Principles and Practice of Radiation Oncology

First Annual Cancer Rehabilitation Symposium
May 31, 2013

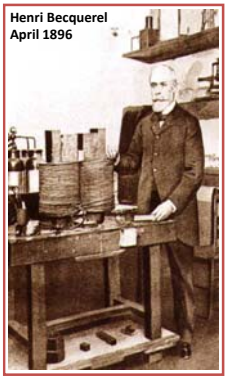
Josh Yamada MD FRCPC
Department of Radiation Oncology
Memorial Sloan Kettering Cancer Center

Disclosures

- Institute for Medical Education
- Varian Medical Systems

Natural Radioactivity

Henri Becquerel
April 1896



Pitchblend
Uranium, Polonium, & Radium

Marie Curie

1896
"Radioactivity"

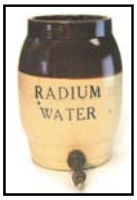
1898
Isolated Radium

Courtesy Michael Tuttle MD

Radium Therapy

1910-1920's: Pitchblende and Carnotite

- Malignancy
- Subacute and Charcot Joint
- Muscular Conditions
- High Blood pressure
- Nephritis
- Simple and Pernicious Anemias



Radium Beer

Courtesy Michael Tuttle MD

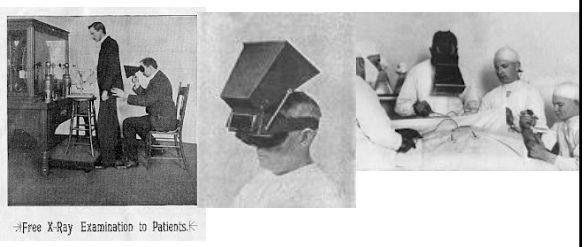
Household Products

Courtesy Michael Tuttle MD

Early x-ray facilities

Courtesy Michael Tuttle MD

Early Radiation Technology: Fluoroscopy



Radiotherapy as an Emerging Technology

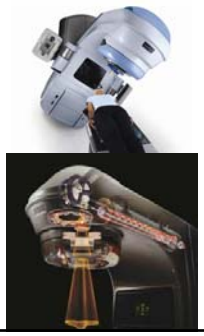
- **1895 - Rontgen discovers x-rays.**
- **1896 - Becquerel discovers radioactivity.**
  - Victor Despeignes reports treating stomach cancer with X rays
- **1901 - Rontgen receives the Nobel Prize in Physics for the discovery of x-rays.**
- **1905 - The first English book on Chest Radiography is published.**
  - Niels Finsen reports 50% success rate treating lupus with x rays
- **1913 -Coolidge introduces the hot cathode tube.**
- **1914 - Von Laue receives the Nobel Prize in Physics for x-ray diffraction from crystals.**
- **1915 - Bragg and Bragg receive the Nobel Prize in Physics for crystal structure derived from x-ray diffraction.**
- **1917 - Barkla receives the Nobel Prize in Physics for characteristic radiation of elements.**
- **1918 - Eastman introduces radiographic film.**
- **1920 - The Society of Radiographers is formed.**
- **1923 – Coutard reports 23% cure rate for head and neck cancers with fractionated RT**
- **1924 - Siegbahn receives the Nobel Prize in Physics for x-ray spectroscopy.**
- **1951 – Co60 Teletherapy**
- **1953 – Linear accelerator**

Radiation Oncology Factoids

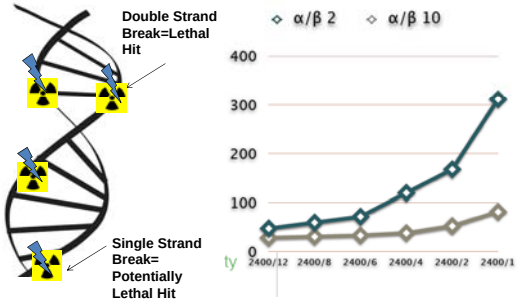
- Nearly 2/3 of cancer patients will receive radiation therapy
- There are over 4,600 licensed radiation oncologists in the US
- In 2004, nearly one million patients were treated with radiation therapy, 60% were first time RT patients
- Overall, 75% of patients were treated with curative intent

Radiotherapy Introduction

- Photons (xrays,gamma rays)
  - Quantum energy
  - Kilovoltage - Diagnostic imaging
  - Megavoltage – Therapeutic
    - Ionizing radiation
    - Radiation dose = Gray (joules/kg)
  - Brachytherapy
- Electrons
  - Superficial treatment
- Protons
  - Charged particles
  - Kinetic energy



Dose Per Fraction: Biologic Effectiveness



Dose and Fractionation

- Dose per fraction
  - High dose per fraction greater likelihood of lethal cell damage (same for tumor and normal tissue)
  - Increasing the dose per fraction has an exponential biologic effect
  - Increasing the number of fractions has a more linear biologic effect
  - Smaller dose per fraction means less injury to normal tissue (and also tumor)
  - Greater volume of irradiated tissue means a greater risk of serious radiation injury

