Decomposition Technique

Yabo Fu¹, Pengpeng Zhang², Qiyong Fan¹, Weixing Cai¹, Hai Pham², Laura Cerviño¹, Jean M. Moran¹, Tianfang Li¹, and Xiang Li¹
¹Division of Radiotherapy Physics and ²Computer Service

Motivation: To support planning margin reduction in lung stereotactic body radiation therapy (SBRT) by enabling direct tumor tracking using on-board imager kilovoltage (kV) images during treatment.

Methods: A patient-specific deep learning model was developed using a conditional generative adversarial network (Pix2Pix) to generate synthetic decomposed target images (sDTIs) from real-time kV projections. This approach enhances tumor visibility by removing overlapping anatomical structures. Fig. 1 shows the target decomposition process. Training data consisted of digitally reconstructed radiographs (DRRs) and corresponding decomposed target images (DTIs), derived from segmented, lung-only simulation CT volumes. Data augmentation involved random 3D translations of the CT to simulate respiratory variability, yielding approximately 9,000 DRR-DTI pairs per patient.

During treatment, triggered intrafraction motion review (IMR) images were processed through the trained model to produce sDTIs in real time. Tumor localization was performed via template matching between sDTIs and DTI templates generated from the planning CT. Nine patient datasets were retrospectively collected under institutional review board-approved protocol MSK14-225 at MSK. Three CalypsoTM beacon transponders (Varian Medical Systems, Palo Alto, CA) were bronchoscopically implanted near each tumor and detected in real time by the Calypso system, serving as surrogates for tumor localization during treatment. Tracking accuracy was validated using Calypso beacon motion as the ground truth.

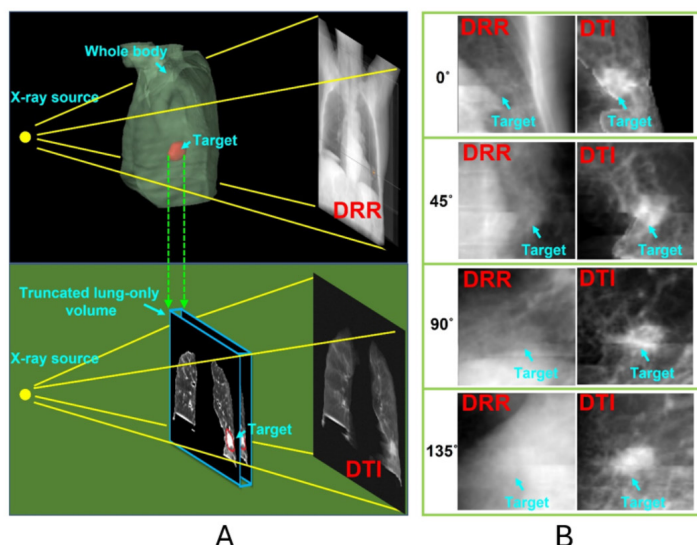


Fig. 1: The target decomposition process. (A): A digitally reconstructed radiograph (DRR) is projected through the whole body, while the decomposed target image (DTI) is projected through the truncated lung-only volume. (B): Target visibility was improved in the DTI when compared with the DRR.

Results: Sub-millimeter tracking accuracy was achieved.

Using the beacon motion as ground truth, the tracking errors were on average $0.8 \text{ mm} \pm 0.7 \text{ mm}$ in the superior-inferior (SI) direction and $0.9 \text{ mm} \pm 0.8 \text{ mm}$ in the in-plane left-right (IPLR) direction. The percentage of successful tracking, defined as a tracking error of less than 2 mm in the SI direction, was 92.2% across the 4,312 tested images. Fig. 2 shows the trajectories comparison between the band pass filter method and the proposed method. It took approximately 35 ms to generate one sDTI, and 13 ms to perform the tumor tracking using template matching.

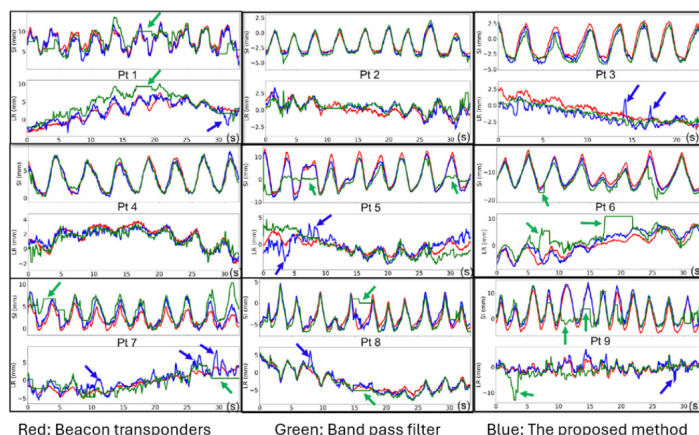


Fig. 2: Two-dimensional tumor trajectories for nine patients. LR: left-right; SI: superior-inferior.

Scientific Significance: The target decomposition technique can significantly enhance tumor contrast, enabling direct tumor imaging during treatment.

Potential Clinical Impact: This technique, when combined with motion compensation, offers a promising solution to improve the target localization accuracy and reduce treatment margins.

Acknowledgments:

This work is supported in part by the Varian Investigator Initiated Research Grant and the MSK Cancer Center Support Grant/Core Grant (P30 CA008748).

References:

Y Fu, P Zhang, Q Fan, W Cai, H Pham, A Rimner, J Cuaron, L Cervino, JM Moran, T Li, X Li (2024), Deep learning based target decomposition for markerless lung tumor tracking in radiotherapy, *Medical Physics*, 51(6):4271-4282.

Y Fu, Q Fan, W Cai, F Li, X He, J Cuaron, L Cervino, JM Moran, T Li, X Li (2023) Enhancing the target visibility with synthetic target specific digitally reconstructed radiograph for intrafraction motion monitoring: A proof of concept study, *Medical Physics*, 50(12):7791-7805.

A Simulation-Free Replacement Solution for Radiation Therapy Immobilization Devices using Computer Numerical Control (CNC) - Milled Polystyrene Molds

Laszlo Voros¹, Victoria Y. Yu¹, Sean Berry¹, Lei Zhang¹, Margie Hunt¹, Paul Booth², Jason Ocana², Joseph O. Deasy³, and Laura Cerviño¹
¹Division of Radiotherapy Physics, ²Biomedical Engineering, and ³Predictive Informatics

Motivation: In radiation therapy (RT), if an immobilization device is lost or damaged, the patient may need to be brought back for re-simulation, device fabrication, and treatment planning, causing additional imaging radiation exposure, inconvenience, higher cost, and delay. We developed and implemented a method for replacing lost or damaged RT immobilization devices to avoid re-simulation and to prevent delays in care.

Methods: Image-based immobilization (IBI) replacement devices were designed using existing simulation scans and then fabricated by computer numerical control (CNC) milling of molds made from extruded polystyrene (XPS) as shown in Fig. 1. XPS material attenuation and bolus properties were evaluated, and a standard workflow was established and published [1]. To allow for broader use of this method in supporting all MSK radiation oncology treatment facilities, we generated a guide and implemented a decision-making process that comprised a team of physicians, medical physicists, and radiation therapists.

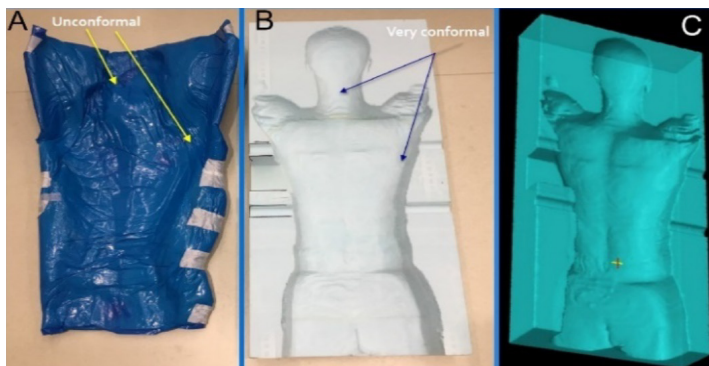


Fig. 1: (A) Original alpha cradle, (B) replacement image-based immobilization mold, and (C) stereolithography design of the replacement mold for mediastinum treatment.

