

The Radiation Fibrosis Syndrome: Neuromusculoskeletal Complications

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American Board of Physical Medicine & Rehabilitation
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Memorial Sloan-Kettering
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Radiation Fibrosis Syndrome Disclosures

None



Radiation Fibrosis Syndrome Neuromuscular Complications

- Cerebroopathy
- Myelopathy
- Radiculopathy
- Plexopathy
- Mononeuropathy
- Myopathy



Stubblefield MD. Radiation fibrosis syndrome: neuromuscular and musculoskeletal complications in cancer survivors. PM R 2011;3(11):1041-54.




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Radiation Fibrosis Syndrome

Myelopathy

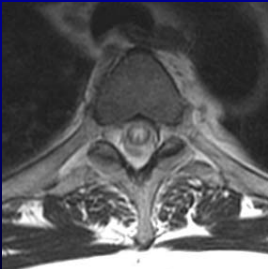

- Subacute myelopathy is estimated to occur in as many as 15% of patients treated with MF irradiation for HD.¹
- Clinical manifestations include:
 - Spasticity
 - Paraplegia / Quadriplegia
 - Spinal ataxia
 - Funicular pain
 - Detrusor sphincter dyssynergia (DSD)
 - Dystonia

Cress NE, Glantz MJ. Neurologic complications of radiation therapy. *Neural Clin N Am*. 2003;21:249-277.



Radiation Fibrosis Syndrome

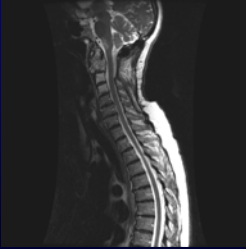

Myelopathy

Radiation Fibrosis Syndrome

Myelopathy of Medulla from Single Fraction Radiation


- C2 Chordoma
- IGRT 2400 cGy x1
- Progressive ataxia and weakness
- Later died of GI bleed

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Radiculopathy

- Incidence ?
- Clinical manifestations include:
 - Mono or poly-dermatomal pain or sensory deficits
 - Mono or poly-myotomal weakness, cramping, or spasm
 - Dystonia, myokymia
 - Often keeps company with other PNS deficits
 - Upper cervical (C-5, C-6) nerve roots commonly and severely affected




Radiation Fibrosis Syndrome

Neuropathology of Nerve Root Injury

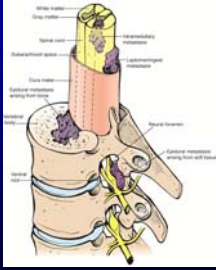
- Demyelination and axon loss with central chromatolysis of the anterior horn cells.
- Irregular thickening and areas of hemorrhage macroscopically and fibrosis with reduced numbers of axons microscopically.
- Clusters of dilated vessels with thickened hyalinized walls compressing adjacent nerve fibers.

Hsieh AW, et al. Post-irradiation polyradiculopathy mimics leptomeningeal tumor on MRI. Neurology 2003;60:1694-6.




