City of Hope®

Multidisciplinary Approaches to Cancer Symposium

Symptom Management of Radiation Toxicities

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City of Hope

Disclosures

- I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

The following CLC & IB components will be addressed in this presentation:

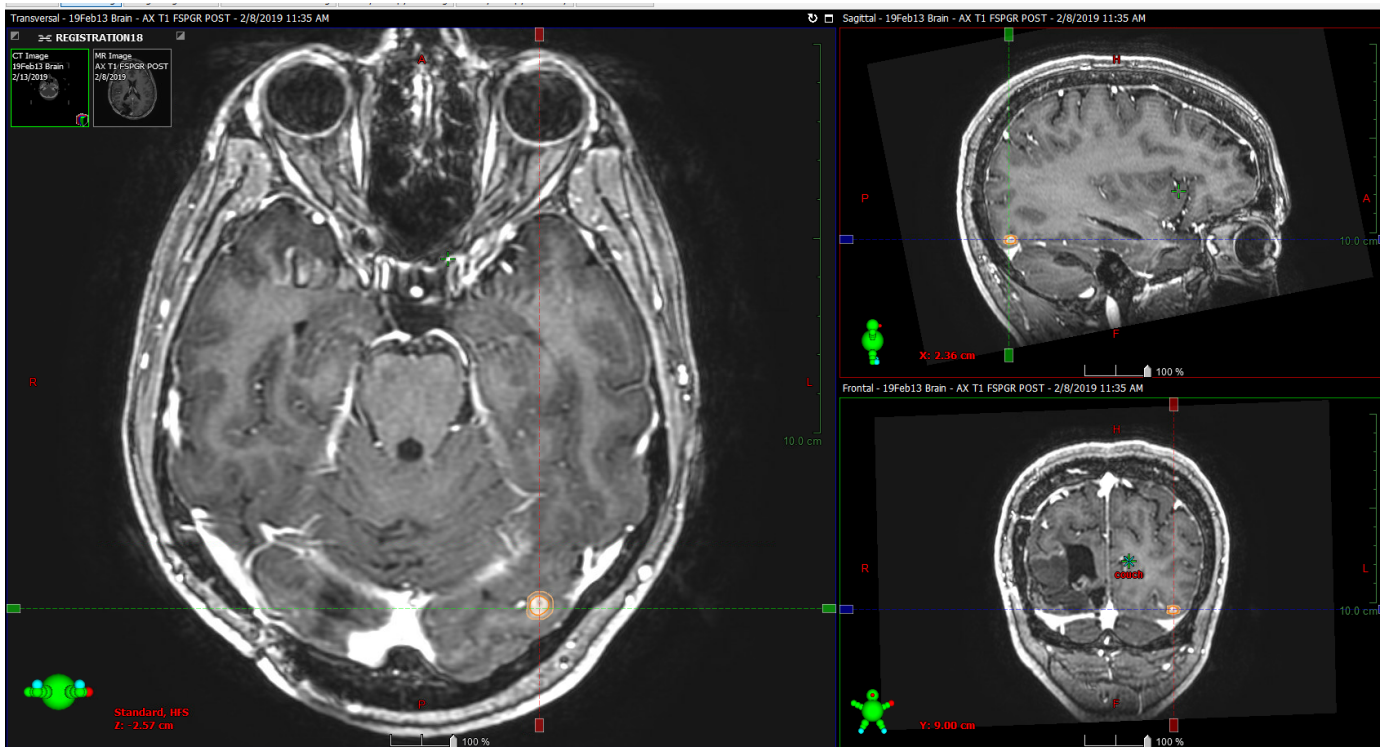
- *Consideration of the management of toxicity for patients of diverse backgrounds.*
- *Barriers in access to various treatments.*