Results: All patients were successfully treated using the CNC-milled replacement molds, and pretreatment imaging verified satisfactory clinical setup reproduction for each case as shown in Fig. 2. Results showed that XPS foam material had less dosimetric impact (attenuation and bolusing) than materials used in standard immobilization devices. The external body contours from the setup cone-beam CT and the original CT simulation with matching superior-inferior extent were compared by calculating the dice similarity coefficient (DSC) and the mean distance to agreement (MDA). The DSC average was 0.966 mm (standard deviation [SD], 0.011), and the MDA average was 2.694 mm (SD, 0.986).

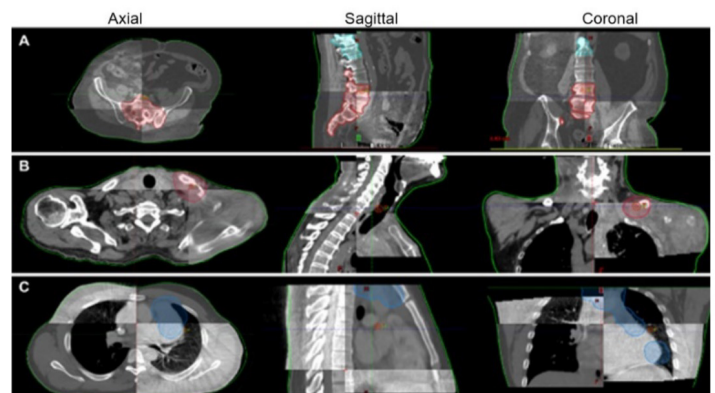


Fig. 2: Simulation CT with original immobilization overlaid with onboard cone-beam CT using an image-based immobilization mold in axial, sagittal, and coronal views. Cone-beam CT with image-based immobilization mold: top left and bottom right; planning CT with original immobilization: top right and bottom left. Green contour: external body contour on planning CT from a few example cases. (A) T12-L1 spine (Cyan) and lumbar to sacral spine. (B) Clavicle. (C) Mediastinum.

Potential Clinical Impact: The convenience and significant time/cost savings for patients, clinicians, and the clinical care team has proven to be extremely valuable. A re-simulation typically requires a repeat visit from the patient, re-contouring of treatment volumes by physicians, and recreation of the treatment plan by the physics team (at least one week of potential delay), whereas the IBI mold replacement process was completed in as little as four hours and typically in less than 24 hours. In many cases, the original simulation was executed along with a CT myelogram for high precision cord delineation, and re-simulation would have meant a repeat of the invasive myelogram as well. Thus, the elimination of re-simulation for these patients avoids significant delays in treatment start and still achieves highly reproducible treatment setups.

Awards: Memorial Sloan Kettering Cancer Center (MSK) Division of Quality and Safety (DQS) Good Catch, Great Care Spotlight Award 2023

Acknowledgments:

Drs. Samuel Hellman, Michael Lovelock, Yoshiya Yamada also contributed significantly to this work. This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

Disclosures:

Drs. Joseph O. Deasy and Dale M. Lovelock hold a related patent on systems and methods for designing and manufacturing custom immobilization molds for use in medical procedures (US Patent No. 11568618, 2023).

References:

1. Hellman, S., Voros, L., et. al. A Simulation-Free Replacement Solution for Radiation Therapy Immobilization Devices Using Computer Numerical Control (CNC) - Milled Polystyrene Molds. *Adv. in Rad Onc* 9.8 (2024): 101544.

Implementation and Clinical Integration of a CBCT-Based Adaptive Radiotherapy Program using the Varian Ethos Platform

Michelle Savacool¹, Grace Tang¹, Jie Yang², Pengpeng Zhang², Seng Boh Lim¹, Michalis Aristophanous¹, and Laura Cerviño¹
¹Division of Radiotherapy Physics and ²Computer Service

Motivation: Adaptive radiotherapy (ART) has the potential to improve treatment precision by accounting for anatomical changes throughout the course of therapy. Clinical adoption has been slowed by workflow complexity and resource demands. The Varian Ethos™ platform (Varian Medical Systems, Palo Alto, CA) introduces a streamlined, cone-beam computed tomography (CBCT)-guided adaptive workflow which integrates high-quality HyperSight™ imaging, contouring, planning, and delivery into a single treatment session. This abstract outlines the clinical deployment of Ethos ART, including commissioning, training, workflow development, and early clinical experience.

Methods: The Ethos adaptive program was launched following extensive commissioning of the treatment planning system, beam model, and quality assurance (QA) tools including SureCalc™, Mobius3D™, and log file analysis for patient-specific QA. Training was conducted for physicists, dosimetrists, and therapists using a structured competency framework. Adaptive workflows were developed for prostate (post-brachytherapy and stereotactic body radiation therapy with nodes) and head and neck (H&N) with disease-specific templates and contouring protocols. On-couch workflows were tested using phantom tests and clinically validated with patient data as shown in Fig. 1. An upgrade to the system (Ethos 2.0) included AI auto-contouring for organs at risk (OARs).

Results: The first Ethos adaptive treatment was successfully delivered in August 2024, with a total treatment time of 50 minutes, including a five-minute delay due to secondary monitor unit calculation issues. Subsequent treatments showed improved efficiency, with total treatment times possible within 30 minutes. The on-couch treatment workflow is shown in Fig. 2. We have treated so far over 20 prostate patients with three different fractionation schedules. Plans consistently met clinical goals, with the adapted plan chosen over 95% of the time. Adapted plan superiority can be seen in the example in Fig. 3. For H&N cases, a single adaptation workflow was developed and tested using the Steeve™ phantom and validated through QA with radiochromic film and myQA-SRS16™. The SureCalc™ on-couch implementation for adaptive plan QA was completed in July 2025, enabling real-time secondary dose verification.

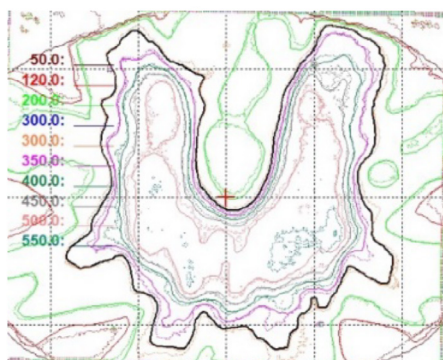


Fig. 1: Film measurements (dotted lines) and Ethos™ Treatment Planning System (Varian Medical Systems, Palo Alto, CA) calculations (solid lines) for a treatment plan during commissioning.

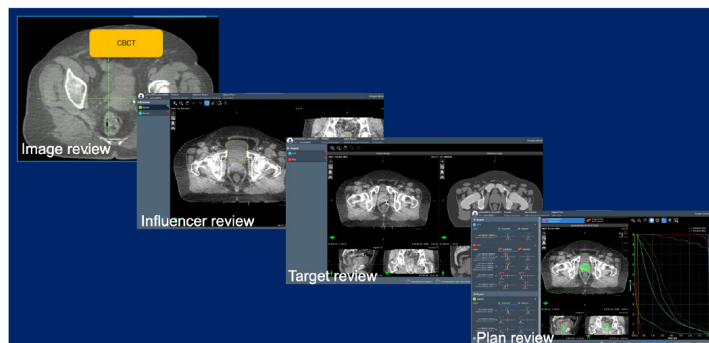


Fig. 2: A schematic of the on-couch treatment workflow.

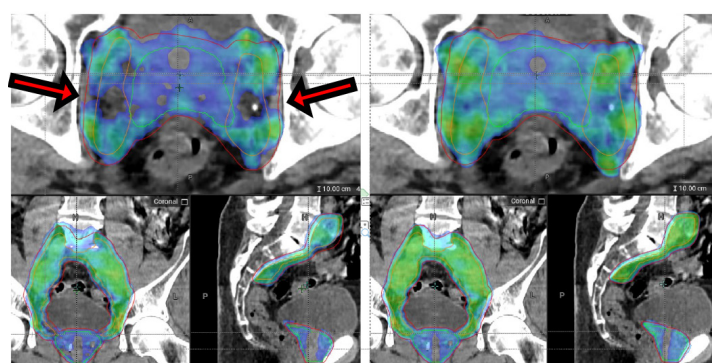


Fig. 3: Example non-adaptive (left) dose map vs adaptive dose (right) comparison. The non-adaptive dose shows cold spots in the target.

Scientific Significance: We successfully integrated CBCT-guided adaptive radiotherapy into routine practice using the Ethos™ platform. Our initial experience demonstrates that the adaptive plan is preferred for most fractions, supporting the idea that ART can improve accuracy in radiotherapy delivery. The improvement in total treatment times demonstrates that, as our teams become more familiar with these workflows, ART can become standard of care for many sites that can benefit from plan adaptation.