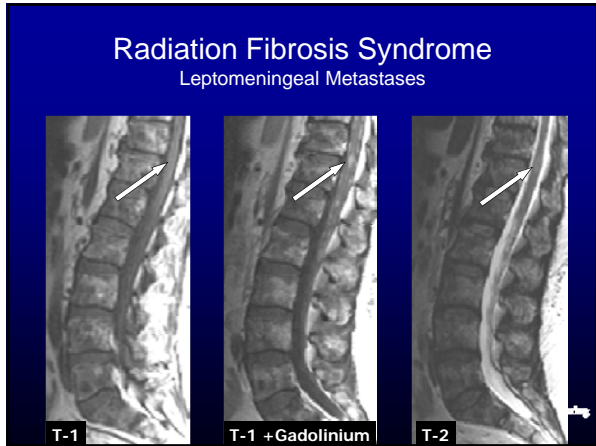
Radiation Fibrosis Syndrome

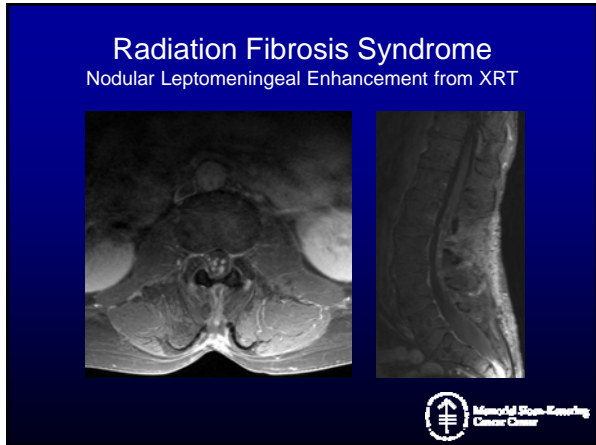
Radiculopathy

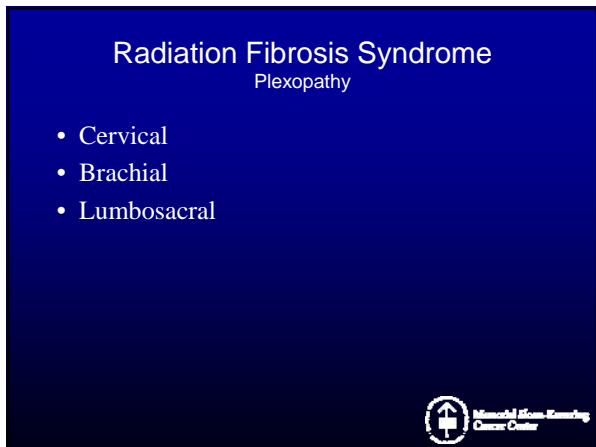


Stubbsfield MD and O'Dell MW, editors. Cancer Rehabilitation: Principles and Practice. New York, NY: Demos Medical Publishing; 2009.










Radiation Fibrosis Syndrome

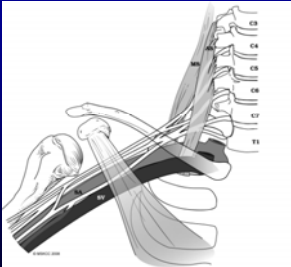
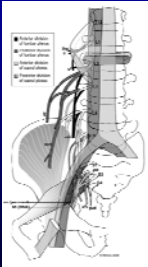
Cervical Plexus

- Ventral rami of C1-C4
- Located deep to the sternocleidomastoid muscle
- Cutaneous branches
 - Lesser occipital nerve (lateral part of occipital region - C2 only)
 - Great auricular nerve (skin near outer ear and ear canal - C2 & C3)
 - Transverse cervical nerve (anterior region of neck - C2 & C3)
 - Supraclavicular nerves (supraspinatus, shoulder, upper thoracic region - C3 & C4)
- Muscular branches
 - Ansa cervicalis (geniohyoid, thyrohyoid, sternothyroid, sternohyoid, omohyoid - C1-C3)
 - Phrenic (diaphragm and pericardium - C3-C5, primarily C4)
 - Segmental branches (anterior and middle scalenes - C1-C4)




Radiation Fibrosis Syndrome

Brachial and Lumbosacral Plexus


Lewis J, Krol G. Principles of Plexus Imaging. In: Stubbelfield MD and O'Dell MW, editors. Cancer Rehabilitation: Principles and Practice. New York, NY: Demos Medical Publishing; 2009. 149-160.