Outline

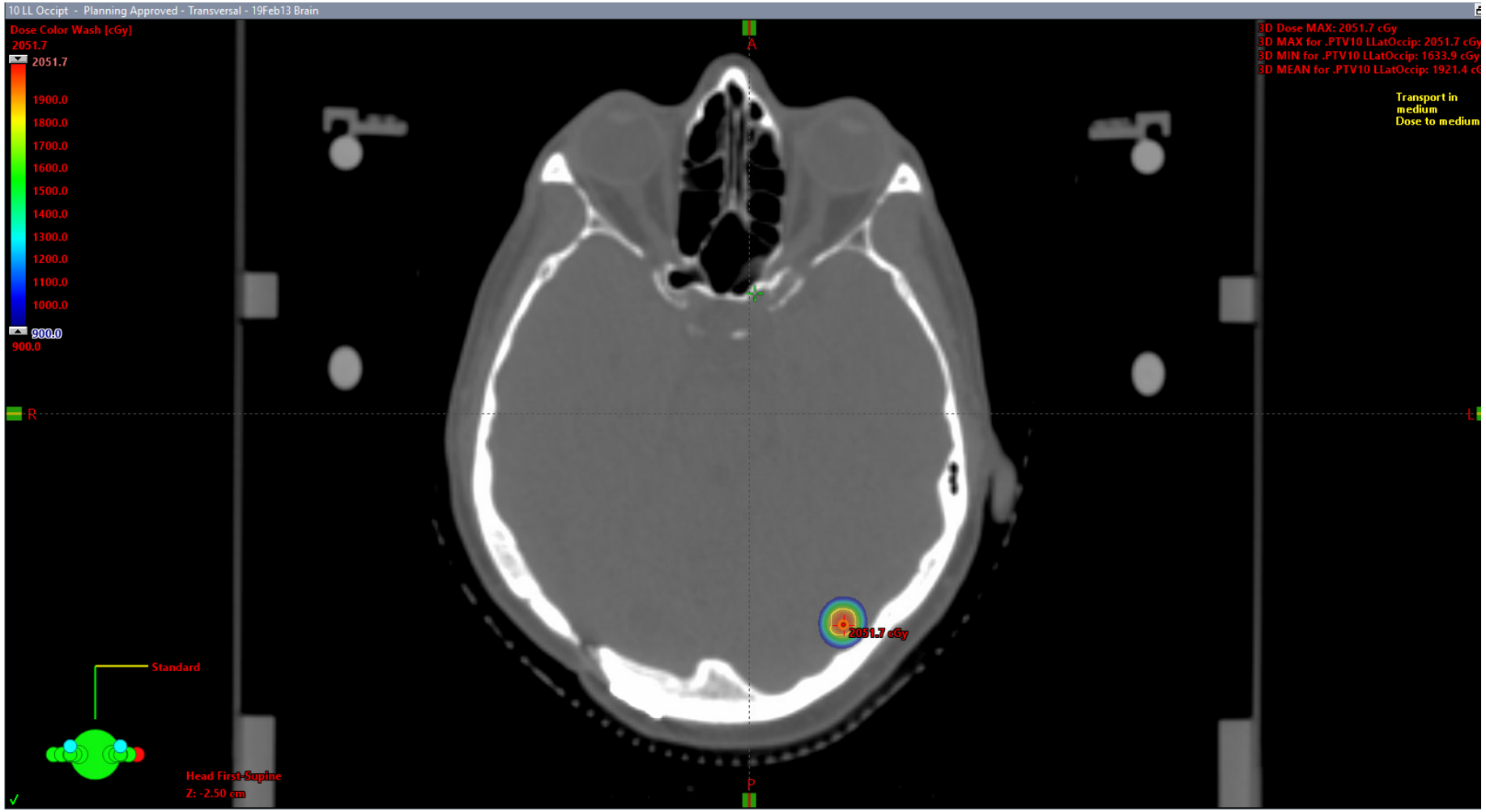
- Common Radiation Induced Toxicities
  - CNS radionecrosis / edema
  - Dysphagia/Odynophagia
  - Xerostomia
  - Dermatitis
  - Nausea
  - Diarrhea
  - Cystitis
  - Proctitis
  - Sexual
  - Lymphedema

CNS radionecrosis / edema

- Case 1: 50 y/o with history of metastatic breast cancer, most recently treated with TDM-1
  - Develops small brain metastasis shown here:



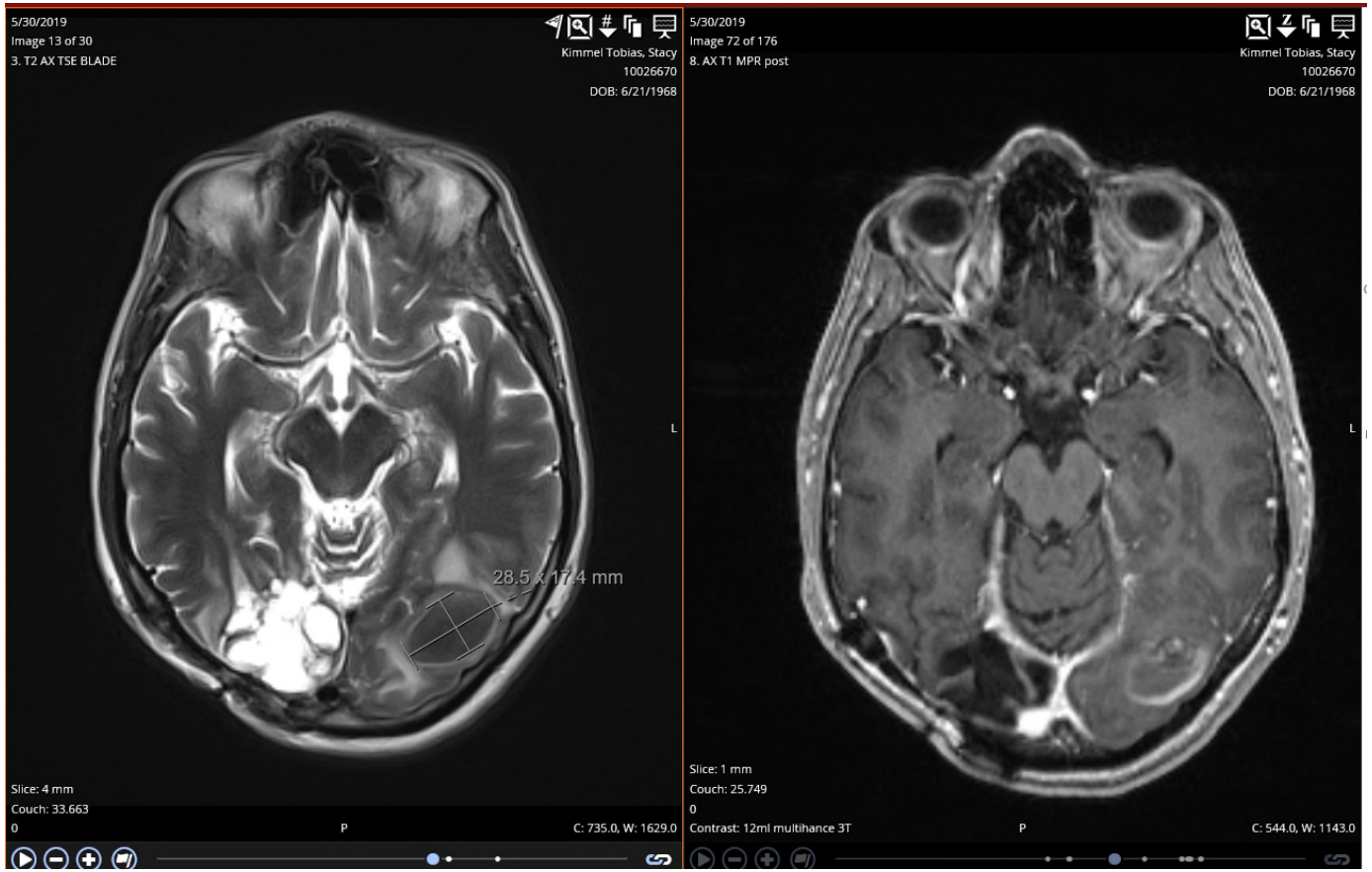
CNS radionecrosis / edema



CNS radionecrosis / edema

- 3 months after she developed headaches, weakness, and visual field deficits. She had progressive blurry vision, and she was unable to recognize faces or read

- MRI showed a 3 cm hematoma in the left occipital lobe, seen on the T2 image on the left. On the T1 image on the right shows the irradiated lesion with surrounding radiation necrosis and the surrounding hematoma