Potential Clinical Impact: CBCT-guided ART using the Ethos™ platform has the potential to significantly enhance treatment personalization and precision across multiple disease sites. By enabling daily plan adaptation based on patient-specific anatomy, this approach can improve target coverage and reduce dose to OARs, particularly in anatomically variable regions such as the pelvis, abdomen and H&N.

Acknowledgments: We would like to acknowledge the many team members and residents in the Division of Radiotherapy Physics and Computer Service that have contributed to the commissioning and implementation.

This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

Novel Script Supporting SRS Treatment Planning - Predictive Models for SRS Plan Quality Evaluation

LiCheng Kuo¹, Michalis Aristophanous¹, and Åse M. Ballangrud¹

¹Division of Radiotherapy Physics

Motivation: Achievable plan quality for cranial multi-lesion stereotactic radiosurgery (SRS) metastases is highly variable and dependent on lesion number, clustering, and characteristics. Predictive models for dose gradient were developed using optimal clinical plans and provide plan quality metrics which guide planners, resulting in increased planning efficiency as well as standardized and improved plan quality.

Methods: Predictive models for plan quality evaluation were developed and refined based on a large cohort of clinical volumetric modulated arc therapy (VMAT) SRS plans, all treated on Varian TrueBeam and TrueBeam STx linear accelerators (Varian Medical Systems, Palo Alto, CA, USA). Gradient Index (GI) Prediction:

The GI, defined as $V50\% / V100\%$, quantifies the dose fall-off outside the target. The predicted GI, pGI , was modeled mathematically as:

Model 1:

$$pGI = a \times (PTV)^b$$

where PTV is the planning target volume in cm^3 , and a and b represent the empirical fitting parameters. The initial empirical model for pGI was developed based on 40 patients with 188 lesions [1]. This model was validated and updated using a larger dataset of 121 cases (444 lesions), resulting in a refined model for tiny lesions ($PTV < 0.35$ cc) [2].

Model 2:

Further analysis on a comprehensive dataset of 652 patients (2,511 lesions) led to a more sophisticated model which accounts for multileaf collimator (MLC) width, the number of lesions (single vs. multiple), and inter-lesion spacing. The shortest surface distance (SSD) to the nearest neighboring lesion was incorporated to account for the complex dose gradient between proximal targets in multi-lesion plans [3]:

$$pGI = (a + c * e^{-d * SSD} \times (PTV)^b$$

Fitting parameters a , b , c , and d were determined for different MLC configurations (2.5 mm and 5 mm).

Results: Table 1 lists the fitted parameters for Model 1 for different conditions. Fig. 1 illustrates the performance of the two prediction models for single-lesion and multiple-lesion plans on the Varian TrueBeam STx (equipped with HD-MLC) platforms using six megavolt flattening-filter-free beams. Compared with the single-lesion model, including the SSD reduced the mean squared error of the pGI for multiple lesions from 0.67 to 0.48 using a 2.5 mm MLC, and from 1.52 to 1.16 using a 5 mm MLC.

Lesions	MLC	Target Size	SSD (cm)	a	b
Single	HD-MLC			3.16	-0.10
	M-MLC			3.69	-0.14
Multiple	HD-MLC	$\geq 1 cm^3$	$\geq 1 cm$	4.23	-0.21
			$< 1 cm$	4.61	-0.23
		$< 1 cm^3$	$\geq 1 cm$	4.14	-0.18
			$< 1 cm$	4.09	-0.24
	M-MLC	$\geq 1 cm^3$	$\geq 1 cm$	4.13	-0.21
			$< 1 cm$	5.60	-0.18
		$< 1 cm^3$	$\geq 1 cm$	4.45	-0.15
			$< 1 cm$	8.55	0.11

Table 1: Parameters of the predicted gradient index (GI) Model 1 for different conditions. HD-MLC: high-definition multileaf collimator; M-MLC: Millennium multileaf collimator

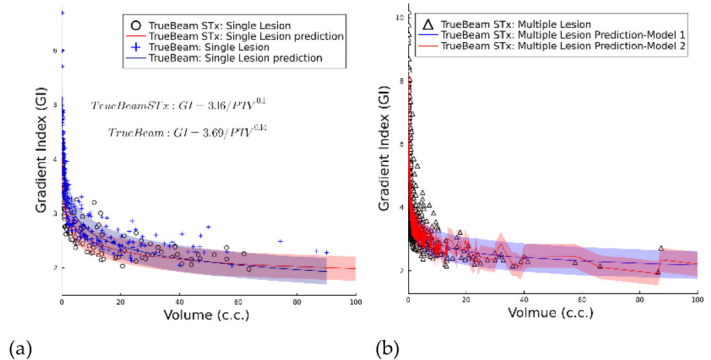


Fig. 1: (a) Single-lesion gradient index (GI) prediction model for TrueBeam and TrueBeam STx (Varian Medical Systems, Palo Alto, CA, USA); (b) Multiple-lesion GI prediction models for TrueBeam STx

Scientific Significance: This work establishes robust, data-driven predictive models for key SRS plan quality metrics. These models serve as objective benchmarks, incorporating MLC type and inter-lesion distance, and provide tools that enable institutions to standardize plan quality.

Potential Clinical Impact: These models provide real-time feedback to planners, improving planning efficiency as well as standardizing and strengthening the plan quality for all SRS plans, reducing the risk of adverse effects and contributing to safer SRS delivery.

Acknowledgments: This research was funded by the MSK Cancer Center Support Grant (P30 CA008748).

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Comprehensive Commissioning of the Motion Management System on the Elekta Unity MR-Linac

William Donahue¹, Shu Xing¹, Lauren Smith¹, Paola Godoy Sripes¹, Eric Aliotta¹, Jim Mechalakos¹, Lakshmi Santanam¹, Neelam Tyagi¹, and Seng Boh Lim¹

¹Division of Radiotherapy Physics, Department of Medical Physics

Motivation: Enabling accurate, real-time magnetic resonance (MR)-guided gating for moving targets with the Elekta Unity MR-Linac (Elekta AB, Stockholm, Sweden) to reduce dose delivered to normal tissues.

Methods: A 3D MRI-compatible motion phantom with 1–3 cm targets was used to assess tracking accuracy across breathing patterns (8–20 breaths per minute [bpm]) and bore positions. Gating latency was measured with and without prediction by comparing beam triggers to known motion.

Simulated clinical plans (prostate, pancreas, liver, and lung) were delivered under exception, free-breathing, and exhale-gating conditions. Films were analyzed for dose differences and gamma pass rates (3% / 2 mm). End-to-end tests replicated full workflows, including adaptive planning and baseline shifts, to assess accuracy.

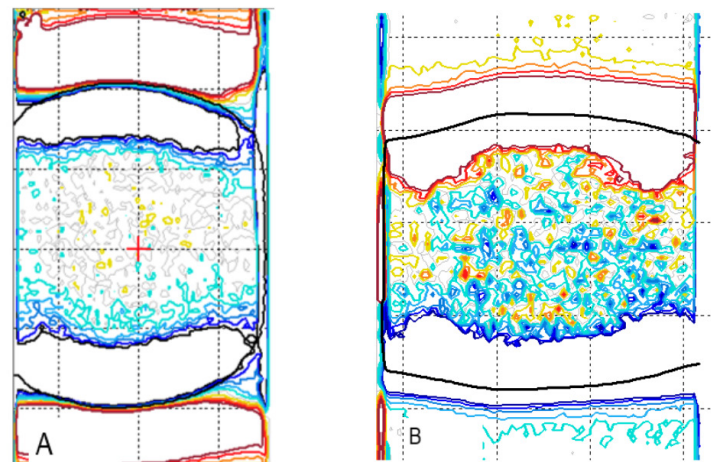


Fig. 1: Dose difference map for liver (A) and lung (B) treatments when no gating is applied. This results in underdosing (blue) of the tumor and increased dose (red) to the surrounding healthy tissues.

Results: Tracking system was found to be acceptable for clinical use.