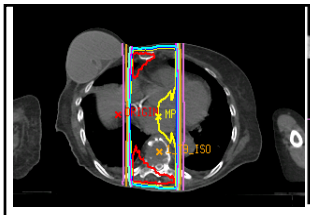
Tumor Control vs Complications

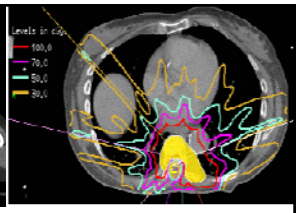
- **Ideal radiation treatment:**
  - **Maximum cell kill in tumor, minimum cell kill in normal tissue**
    - **Concentrate radiation in tumor, *limit dose* and volume of irradiated surrounding normal tissue**
  - **Normal tissues to be aware of in spine:**

•Spinal cord
•Esophagus
•Nerve plexus
•Bone Marrow

•Heart
•Lung

Tissue	Tolerated Dose	Complication
Spinal cord	50Gy in 25 fractions/ 14 Gy in 1 fraction	Myelitis
Peripheral N	60Gy in 30 fractions/ 20Gy in 1 fraction	Neuropathy
Small Bowel	60Gy in 30 fractions/ 18Gy in 1 fraction	Ulceration/perforation





- **Conventional XRT**
- Lower doses per fraction
- More fractions
  - Less complex
  - Fast
  - Larger volumes (multiple spine segments)
  - Cheaper
  - Hot spots near surface
- **Conformal XRT**
- High doses per fraction
  - Less normal tissue dose
    - Smaller margins
    - Important for surgical complication risks!
  - Higher dose to tumor
  - More technical/labor intensive
  - More expensive

	Conventional RT	Conformal RT
Dose per fraction	Lower	Higher
Treatment Volume	Bigger	Smaller
Normal Tissue	More	Less

- Conventional RT:
  - •Larger volumes to lower doses per fraction (radiosensitive)
  - •ie: Regional LN, multi level spine disease
- Conformal RT:
  - •Smaller volumes to higher doses per fraction (radioresistant)
  - •Discrete targets
  - •ie: Metastases in brain, lung, liver, spine

Advantages of RT

- Local/Local Regional
  - Not anatomically restricted
  - Limit high dose regions to tumor bearing tissue
- Non invasive
  - Curative tx for inoperable tumors
    - To extensive for surgery
    - Medically unfit for curative surgery
    - Adjuvant tx
- Effective palliation

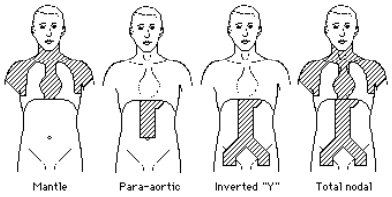
Risk Factors for Radiation Damage

- **Radiation Factors**
  - **Dose per fraction**
  - **Total dose**
  - **Total duration of tx**
  - **Volume of irradiated tissue**
- Host Factors
  - Age
  - Genetic predisposition
  - Infection
  - Systemic diseases
    - HTN
    - Diabetes
    - Autoimmune
  - Chemotherapy
  - Lifestyle (smoking)

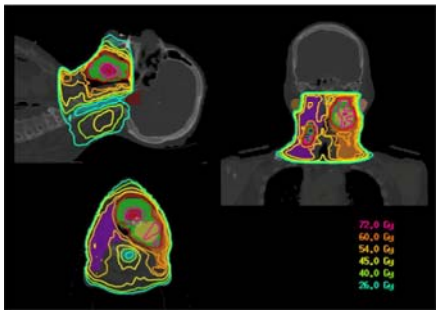
Radiation Induced Injury

- Direct Injury
  - Loss of functional cells
    - Pediatric
      - Mental function
      - Growth plates
    - Hematopoetic
- Indirect
  - Blood vessels
  - Fibrosis
  - RT induced tumors

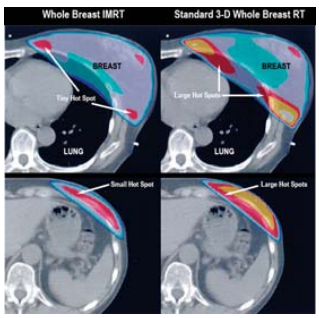
Hodgkin's Lymphoma Radiation Ports



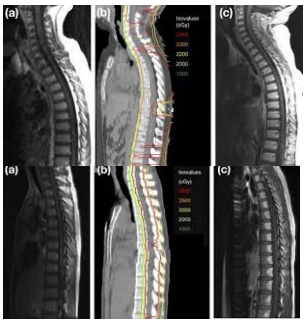
Head and Neck Radiation Fields- IMRT



Breast Cancer

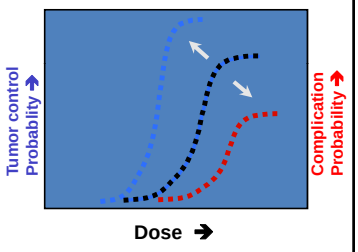


Proton Cranio Spinal RT



The Therapeutic Ratio

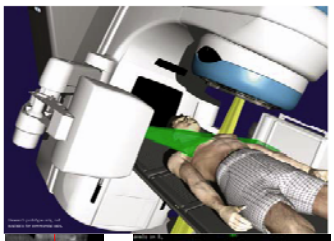
- *Improving the therapeutic ratio:*
- *Increase separation of tumor control curve and toxicity curve*
- Reduce toxicity:
  - Significant reduction in volume of volume sensitive toxicity
  - Reduce dose to dose sensitive toxicity
- Improve tumor control:
  - Tumor dose is critical