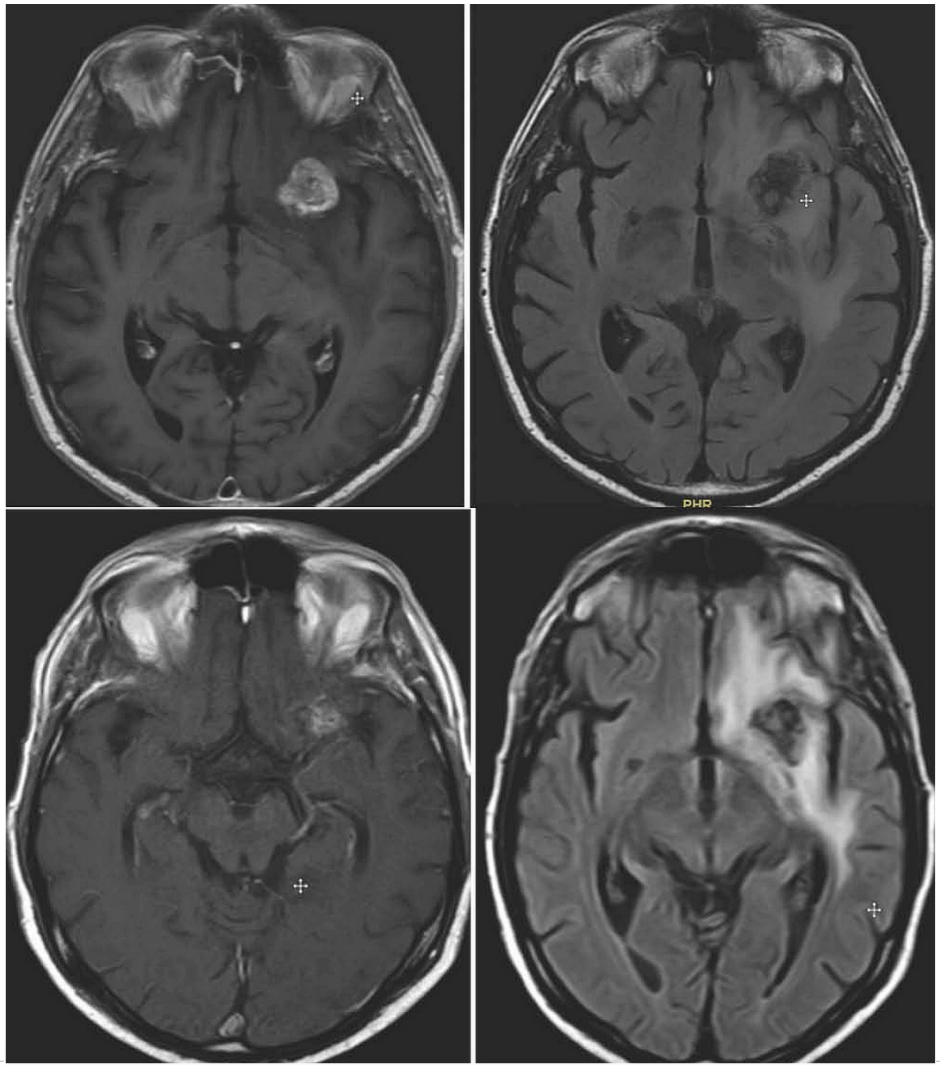


CNS radionecrosis / edema

- Treatment of this case:
  - 4 mg Decadron TID
  - Neurosurgery consulted
  - Monthly MRI brain
  - 1 month later, patient reports significant headache improvement, vision improved by 80%
  - Walking without difficulty

CNS radionecrosis / edema

- Symptomatic necrosis in single-fraction SRS occurs in
  - 20% of patients receiving V12 > 15 cm^3
  - 15% of patients receiving V12 > 10 cm^3
  - 10% of patients receiving V12 > 5 cm^3
- Brain – GTV V12 < 10 cc
- Optic pathway point max < 10 Gy
- Brainstem point max < 16 Gy
- 3-fraction SRS: V20 < 20 cm^3 and 5-fraction V24 < 20 cm^3
  - <10% risk of necrosis or edema
  - <4% risk of radionecrosis requiring resection
- Synergy with certain systemic therapies
  - TDM-1, Methotrexate, Enhertu?



CNS radionecrosis / edema

- Differential Diagnosis:
  - Progression
  - Pseudoprogression
    - Usually presents earlier at 2-5 months and resolves
    - Self-limited
  - AVM
  - Hemorrhagic Stroke
  - Dural Thrombosis

CNS radionecrosis / edema

- Corticosteroids
  - Inhibit pro-inflammatory cascade
  - Long-term complications
- Hyperbaric oxygen
- Surgical excision
- Bevacizumab 5 mg/kg biweekly
  - Anti-*VEGF* monoclonal antibody
  - *VEGF* normally causes angiogenesis and increases capillary permeability
  - Blocks *VEGF* from reactive astrocytes

Case Example #2:

57 yo male, heavy smoker

T3 N2 M0 AdenoCa of the Right Upper Lobe

Coronal PET/CT

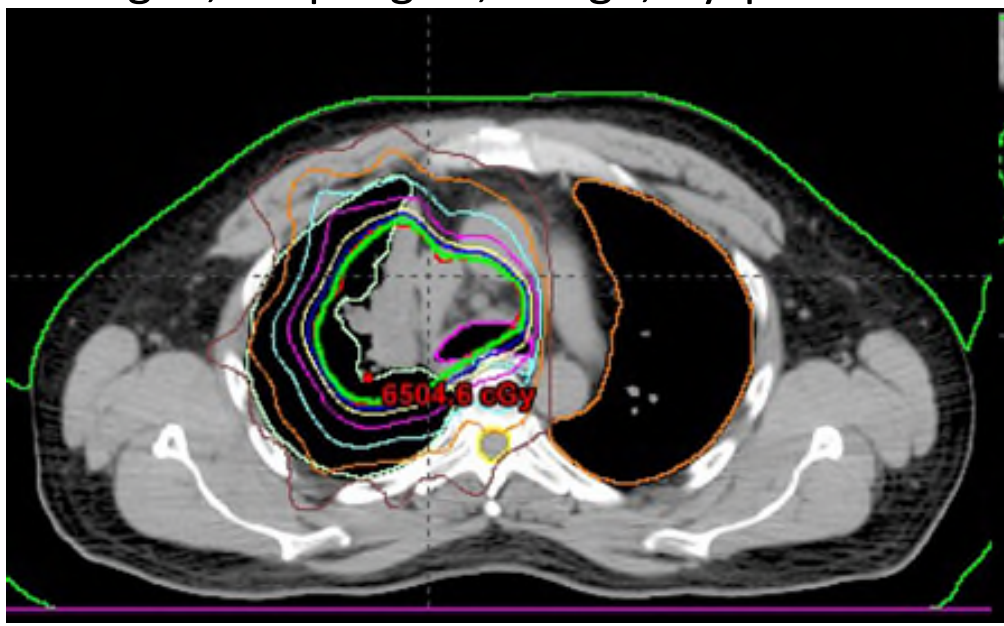
Recommended:

60 Gy delivered in 30 fractions (2-Gy per treatment) over 6 weeks

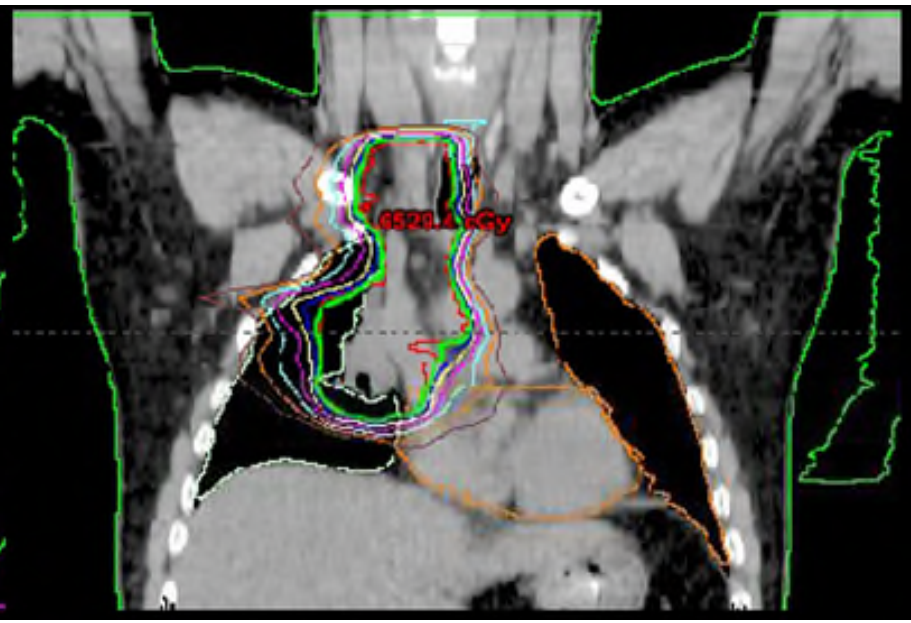
Delivered with concurrent cisplatin/etoposide chemotherapy

Potential Side Effects:

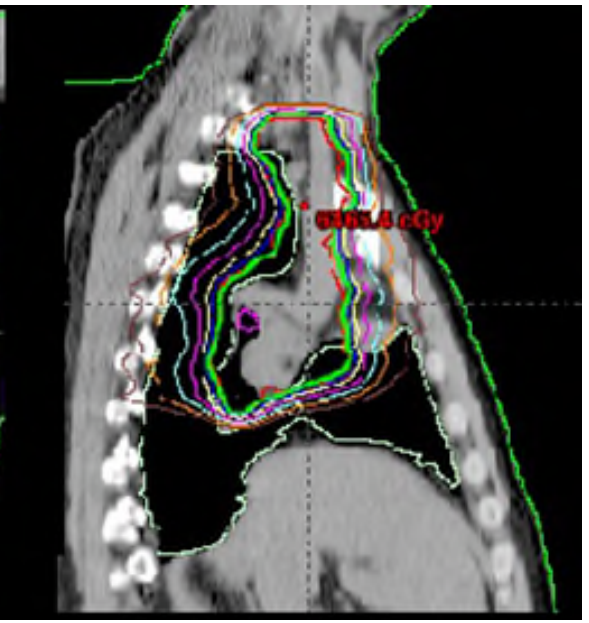
Fatigue, Esophagitis, Cough, Dyspnea



Axial



Coronal



Sagittal

Dysphagia/Odynophagia (Mucositis)