Mean tracking errors were < 1 mm for 2–3 cm targets. Errors increased with breathing rate, and 1 cm targets showed tracking failures due to through-plane motion. System latency without prediction was ~350 ms; with prediction, latency dropped to below 120 ms (95th percentile). Dose differences for ungated treatments are shown in Fig. 1 for reference, with significant areas of over- and under-dosing >10%. Dose differences were < 2% for most cases, and free-breathing and exhale-gating strategies reduced motion blur (Fig. 2). Exhale gating showed systematic dose shifts related to gating window timing (seen in Fig. 3). In end-to-end testing, localization accuracy was < 1.4 mm, and dose differences were within 3.1%, which is acceptable given the uncertainties in the tracking algorithm.

Scientific Significance: The Elekta Unity MR-Linac meets the needs of real-time gating. The presented work provides the community with a baseline characterization of the gating system for comparison during commissioning.

Potential Clinical Impact: The motion management system may allow for reduced treatment volumes, which could enable dose escalation to the tumor.

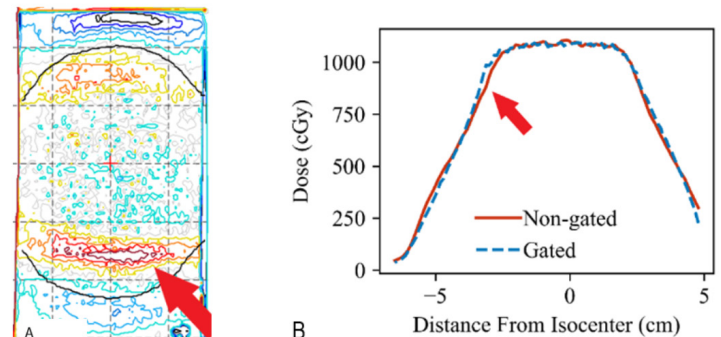


Fig. 2: Dose difference map for a liver case (A) and the dose profile in the motion direction (B) when gating is utilized. The hotspot is caused by the system improving the penumbra and increasing the dose to the tumor.

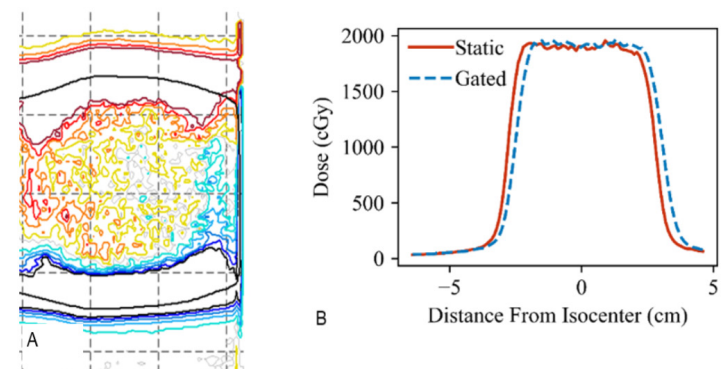


Fig. 3: Dose difference map for a lung case (A) and the dose profile in the motion direction (B) when gating is utilized. The hot and cold spots are caused by a systematic dose shift related to gating window size and system latency. There is improvement compared to the no gating case, reducing the effect by more than 30%.

Acknowledgments:

We thank Elekta AB for including us in the pilot program for the gating upgrades and for working closely with us to address issues. This work is also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Donahue W, Xing S, Smith L, Godoy Sripes P, Aliotta E, Mechalakos J, Santanam L, Tyagi N, Lim SB. Characterizing the motion management system accuracy on a 1.5T MR-Linac. *Physica Medica*. 2025 Nov;139:105189. Epub 2025 Oct 14.

MRSIGMA-MLC Tracking for Real-Time Adaptive Radiation Therapy on the MR-Linac

Grace Tang¹, Justin Yang², Aniket Pramanik², Can Wu², Victor Murray², William Donahue¹, Neelam Tyagi¹, and Ricardo Otazo²
¹Division of Radiotherapy Physics and ²MRI Physics

Motivation: The current standard for motion management in radiotherapy includes expanding the treatment margin, controlling the patient's breathing patterns, or controlling the linear accelerator (Linac) to irradiate only when the target is within a certain positional range (gating). While these procedures are widely used in the clinic, improvements can be made to reduce target margins, increase patient comfort, as well as increase clinical throughput. This can be achieved through multileaf collimator (MLC) tracking, whereby the MLC dynamically adapts to the instantaneous changes in the shapes and positions of the target and normal tissue due to respiratory motion during radiation therapy.

Methods: Magnetic Resonance Signature Matching (MRSIGMA) is a real-time 3D MRI technique developed at MSK (1), with total imaging latency lower than 200 ms and high spatial resolution in the order of 1-2 mm in-plane and 2-4 mm through-plane, which enables real-time intra-fractional motion imaging during treatment on the MR-Linac. An MLC tracking interface for the Elekta Unity MR-Linac system was developed to use the real-time target position derived from MRSIGMA to adapt the MLC aperture of a treatment plan. To account for the imaging and MLC motion latencies, a Kalman filter was used. Within the research environment of the Linac, the MLC tracking interface obtains control of the treatment machine, allowing the MLC positions are adjusted instantaneously (Fig. 1). Initial testing was performed on a dynamic motion platform with a MR-visible target embedded on a solid water phantom.

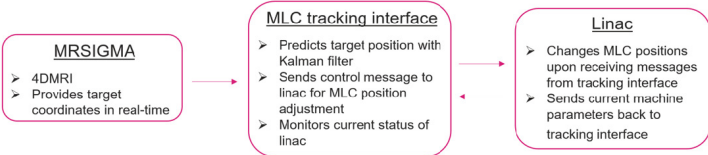


Fig. 1: Magnetic Resonance Signature Matching-Multileaf Collimator (MRSIGMA-MLC) tracking workflow.

Results: For a sinusoidal motion with peak-to-peak displacement of 15 mm, the Kalman filter achieved accurate position predictions, with a room mean square error (RMSE) of < 0.7 mm, for time periods of 3, 4, 5, 6, 7, and 8 seconds (see Table 1). Subsequently, the geometric error of MLC tracking for a simple field with a circular MLC aperture was within 0.54 mm of RMSE for the same motion traces as shown in Table 1. The overall latency was < 40 ms, with the control message rate occurring every 40 ms. Dosimetric performance was quantified by film measurement as shown in Fig. 2, where the overall dose differences between planned delivery (reference) and MLC tracking delivery was remarkably improved. Further work with patient motion traces and clinical treatment plans are in progress.

Period(s)	MLC tracking RMSE (mm)	Latency (ms)
3	0.54	39
4	0.39	38
5	0.38	38
6	0.28	33
7	0.24	33
8	0.23	30

Table 1: Geometric uncertainty (quantified using root mean square error [RMSE]) and overall multileaf collimator (MLC) tracking latency for a sinusoidal motion with a peak-to-peak displacement of 15 mm.

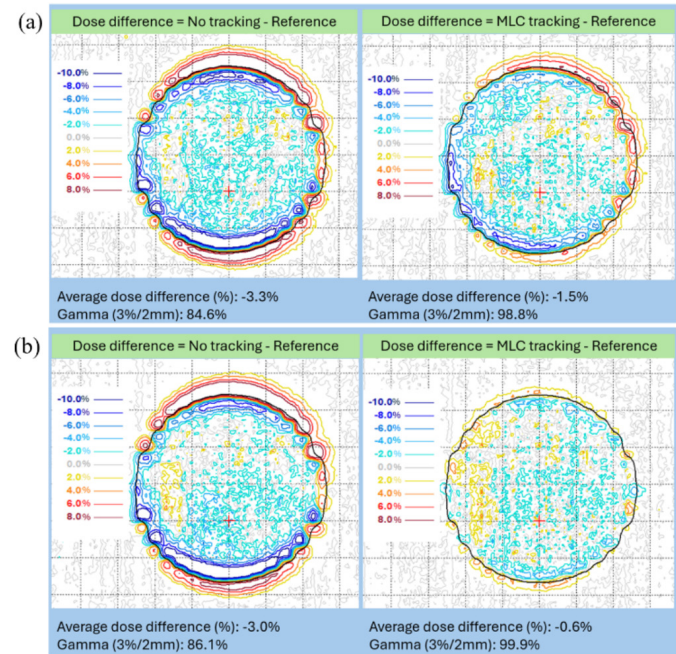


Fig. 2: Film measurements for sinusoidal traces with 15 mm peak-to-peak displacement and time periods of (a) 6 s and (b) 8 s. Local dose differences and gamma passing rates improved with MLC tracking compared to delivery with no tracking.

Scientific Significance: MRSIGMA-MLC tracking workflow has been successfully developed and implemented on the MR-Linac.