Radiation Fibrosis Syndrome

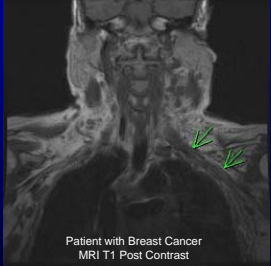
Plexopathy

- Incidence ?
- Clinical manifestations include:
 - Pain or sensory deficits in distribution of affected plexus structure
 - Weakness, cramping, or spasm in distribution of affected plexus structure
 - Dystonia, myokymia
 - Often keeps company with other PNS deficits
 - Upper brachial plexus most commonly and severely affected

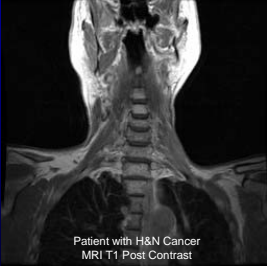


Radiation Fibrosis Syndrome

Radiation Plexopathy




Patient with Breast Cancer
MRI T1 Post Contrast



Patient with H&N Cancer
MRI T1 Post Contrast

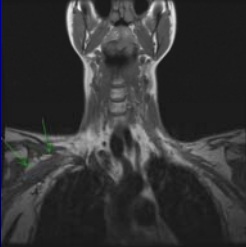
Shubfield MD and O'Dell MW, editors. Cancer Rehabilitation: Principles and Practice. New York, NY: Demos Medical Publishing; 2010.




Radiation Fibrosis Syndrome

Radiation Plexopathy from XRT for Hodgkins and Breast CA

T1 Post gadolinium MRI demonstrating a severe radiation-induced brachial plexopathy in a patient with Hodgkin lymphoma treated with 10 cycles of alternating MOPP/ABVD chemotherapy and mantle field radiation (dose unknown) in 1983. In 2005 she was diagnosed with right sided breast cancer treated with bilateral mastectomy, ACT chemotherapy and radiation including 5040cGy in 28 fraction to the right chest wall and 4500cGy in 25 fractions to the right subclavian lymph nodes.






Radiation Fibrosis Syndrome

Neuropathy

- Incidence ?
- Clinical manifestations include:
 - Mono or poly-neuronal pain or sensory deficits
 - Mono or poly-neuronal weakness, cramping, or spasm
 - Dystonia, myokymia
 - Often keeps company with other PNS deficits
 - Only affects nerves that are in or traverse the radiation field
 - Bilateral phrenic nerves can be compromised from mantle radiation!


Avila EK, Goerka A, Fontana S. Bilateral phrenic nerve dysfunction: a late complication of mantle radiation. J Neurooncol 2010.



Radiation Fibrosis Syndrome

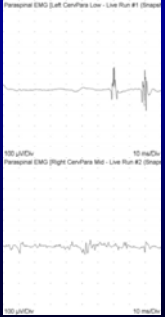
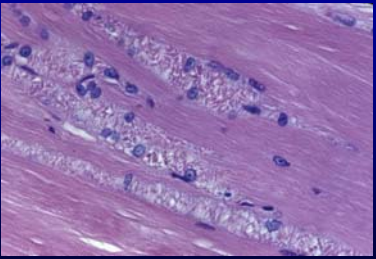
Myopathy

- Incidence ?
- Clinical manifestations include:
 - Pain, weakness, cramping, or spasm
 - Dystonia, myokymia
 - Often keeps company with other PNS deficits




Radiation Fibrosis Syndrome

Nemaline Rod Myopathy

Portlock CS, Boland P, Hays AP, Antonescu CR, Rosenblum MK. Nemaline myopathy: a possible late complication of Hodgkin's disease therapy. Hum Pathol. 2003;34:119-24.



Radiation Fibrosis Syndrome


Clinical Neuromusculoskeletal Syndromes




Radiation Fibrosis Syndrome

Malignancies Commonly Complicated by RFS

- Hodgkin Lymphoma
- Head and Neck Cancer
- Metastatic Disease
- Recurrent Breast Cancer



Stubblefield MD. Radiation fibrosis syndrome: neuromuscular and musculoskeletal complications in cancer survivors. PM R 2011;3(11):1041-54.