- Common in patients getting radiation to the head and neck region, thorax (lung, esophagus)
- May be exacerbated by certain systemic therapies (i.e. 5-Flurouracil)
- Is patient able to eat or drink? If not and/or patient is altered, not responding well, consider ETC or ER
    - May need to have a PEG tube placed
- If eating and drinking, then medical management
    - Smoothies, supplements (Ensure, Boost)
    - MD can prescribe medications
        - Radiomix, Carafate, PPI, Dexamethasone, Opioids if needed, Glutamine

Dysphagia/Odynophagia (Mucositis)

- Oral mucositis: multiple options (nothing ground breaking)
  - Oral rinses (baking soda), Magic mouthwash (lidocaine/maalox/benadryl), NSAIDS, gabapentin, narcotics, steroids, red light therapy

Xerostomia

- Common side effect of head and neck radiotherapy
    - Decreased rates in the era of IMRT. Randomized trial showed that by switching from older radiation techniques to IMRT the rates of grade 2+ xerostomia decreased from 75% to 25%

- Treatment options:
    - Biotene mouthrinse
    - Ginger ale
    - Acupuncture
    - Bethanechol
    - Submandibular gland transfer

Applied Cancer Research. 37. 10.1186/s41241-017-0037-5.

Dermatitis

- Radiation can cause skin erythema -> desquamation
- Results from superficial dose due to superficial tumor sites
    - Common in breast cancer, head and neck cancer, anal cancer, vulvar cancer
    - Rare to nonexistent in cancers of deeper locations such as prostate cancer, esophageal cancer, lung cancer, rectal cancer, upper GI cancer
- Urgent/Emergent if patient has fevers
- Management
    - Skin creams (Aquaphor, Miaderm, Aloe Vera) – grade 1-2
    - Grade 2-3+ Mepilex pads, Silvadene cream, break from radiation

Nausea

- Less common than with chemotherapy
- Typically when treating brainstem, lower esophagus, abdomen
- Ondansetron (preferred), Prochlorperazine (can add), Ativan, Phenergan, hydration
- One nausea develops, patients often need anti-nausea med daily through the remainder of the radiation course to minimize further episodes.
    - With medical management usually can be well controlled

Cystitis

- Common with pelvic radiotherapy (prostate and GYN)
- Urinary frequency, urgency, hesitancy, leakage, dysuria, hematuria, nocturia
- Should rule out UTI, especially if prior UTI history, more than minimal to mild symptoms, fevers
- Generally non-urgent – can try Ibuprofen/Advil and Pyridium (available OTC, brand=AZO, turns urine orange)
    - Should have UA done but non-urgent if afebrile
- Urgent – fevers/chills; should have evaluation to rule out UTI

Late Complications: Cystitis

Radiation-induced cystitis treated with hyperbaric oxygen therapy (RICH-ART): a randomised, controlled, phase 2–3 trial

Nicklas Oscarsson, Bernd Müller, Anders Rosén, Pär Lodding, Johan Mölne, Daniel Giglio, Karin M Hjelle, Guro Vaagbø, Ole Hyldegaard, Michael Vangedal, Lisbeth Salling, Anders Kjellberg, Folke Lind, Otto Ettala, Olli Arola, Helén Seeman-Lodding

Lancet Oncol 2019; 20: 1602–14

- 87 patients randomized to +/- hyperbaric oxygen
- Pelvic RT >6 mo prior, <80 EPIC urinary score, >100 cc bladder, no catheter, no fistula, no recent blood transfuse
- 30-40 1.5 hour sessions breathing O_2 at 240-250 kPa
- Improvement in EPIC score of 17.8 vs 7.7 points (p=0.01)
- 41% transient grade 1-2 vision or hearing AE

•Cystitis

- Other management options: anticholinergics (oxybutynin), tamsulosin, Kegel exercises
- Other treatment options for Hemorrhagic cystitis
  - Oral therapy (sodium pentosan polysulphate or tranexamic acid)
  - Ablation of bleeding or imminently bleeding vessels
  - Intravesicular aluminum
  - Urinary diversion
  - Intravesicular formalin
  - Cystectomy

- Smit, S. G. & Heyns, C. F. *Nat. Rev. Urol.* 7, 206–214 (2010)