Potential Clinical Impact: Preliminary data shows promising results for real-time MLC tracking on the MR-Linac, with the potential to improve treatment efficiency and efficacy of tumors affected by continuous motion.

Acknowledgments: This work was supported by NIH R01-CA255661 and is supported in part by the MSK Cancer Center Support Grant P30 CA008748.

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Modernizing Linac QA with Automated Onboard Imaging

William Donahue¹, Seng Boh Lim¹, and Jean Moran¹

¹Division of Radiotherapy Physics, Department of Medical Physics

Motivation: Routine quality assurance (QA) for linear accelerators (Linacs) is essential but time-consuming. By using automated analysis of onboard imaging, we aim to modernize QA processes, saving time, improving consistency, and enhancing patient safety.

Preliminary Work: Evaluation of an Existing QA Solution

The Automated QA (AQA) Consortium is a group of international organizations that developed and used an online platform to analyze data collected with on-board imaging systems for Linac beam QA. We used their open-source platform to explore the concept of performing this procedure at MSK.

Methods: We performed our standard practice (SP) Linac QA and delivered the standardized AQA plans for seven months. We analyzed the resultant images using the AQA's online platform and compared the results with routine QA. We quantified the differences in trends between manual and AQA deliveries.

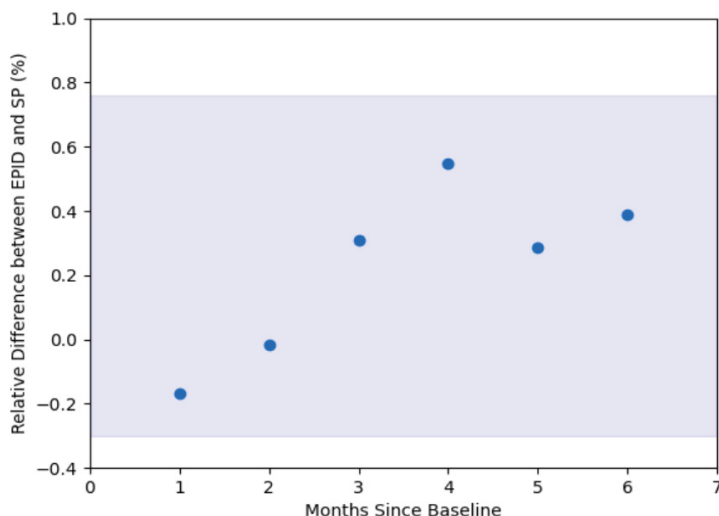


Fig. 1: Plot of the relative difference between outputs calculated using an electronic portal imaging device (EPID) and standard practice for 6MV photons. The blue box indicates the confidence interval. The upward trend is primarily associated with a change in the sensitivity of the detector panel due to radiation damage.

Results: The AQA demonstrated a potential reduction in effort of 18 full-time equivalent (FTE) days for three tests alone:

- Excellent agreement was observed between standard measurements for output, flatness, and symmetry (shown in Figs. 1 and 2)
- QA time was reduced from 40 minutes to 5 minutes for these critical tests.
- For the first three months of testing, all data was within tolerance, with the only data point outside of tolerance being due to a defective panel (Fig. 2).

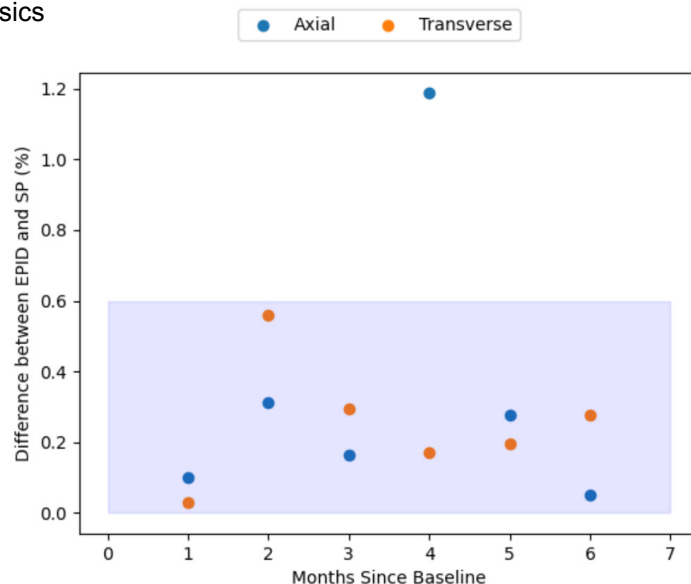


Fig. 2: Plot of the difference between the changes in symmetry relative to baseline, calculated using an electronic portal imaging device (EPID) and current standard practice for 6MV photons. The blue box indicates the confidence interval. The axial outlier was attributed to a defective detector.

Ongoing Efforts: Meeting MSK needs

The preliminary results demonstrated that the approach is feasible. However, to automate additional QA at MSK, the following needs to be addressed:

- Inclusion of new Linac models (Halcyon and Ethos Adaptive [Varian Medical Systems, Palo Alto, CA])
- Use of a phantom to allow for checking the mechanical accuracy of Linacs
- Addition of tests that are specific to the MSK process

Accordingly, we are developing a customized version of AQA to address these. Work is currently focused on developing algorithms for our new Linacs before deployment across the broader Linac fleet.

Scientific Significance: The work described demonstrates the development of well-characterized and scalable algorithms for investigating machine performance, paving the way for future research.

Potential Clinical Impact: Automating Linac QA ensures safer treatments and frees up to 168 FTE-days per year for other clinical tasks. MSK will have a unified, scalable QA solution that supports advanced radiotherapy across all major platforms, helping to maintain its leadership in precision cancer care.

Acknowledgments: This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Donahue W, Irrer J, Barnes M, DeMarco J, Moran J, Lim SB. Commissioning of EPID-Based Dosimetry QA for Linear Accelerators. Poster presented at the 65th Annual Meeting of the American Association of Physicists in Medicine (AAPM); July 23-27, 2023; Houston, TX, USA.

Real-Time Motion-Including Prostate and Bladder Dose Reconstruction During Prostate Radiotherapy Delivery

Grace Tang¹, Laura Happersett¹, Perry Zhang², Brian Leong¹, and Hai Pham²

¹Division of Radiotherapy Physics and ²Computer Service

Motivation: The in-house developed megavoltage/kilovoltage (MV/kV) intrafractional motion monitoring program for prostate stereotactic body radiation therapy (SBRT) has been successfully implemented at MSK for the past decade, achieving a greater clinically significant reduction in late urinary toxicity compared to a commercial solution (intrafraction motion review, Varian Medical Systems)¹. To further investigate the efficacy of the current implementation, which uses geometric localization of fiducial markers, online real-time motion-including dose reconstruction was performed.

Methods: The online dose reconstruction software, Dose-Tracker², developed at Aarhus University in Denmark, was integrated into the MV/kV workflow. Real-time motion-including dose reconstruction of the prostate and bladder was performed during treatments of twenty prostate SBRT patients (800 cGy × 5 fractions). The dose received by 95% ($D_{95\%}$) of the prostate clinical target volume (CTV), and the volume of the bladder receiving at least 36 Gy ($V_{36\text{Gy}}$) were calculated. For comparison, dose distributions were also simulated offline without MV/kV guidance.

Results: Under MV/kV guidance, the planning criteria of prostate CTV $D_{95\%} > 95\%$ was fulfilled at all treatment fractions except for one, and the criterion of bladder $V_{36\text{Gy}} < 10\%$ was fulfilled for all fractions, as shown in Fig. 1. Without MV/kV guidance, the planning criteria would have been violated for 9 of 92 fractions (CTV $D_{95\%}$) and 4 of 92 fractions (bladder $V_{36\text{Gy}}$). The mean (standard deviation, range) motion-induced dose differences were -0.6% (1.1%, [-5.6, +1.6]%) for CTV $D_{95\%}$ and +0.1% (0.5%, [-1.0, +1.3]%) for bladder $V_{36\text{Gy}}$ with MV/kV guidance, and increased to -2.0% (6.6%, [-42.5, +1.8]%) for the prostate and +4.1% (2.0%, [-5.8, +10.1]%) for the bladder without MV/kV guidance.

Scientific Significance: This work presents the first reported clinical real-time dose reconstruction during prostate radiotherapy.

Potential Clinical Impact: This ongoing study provides direct insight into geometrically driven versus dosimetrically driven localization using MV/kV guidance, improving the efficacy of motion monitoring and clinical outcomes.