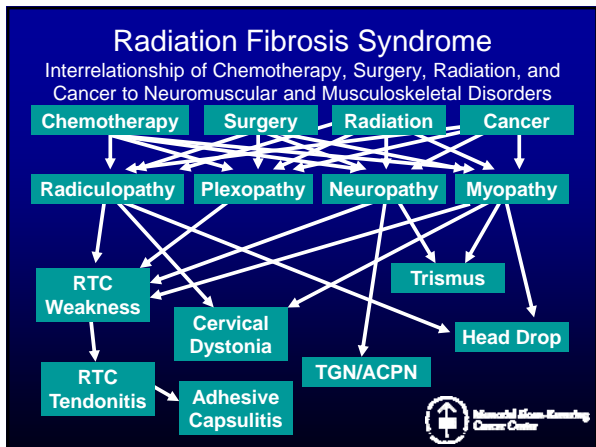
Radiation Fibrosis Syndrome

Common Neuromusculoskeletal Disorders

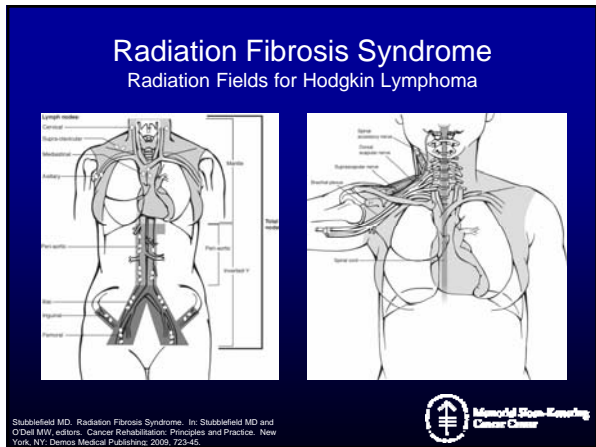
- Myelo-radiculo-plexo-neuro-myopathy
- Cervical dystonia
- Neck extensor weakness
(a.k.a., “dropped head syndrome”)
- Trigeminal/ anterior cervical plexus neuralgia
- Trismus (oropharyngeal dystonia)
- Mononeuropathies
- Shoulder Dysfunction

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Radiation Fibrosis Syndrome

Hodgkin Lymphoma




Radiation Fibrosis Syndrome

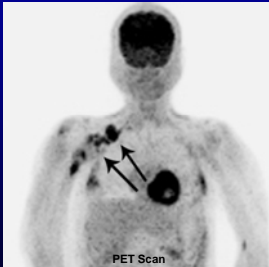
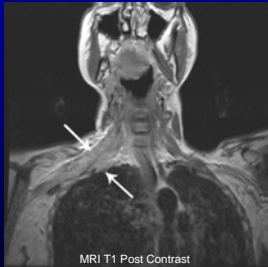
Nodular Plexopathy in a Hodgkin Lymphoma Survivor 37 Years After Mantle Radiation