Proctitis / Enteritis

- Common in patients getting radiation for Lower GI cancers (pancreas, gastric, rectal), Prostate, or GYN
- Start with OTC Imodium (make dose is 4 mg, 4 times daily)
- If Imodium is not enough, can add lomotil
- Can consider dexamethasone short course
- Hydration!
- Urgent if patient altered, confused, or if significant amounts of bright red blood

Review Article

Radiation Proctitis: Current Strategies in Management

Nhue L. Do, Deborah Nagle, and Vitaliy Y. Poylin

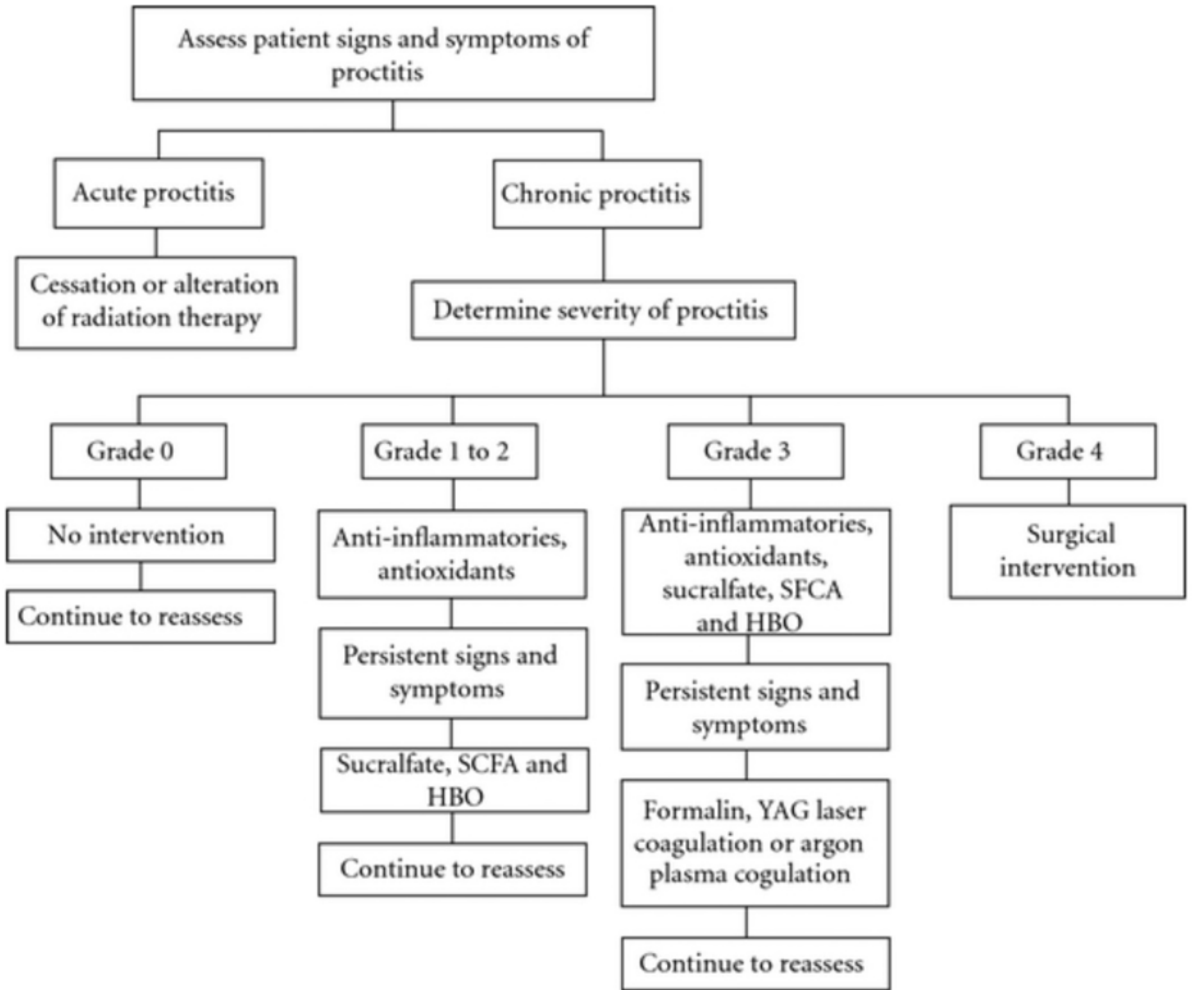
Division of Colon and Rectal Surgery, Beth Israel Deaconess Medical Center, Harvard Medical School Boston, 330 Brookline Avenue, Stoneman 9, Boston, MA 02215, USA

Gastroenterology Research and Practice Volume 2011, Article ID 917941, 9 pages doi:10.1155/2011/917941