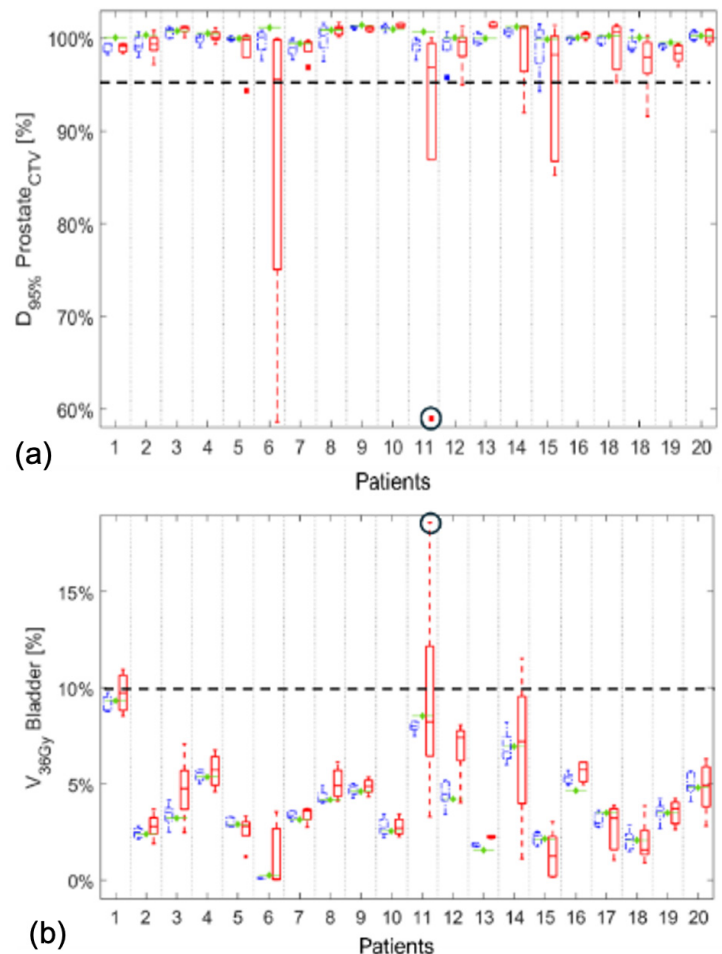


Fig. 1: (a) Prostate clinical target volume (CTV) dose received by 95% of the volume ($D_{95\%}$) and (b) volume of the bladder receiving at least 36 Gy ($V_{36\text{Gy}}$). The blue boxes correspond to the delivered dose distribution with megavoltage/kilovoltage (MV/kV) guidance, and the red boxes represent the simulated treatment without intra-treatment image guidance. The green diamonds indicate the planned values, assuming no motion.

Acknowledgments: This work was conducted in collaboration with Karolina Klucznik, Thomas Ravkilde, Simon Skouboe and Per Poulsen from Aarhus University, and with Paul Keall from University of Sydney. This work was also supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Radiotherapy Dose Accumulation Routine (RADAR) - Accounting for Dose Accumulation Uncertainty in External Beam Reirradiation

Jim Mechalakos¹, Yu-Chi Hu², LiCheng Kuo¹, Lei Zhang¹, Niral Shah¹, Ellen Yorke¹, Ase Ballangrud-Popovic¹, Yilin Liu¹, Laura Cerviño¹, Andrew Jackson¹, Jean Moran¹, Joseph Deasy³, and Perry Zhang²

¹Division of Radiotherapy Physics, ²Computer Service, and ³Predictive Informatics

Motivation: With recent advances in the accuracy of positioning and dose delivery, reirradiation is becoming more common, yet determining the composite dose received by organs-at-risk (OARs) across multiple radiation courses remains challenging, largely due to uncertainty in image registration.

Methods: Given the need for dose accumulation software that is more robust to uncertainty in image registration as well as other sources of uncertainty, such as organ motion and deformation, we have developed an in-house application, Radiotherapy Dose Accumulation Routine (RADAR), which incorporates user-specified uncertainty estimates directly into the computation of accumulated dose.

Results: RADAR incorporates uncertainty into the dose accumulation by “smearing” the dose delivered in previous courses at the voxel level according to an uncertainty specified by the user. As shown in Fig. 1, for each voxel of the previous dose distribution, RADAR searches for the maximum dose within an “uncertainty ellipsoid” centered on that voxel and uses that local maximum for the dose accumulation rather than the dose to the voxel itself. The size of this ellipsoid can be varied for different structures because the positional and registration uncertainty can be smaller for more rigid structures, such as the brain, and larger for more mobile structures, such as the esophagus or bowel. In addition, RADAR can limit the reach of these uncertainty ellipsoids such that they only search within the OAR of interest, preventing the search from yielding an unreasonably high OAR dose because the ellipsoid reaches into a nearby target. RADAR is accessed from within the Eclipse application (Varian Medical Systems, Palo Alto, CA) via the Eclipse scripting application programming interface (ESAPI).

If dose accumulation software is not available, the approach of simply adding the individual maxima from each plan can be followed to estimate a particular cumulative dose index such as the D0.035cc of the spinal cord. This is overly conservative, as these “max-like” dose points are usually not in the same geometric location. A dose accumulation from RADAR yields a more realistic estimate of the actual spinal cord D0.035cc with uncertainty included. A comparison between RADAR dose accumulation results and the more conservative approach averaged over nine patients that had undergone stereotactic body radiation therapy spine reirradiation is shown in Table 1. On average, RADAR provides predictably lower but more realistic estimates of the dose indices associated with the composite dose distribution.

Scientific Significance: Armed with the tools provided by RADAR to add dose more safely and reliably from consecutive courses of radiation, the ideal uncertainty estimates for different organs in different irradiation settings to use in the program are yet to be determined. It also remains to

reframe our institutional dose constraints in a more universal manner using a 2 Gy/fx equivalent dose, which RADAR can incorporate. RADAR also offers the opportunity to apply “dose discounts” based on the time elapsed between courses, allowing for tissue repair. All these parameters can be entered into site-specific templates, thereby minimizing the need for users to manually enter values and enhancing the overall safety of the program.

Future developmental work for RADAR includes going beyond a user-specified structure-based uncertainty in the current implementation to the specification of voxel-specific uncertainty that would be estimated using an automated AI-based pipeline.

Potential Clinical Impact: Using RADAR for dose accumulation represents a paradigm shift in the manner in which reirradiation is analyzed at MSK by incorporating the latest in 3D dose accumulation with a novel built-in safety valve for uncertainty. This is the only dose accumulation routine that incorporates a user-defined uncertainty directly into the dose accumulation in a consistent, objective fashion rather than relying on the user to subjectively estimate uncertainty for each individual case. With this tool, radiation oncologists can make more informed decisions about treatment and even sculpt reirradiation dose distributions over previously irradiated areas at the voxel level, thereby offering treatments customized to each individual patient’s radiation history.

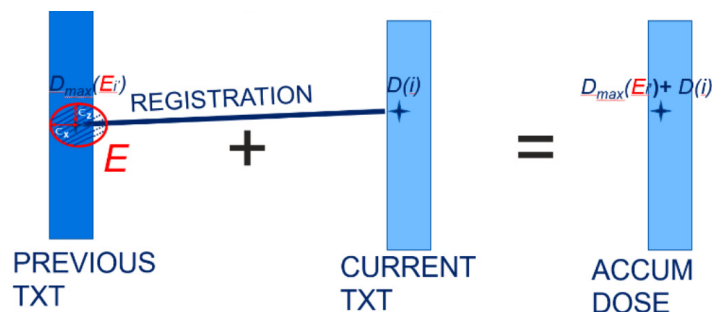


Fig. 1: A diagram illustrating dose accumulation using Radiotherapy Dose Accumulation Routine (RADAR).

Structure	Index	Difference between RADAR and sum of individual plans		
		Average	Min	Max
Spinal Cord	D0.035cc	-12.8%	-46.3%	2.6%
Esophagus	D0.035cc	-8.6%	-50.8%	1.0%

Table 1: Comparison between Radiotherapy Dose Accumulation Routine (RADAR) dose accumulation results and a simple sum of individual dose indices for patients who underwent spine reirradiation.