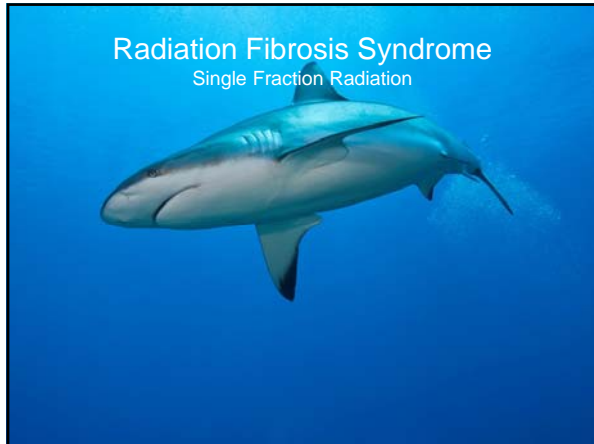
Radiation Fibrosis Syndrome

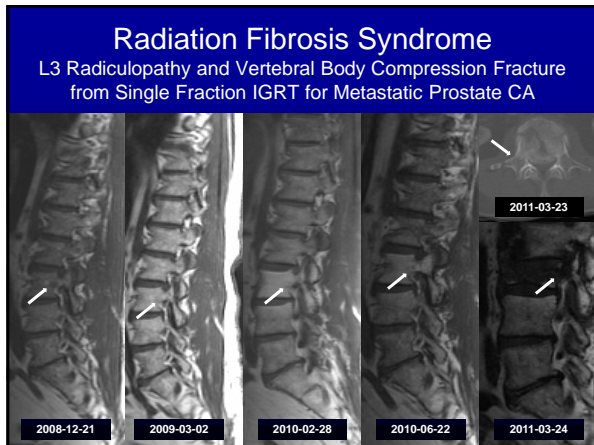
Radiation-induced Sarcoma (MPNST) from Mantle Radiation for Hodgkin Lymphoma

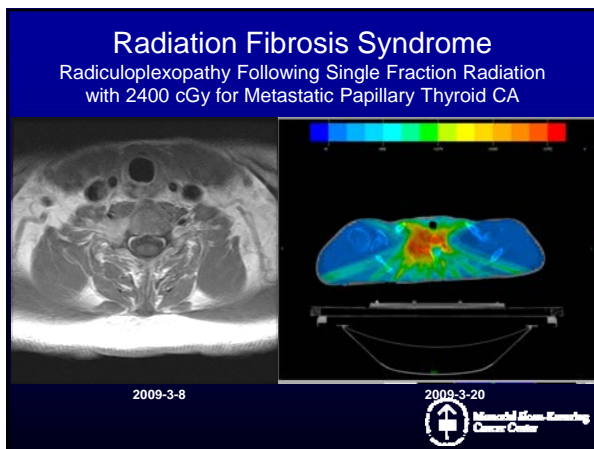



Stubblefield MD and O'Dell MW, editors. Cancer Rehabilitation: Principles and Practice. New York, NY: Demos Medical Publishing; 2009.









Radiation Fibrosis Syndrome

Radiculoplexopathy Following Single Fraction Radiation with 2400 cGy for Metastatic Papillary Thyroid CA

2011-5-11

2011-6-7

Radiation Fibrosis Syndrome

Head and Neck Cancer

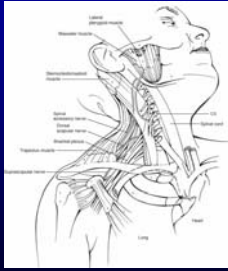
Radiation Fibrosis Syndrome

100% Isodose Curves for a Nasopharyngeal Carcinoma

Stubblefield MD. Radiation Fibrosis Syndrome. In: Stubblefield MD and O'Dell MW, editors. Cancer Rehabilitation: Principles and Practice. New York, NY: Demos Medical Publishers; 2009. 723-45.

Radiation Fibrosis Syndrome

Structures at Risk in the Treatment of H&N Cancers



Stubblefield MD. Radiation Fibrosis Syndrome. In: Stubblefield MD and O'Dell MW, editors. Cancer Rehabilitation: Principles and Practice. New York, NY: Demos Medical Publishing; 2009. 723-45.



Radiation Fibrosis Syndrome

Radiation-induced Cervical Dystonia from XRT for Nasopharyngeal Carcinoma



Radiation Fibrosis Syndrome

Myelo-radiculo-plexo-neuro-myopathy from XRT for Nasopharyngeal Carcinoma with Neck Drop

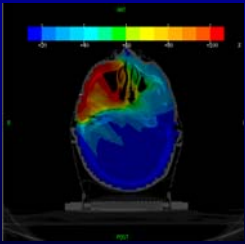


Stubblefield MD. Radiation Fibrosis Syndrome. In: Cooper G, ed. Therapeutic Uses of Botulinum Toxin. Teaneck, NJ: Humana Press; 2007:19-34.




Radiation Fibrosis Syndrome

100% Isodose Curves for a Parotid Malignancy





Stubblefield MD. Radiation Fibrosis Syndrome. In: Stubblefield MD and O'Dell MW, editors. Cancer Rehabilitation: Principles and Practice. New York, NY: Demos Medical Publishing; 2009. 723-45.