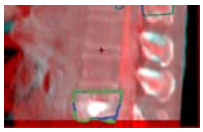


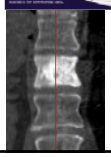
	Curative (RCT)	Standard of Care	Comments
CNS	✔✔✔✔✔	✔✔✔✔✔	RT shown benefit in almost every adult CNS disease
H and N	✔✔✔✔✔	✔✔✔✔✔	ChemoRT definitve for most cases
Lung	✔✔✔✔✔	✔✔✔✔✔	RT beneficial in every stage of lung cancer including stage I (SBRT)
Breast	✔✔✔✔✔	✔✔✔✔✔	Breast conserving RT
GI	✔✔✔✔	✔✔✔✔	ChemoRT most cases significant survival advantage, no role for colon ca. Sign benefit for rectal ca.
Gyne	✔✔✔✔✔	✔✔✔✔✔	RT/SurgeryRT/Chemotx
GU	✔✔✔✔✔	✔✔✔✔	Surgery vs RT as curative tx for prostate cancer, testicular, bladder. no role in adjuvant for renal cell.
Lymphoma/Leukemia/Myeloma	✔✔✔	✔✔✔✔	Ongoing dose reduction chemoRT, RT curative for many low grade lymphomas, less RT for leukemias
Sarcoma	✔✔✔✔✔	✔✔✔✔✔	Limb sparing RT, primary tx for unresectable tumors, no effective chemotx
Skin	✔✔	✔✔	Adjuvant or upfront for unresectable
Pediatric	✔✔✔✔	✔✔	Less of a role for RT, more chemo

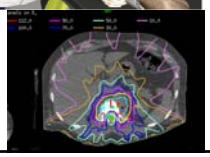
Image Guided Radiotherapy

- Near real time 3D imaging for position verification
- Positional corrections in X, Y,Z planes
- Accuracy within +/- 1mm



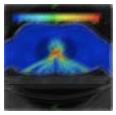


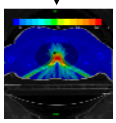




Spine Radiosurgery: Proof of Principle of the IGRT Hypothesis

- **Hypothesis: IGRT will improve outcomes by:** } ↓Uncertainties and Errors
  - **↓Toxicity**
  - **↑Tumor control**
- ***Spine Radiosurgery a test of the IGRT paradigm***
  - Proximity of sensitive structures:
    - Demands high precision
    - Rapid dose fall off to limit dose to spinal cord/bowel etc.
  - Many tumors are "resistant" to conventional fractionation
    - Significant experience with high dose single fraction radiation for intracranial brain metastases of radioresistant histologies





Competing Risks Analysis N = 413

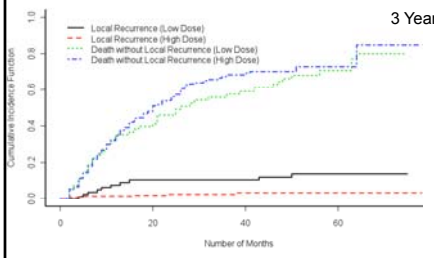


Figure 1: Local recurrence analysis – cumulative incidence functions for the two competing risks stratified by dose level.

3 Year Recurrence Rates

1800-2300cGy = 0.104

2400cGy = 0.024

All Patients = 0.040

Non surgical tx for spinal mets

Tumor	Neurologic	Pain	Function
Breast	93%	87%	93%
Prostate	91%	64%	82%
Myeloma	90%	100%	90%
SCLC	86%	86%	86%
Ovarian	100%	100%	100%
RESPONSIVE	87%	83%	85%
NSCLC	47%	65%	53%
Hepatocellular	33%	44%	33%
Gastric	50%	50%	25%
Colon	50%	50%	75%
Cholangio	50%	0	50%
Renal	67%	67%	67%
Sarcoma	50%	100%	50%
Thyroid	0	0	0
RESISTANT	49%	55%	47%
Total	67%	67%	64%

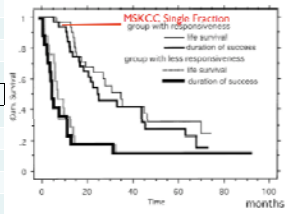


Fig. 4. Survival and duration of success in the group with responsiveness and the one with less responsiveness.

Hosoghi et al., Int J Radiat Oncol Biol Phys 42(5): 1127-1132

Radiation Therapy Summary

- Radiation therapy is beneficial both in terms of cure and palliation of cancer in almost all types of cancer
- The effects of radiation depend upon dose and volume of irradiated tissue
- Modern radiotherapy is able to minimize dose to normal tissue and maximize dose to tumor