Acknowledgments:

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Simultaneous Tracking of Prostate and Rectum for Intrafractional Motion Management of Prostate SBRT

Laura Happersett¹, Sarah Burleson¹, Hai Pham¹, Yabo Fu¹, Himanshu Nagar², Antonio Damato¹, and Pengpeng Zhang¹

¹Department of Medical Physics and ²Department of Radiation Oncology

Motivation: Conventional intrafractional motion management (IMM) implemented on an X-ray image-based platform relies on tracking the prostate-implanted fiducials but lacks information on the motion of adjacent organs at risk needed for the design of a gating strategy and subsequent reconstruction of the delivered dose. We developed a program to simultaneously track the prostate and rectum, thereby enhancing the technical capability and potential benefit of IMM.

Methods: Ten SBRT prostate patients were treated with 40 Gy in five fractions using two volumetric modulated arc therapy (VMAT) arcs. A radio-opaque hydrogel spacer was injected between the prostate and rectum to reduce the rectal dose. The spacer is visible on kilovoltage (kV) images, providing a reliable motion surrogate of the adjacent rectal wall residing in the high-dose region. Three fiducials were also implanted into the prostate for setup and IMM of the target volume. The spacer and fiducials can be seen in Fig. 1. During treatment, kV images were acquired at every 20° gantry rotation.

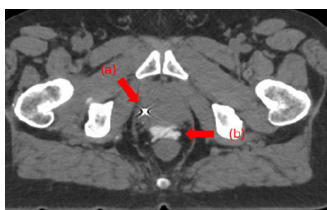


Fig. 1: Example of a patient with (a) implanted fiducials and (b) radio opaque spacer in the axial view.

Retrospectively, the prostate and the rectum were localized using on-treatment kV images by selecting either the spacer or the fiducials as the matching structure. Such images were registered using previously generated templates derived from the planning CT image. These templates were created to highlight the spacer or the fiducials at each gantry angle. An example of an on-treatment kV projection is shown in Fig. 2a. The corresponding template DRR highlighting the spacer or fiducials is shown in Fig. 2b. Beam's-eye-view deviations were quantified for each method and are shown in Fig. 2c.

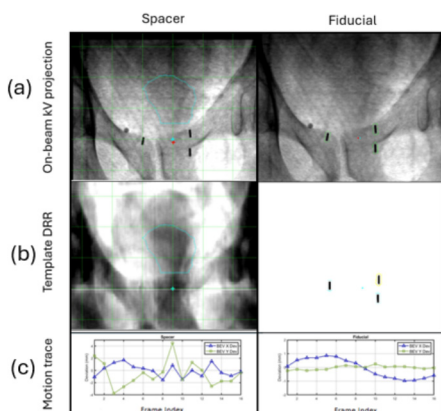


Fig. 2: An in-house program, SeqReg, was used to track the spacer and prostate during VMAT delivery. In this example, the on-beam kV image (a) was registered to the template DRR (b) to generate the motion trace for the rectum and prostate in the kV beam eye view (c).

Results: Although the image quality and contrast of the spacer were often compromised by the overlapping bony structures, the spacer was robustly detected in 40% of the kV images, primarily around the anterior-posterior imaging angles. The 2D displacement measured using the prostate fiducials was 1.0 ± 0.6 mm in the kV beam's-eye view during the treatment, compared with a larger displacement of the spacer (2.1 ± 1.2 mm). The relative motion between the fiducials and the spacer was 2.2 ± 1.3 mm. The motion patterns of the fiducials and spacer differed significantly (t-test, $p < 0.05$) in 70% of the fractions.

Dose recalculations for one patient using motion traces obtained from both spacer-matching and fiducial-matching methods are shown in Fig. 3. The rectum maximum dose to 1 cm^3 (D1cc) and dose covering 99% of the clinical target volume (CTV D99) differed by 1 Gy and 0.6 Gy, respectively, on average if reconstructed using spacer-derived traces rather than fiducial-derived traces.

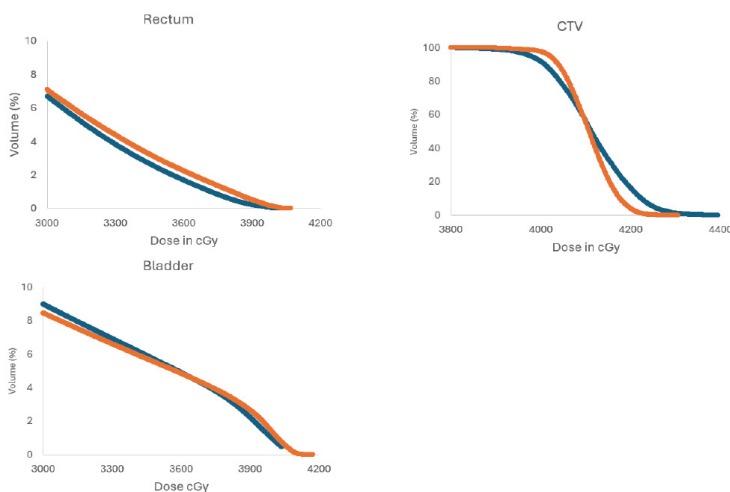


Fig. 3: Recalculated dose-volume histograms (DVHs) for rectum, bladder, and clinical target volume (CTV). Orange and blue lines were created using traces from fiducial-matching and spacer-matching methods, respectively.

Scientific Significance: Simultaneous tracking of the fiducials and spacer is feasible with X-ray imaging for prostate stereotactic body radiation therapy (SBRT). The amplitude and patterns of intrafractional motion appear to be independent between the prostate and spacer, supporting a more comprehensive tracking strategy during treatment.

Potential Clinical Impact: These findings could lead to a more sophisticated gating strategy that employs a structure-specific action threshold to ensure accurate dose delivery and more accurate dose reconstruction for outcome research. It may positively impact treatment quality and benefit prostate patients.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

Can the Risk of Dysphagia in Head and Neck Radiation Therapy be Predicted by Automated Transit Fluence Monitoring During Treatment? A Comparative Study of Patient-Reported Quality of Life and a Fluence-Based Decision Support Metric

Seng Boh Lim¹, Nancy Lee¹, Kaveh Zakeri¹, Peter Greer^{2,3}, Todsaporn Fuangrod⁴, Frederick Coffman⁵, Laura Cerviño¹, and Michael Lovelock¹⁴

¹Memorial Sloan Kettering Cancer Center, ²Calvary Mater Newcastle Hospital, ³University of Newcastle, ⁴HRH Princess Chulabhorn College of Medical Science, Chulabhorn Royal Academy, and ⁵School of Health Professions, Rutgers University

Motivation: The additional personnel and imaging procedures required for adaptive radiation therapy (ART) pose a challenge to broad implementation. We hypothesize that a change in transit fluence during the treatment course is correlated with a change in quality of life and thus can be used as a replanning trigger.

Methods: Twenty-four head and neck cancer (HNC) patients filled out the MD Anderson Dysphagia Inventory (MDADI) questionnaire before and after the radiotherapy treatment course. The transit fluence was measured using the watchdog (WD) in-vivo portal dosimetry system. The patients were monitored with daily WD measurements and weekly cone-beam computed tomography (CBCT) scans. The region of interest (ROI) for each patient was defined as the outer patient contour between approximate cervical spine levels C1 to C4, corresponding to the neck and mandible within the beam's-eye view. The n^{th} -day integrated transit fluence change ($\Delta\phi_n$) and the ROI volume change (ΔV_{ROI}) for each patient were calculated from the corresponding WD and CBCT measurements (as shown in Fig. 1). The correlation between MDADI scores and age, gender, planning mean dose to the salivary glands ($\langle D_{\text{sg}} \rangle$), change in weight (ΔW), ΔV_{ROI} , and $\Delta\phi_n$ was analyzed using the ranked Pearson correlation.