Radiation Fibrosis Syndrome

Radiation Induced Trismus



Treatment of RFS




Radiation Fibrosis Syndrome

Commonly Seen Disorders

- Cervical dystonia
- Head drop/neck weakness
- Trismus
- Axial spinal pain
- Spasticity
- Trigeminal & anterior cervical plexus neuralgia
- Mononeuropathy
- Shoulder dysfunction

Stubblefield MD. Radiation fibrosis syndrome: neuromuscular and musculoskeletal complications in cancer survivors. *PM R*. 2011;3(11):1041-54.



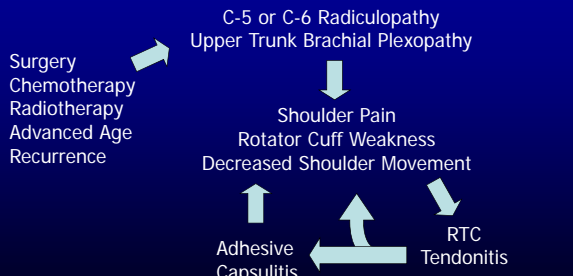
Cancer Rehabilitation

58 women s/p MRN dissection and XRT with Rt. Trapezius Atrophy and Lateral Scapula Winging





Radiation Fibrosis Syndrome

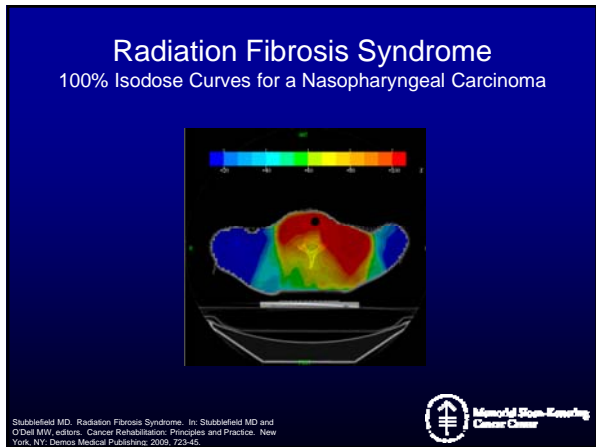
Upper Extremity Pain Cycle

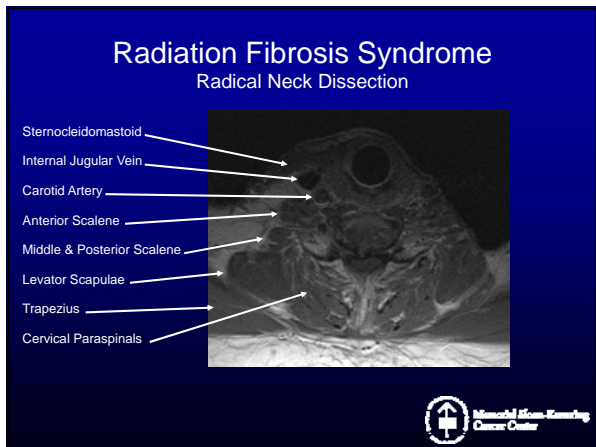


Stubblefield MD, Custodio CM. Upper-extremity pain disorders in breast cancer. *Arch Phys Med Rehabil*. 2009;27(3 Suppl):94-9.










Radiation Fibrosis Syndrome

Treatment of Radiation-induced Cervical Dystonia

- Physical Therapy
- Nerve Stabilizing Agents
 - Pregabalin/Gabapentin
 - Duloxetine
- Botulinum Toxin Injection





Radiation Fibrosis Syndrome

Treatment of Neck Extensor Weakness


- Physical Therapy
 - Neuromuscular Reeducation
 - Postural correction
 - Proprioceptive reeducation
 - Core strengthening
 - Scapular retraction/depression
 - Muscle balancing
 - MLD
 - Soft Tissue Mobilization
 - Advanced myofascial techniques
 - Craniosacral
 - Visceral





Shubblefield MD. Radiation fibrosis syndrome: neuromuscular and musculoskeletal complications in cancer survivors. PM R 2011;3(11):1041-54.