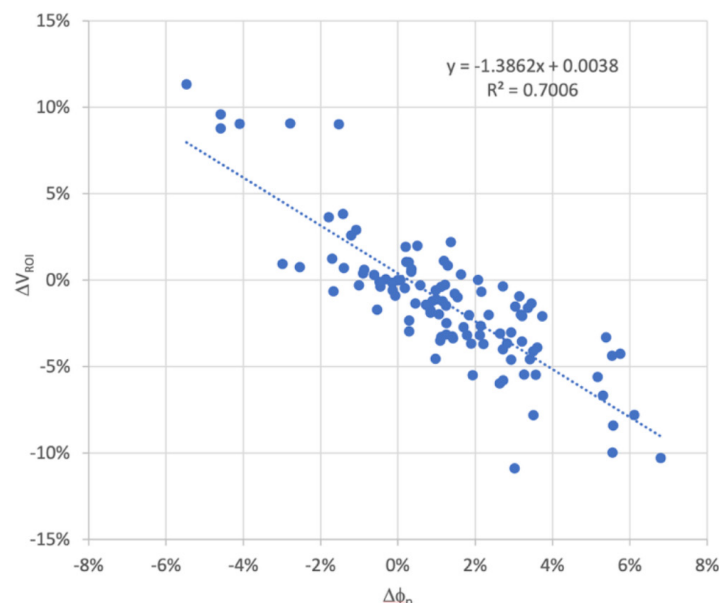


Fig. 1: Scatter plot of transit fluence variation and cone-beam computed tomography (CBCT)-derived volumetric changes of all 24 patients, used to assess the correlation between fluence and volume change during the treatment course.

Results: Suitable markers were identified

No statistically significant correlation was found for age, gender, and DW. The planning mean dose to the salivary

glands ($\langle D_{\text{sg}} \rangle$) was found to have a clinically important correlation with functional MDADI scores ($r = -0.39$, $p = 0.081$). The ROI volume change (ΔV_{ROI}) was found to have statistically significant correlations of 0.44, 0.47, and 0.44 with global, physical, and functional MDADI scores, respectively (p -value < 0.05). The Dfn was found to have statistically significant ranked correlations of -0.46, -0.46, and -0.45 with physical, functional, and total MDADI scores, respectively (p -value < 0.05) (as shown in Fig. 2).

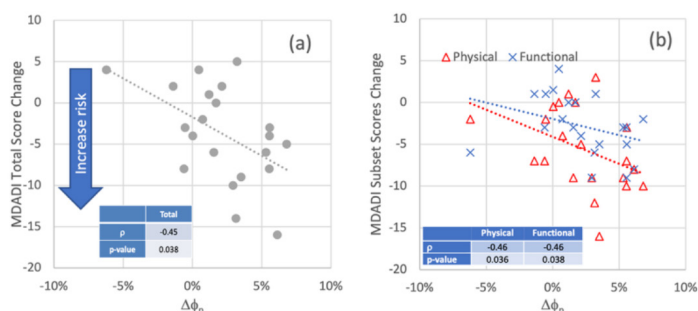


Fig. 2: The relationship between transit fluence change ($\Delta\phi_n$) and (a) total MD Anderson Dysphagia Inventory (MDADI) score change and (b) functional and physical MDADI subset scores change. The negative score changes indicate an increased risk of quality-of-life degradation.

Scientific Significance: A transit fluence-based decision support metric (DSM) is statistically correlated with dysphagia risk.

Potential Clinical Impact: The metric can not only be used as an early indicator to assist clinicians in ART patient selection for replanning, but also reduces the resource barrier to ART implementation.

Acknowledgments:

This work is supported in part by the MSK Cancer Center Support Grant (P30 CA008748).

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Lim SB, Lee N, Zakeri K, et al. Can the Risk of Dysphagia in Head and Neck Radiation Therapy Be Predicted by an Automated Transit Fluence Monitoring Process During Treatment? A First Comparative Study of Patient Reported Quality of Life and the Fluence-Based Decision Support Metric. *Technol Cancer Res Treat*. 2021 Jan-Dec

Lim SB, Tsai CJ, Yu Y, et al. Investigation of a Novel Decision Support Metric for Head and Neck Adaptive Radiation Therapy Using a Real-Time In Vivo Portal Dosimetry System. *Technol Cancer Res Treat*. 2019 Jan 1

Additional Abstracts from the Division of Radiotherapy Physics

Commissioning of a 2D Complementary Metal-oxide Semiconductor (CMOS) Array Detector (myQA Stereotactic Radiosurgery [SRS]) for Efficient End-to-End Tests and Patient-Specific Quality Assurance
Shih-Chi Lin¹, Åse Ballangrud-Popovic¹, Grace Tang¹, and Gary Lim¹

¹Division of Radiotherapy Physics

Cranio-Spinal Irradiation (CSI) using Volumetric Modulated Arc Therapy (VMAT)

Adam Buell¹, Lindsey Claps¹, Katherine Chapman¹, Joseph Jancasz¹, Claire Nerbun¹, Alex Kowalsky¹, Joshua Feldman¹, Rene Britto¹, Cristina Saez², Luke Pike², Michalis Aristophanous¹ and Cesar Della Bianca¹

¹Department of Medical Physics and ²Department of Radiation Oncology

Developing AlignRT in Bore QA and Setup Procedures to Enhance Ethos Surface-guided Radiotherapy (SGRT)

Guang Li¹, Xiaoning Liu¹, Sebastian Meyer¹, Michelle Savacool¹, Michalis Aristophanous¹, and Laura Cerviño¹

¹Division of Radiotherapy Physics

Improving Operational Efficiency and Streamlining the Workflow with an Automatic Plan Documentation Application

Jeonghoon Park¹, LiCheng Kuo¹, Warren Fong², Anyi Li³, and Laura Cerviño¹

¹Division of Radiotherapy Physics, ²Formerly at MSK, and ³Computer Service

Longitudinal Tracking of Brain Metastases

Dylan Hsu¹, Åse Ballangrud-Popovic¹, Joseph Deasy¹, Laura Cerviño¹, Aditya Apte¹, Luke Pike², Rob Young³, Nate Swinburne³, and Michalis Aristophanous¹

¹Department of Medical Physics, ²Department of Radiation Oncology, and ³Department of Radiology

Managing Commonly Implantable Medical Devices for Radiotherapy Patients

Maria Chan¹, Claire Young¹, Daphna Gelblum², Carolanne Rincon³, Elizabeth Hipp¹, Jingdong Li¹, and Dongxu Wang¹

¹Department of Medical Physics, ²Department of Radiation Oncology, and ³Advanced Practice Providers

Next-generation Nonstop Gated Cone-Beam CT (CBCT) for Respiratory Gating Lung Stereotactic Body Radiation Therapy (SBRT)

Mitchell Yu¹, Sean Berry¹, Yabo Fu¹, Wendy Harris¹, Xiuxiu He¹, Weixing Cai¹, LiCheng Kuo¹, Michael Ziegenfus³, Noah Silverberg³, Daphna Gelblum², Boris Mueller², Laura Cerviño¹, Tianfang Li¹, Xiang Li¹, Jean Moran¹, and Hao Zhang³

¹Department of Medical Physics, ²Department of Radiation Oncology, and ³Formerly at MSK

Novel Scripting in Support of SRS Treatments-Implementation and Validation of an In-House Geometry Optimization Software For SRS VMAT Planning of Multiple Cranial Metastases

LiCheng Kuo¹, Pengpeng Zhang², Hai Pham², and Åse Ballangrud-Popovic¹

¹Division of Radiotherapy Physics and ²Computer Service

Predictive Quality Assurance for Linear Accelerator (Linac) Target Failure Using Statistical Process Control

Jingdong Li¹, Dongxu Wang², and Maria Chan²

¹Formerly at MSK and ²Division of Radiotherapy Physics

Predictive Models for Gradient Index and Brain Dose Parameters for Cranial Single Isocenter Multi-Target SRS (SIMT-SRS) planning

LiCheng Kuo¹, Fiona Kuo², Michalis Aristophanous¹, and Åse Ballangrud-Popovic¹

¹Division of Radiotherapy Physics and ²Formerly at MSK

Surface Imaging for Breast Radiotherapy with Deep-Inspiration Breath Hold

Wei Lu¹, George Li¹, Linda Hong¹, Ellen Yorke¹, Jim Mechalakos¹, Perry Zhang², Laura Cerviño¹, Paul Romesser³, Simon Powell³, and Sean Berry¹

¹Division of Radiotherapy Physics, ²Medical Physics Computer Service, and ³Department of Radiation Oncology

Validation and Implementation of Moldless Radiation Therapy for Prostate patients

Victoria Yu¹, Laura Happersett¹, Antonio Damato¹, Joseph Englese², Andrew Tama², Ozlem Dodge², Michael Cebisch², and Sean McBride²

¹Division of Radiotherapy Physics and ²Department of Radiation Oncology



Memorial Sloan Kettering
Cancer Center

Department of Medical Physics
Memorial Sloan Kettering Cancer Center
1275 York Avenue
New York, NY 10065

Chair

Joseph O. Deasy, PhD
deasyj@mskcc.org
212-639-8413

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