Radiation Fibrosis Syndrome

Treatment of Neck Extensor Weakness



- Nerve Stabilizing Agents
 - Pregabalin/Gabapentin
 - Duloxetine
- Analgesics
- Orthotics
 - Headmaster® Cervical Collar



Stubbelfield MD. Radiation fibrosis syndrome: neuromuscular and musculoskeletal complications in cancer survivors. PM R. 2011;3(11):1041-54.

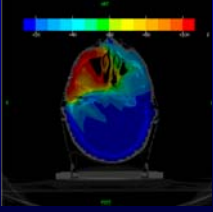



Trismus

Radiation Fibrosis Syndrome

Treatment of Radiation-induced Trismus

- Physical Therapy
 - Soft Tissue Mobilization
 - Advanced myofascial techniques
 - “Facia is the arch-nemesis”
 - Neuromuscular Reeducation
 - Postural correction
 - Proprioceptive reeducation
 - Muscle balancing
 - MLD
- Nerve Stabilizing Agents
 - Pregabalin/Gabapentin/Duloxetine
- Jaw Opening Device
- Botulinum Toxin Injection






Stubbelfield MD, Levine A, Custodio CM, Fitzpatrick T. The role of botulinum toxin type A in the radiation fibrosis syndrome: a preliminary report. Arch Phys Med Rehabil. 2008;89(5):417-21.
 Stubbelfield MD, Mansfield L, Reedel ER. A Preliminary Report on the Efficacy of a Dynamic Jaw Opening Device (Dynamic Trismus System) as part of the Multimodal Treatment of Trismus in Patients with Head and Neck Cancer. Arch Phys Med Rehabil. 2010;91:1278-82.
 Stubbelfield MD. Radiation fibrosis syndrome: neuromuscular and musculoskeletal complications in cancer survivors. PM R. 2011;3(11):1041-54.

Radiation Fibrosis Syndrome

Jaw Opening Devices for Trismus



Stubblefield MD. Radiation Fibrosis Syndrome. In: Stubblefield MD and O'Dell MW, editors. Cancer Rehabilitation: Principles and Practice. New York, NY: Demos Medical Publishing; 2009. 723-45.

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Radiation Fibrosis Syndrome

Changes in Maximal interincisal Distance (MID) Before and After Treatment with Dynasplint Trismus System

Patients	Pretreatment		Posttreatment		Difference in Scores Median (Range)*	p-value [†]
	No.	Score Median (Range)	Score Median (Range)	Score Median (Range)		
All	20	16.5 (9 to 41)	23.5 (10 to 47)	5 (-4 to 15)	.0003	
Compliant	15	16 (11 to 41)	27 (11 to 47)	7 (0 to 15)	.0001	
Noncompliant	5	17 (9 to 30)	22 (10 to 26)	-1 (-4 to 5)	.88	

*Based on the difference of the preintervention and postintervention values for each individual patient.
[†]P values were calculated for differences in the pretreatment and posttreatment scores using the Wilcoxon sign-rank test.

Stubblefield MD, Manfield L, Riedel ER. A Preliminary Report on the Efficacy of a Dynamic Jaw Opening Device (Dynasplint® Trismus System) as part of the Multimodal Treatment of Trismus in Patients with Head and Neck Cancer. Arch Phys Med Rehabil. 2010;91:1278-82.

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Radiation Fibrosis Syndrome

Conclusion

- RFS is a common complication of cancer treatment and includes a number of neuromuscular and musculoskeletal sequelae.
- Radiation fibrosis cannot be prevented but RFS can be treated and its complications minimized.
- The principles of treatment of neuromuscular and musculoskeletal complication of RFS are similar to the treatment of other neuromuscular and musculoskeletal disorders.

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