Grade	Symptoms or signs	Overall management
0	No symptoms	None
1	Occasional urgency and occasional pain; superficial ulceration <1 cm^2, occult bleeding, and mild stricture	Outpatient management; no lifestyle adjustments
2	Intermittent urgency and intermittent pain; superficial ulceration >1 cm^2, occasional bleeding, and moderate stricture	Outpatient management; some lifestyle adjustments
3	Persistent urgency and persistent pain; deep ulceration, persistent bleeding, severe stricture	Possible short hospital admission or minor surgical intervention; major lifestyle adjustments
4	Refractory urgency and uncontrollable pain; gross hemorrhage, perforation, fistula, complete obstruction	Long-term hospital admission or major surgical intervention
5	Sepsis, multiorgan failure, and death	Fatal complications

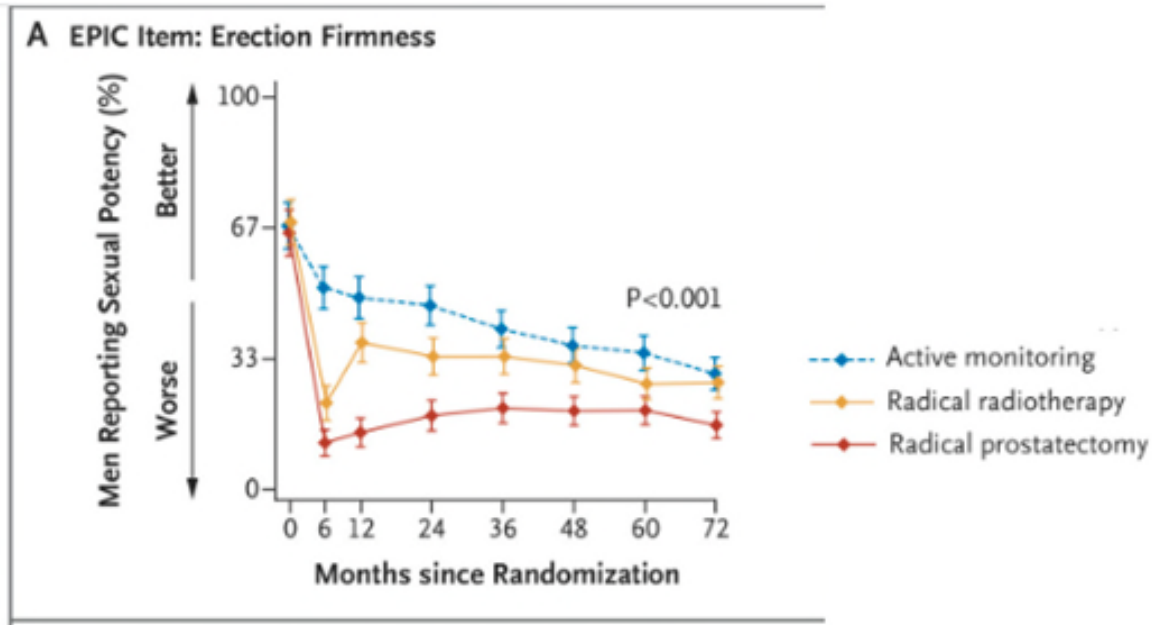
Late Complications: Proctitis

- Treatment
  - Anusol HC suppository
  - Proctosol cream
  - Short Chain Fatty Acids
  - Sucralfate
  - Hyperbaric Oxygen
  - Laser coagulation



Sexual

- Radiotherapy can effect the sexual function of all genders
- Historically more focus on male sexual health though this is changing
- Lots of research on prostate cancer patients and effect of surgery or radiotherapy on sexual health:
    - PDE-5 Inhibitors
    - Injections
    - Pumps
    - Implants



PROTECT Randomized Trial, NEJM 2016

Sexual

- For patients treated with radiotherapy for gynecological or lower GI cancer:
  - Vaginal Dialtor to prevent stenosis/fibrosis
  - Selective use of estrogen supplementation
  - Pomegranate oil, vitamin A, vitamin E

Review

Interventions Preventing Vaginitis, Vaginal Atrophy after Brachytherapy or Radiotherapy Due to Malignant Tumors of the Female Reproductive Organs—A Systematic Review

Adrianna Wierzbicka [1,†], Dorota Mańkowska-Wierzbicka [2,†], Stanisław Cieślewicz [3], Marta Stelmach-Mardas [1,*] and Marcin Mardas [3]

Int. J. Environ. Res. Public Health **2021**, *18*, 3932. https://doi.org/10.3390/ijerph18083932

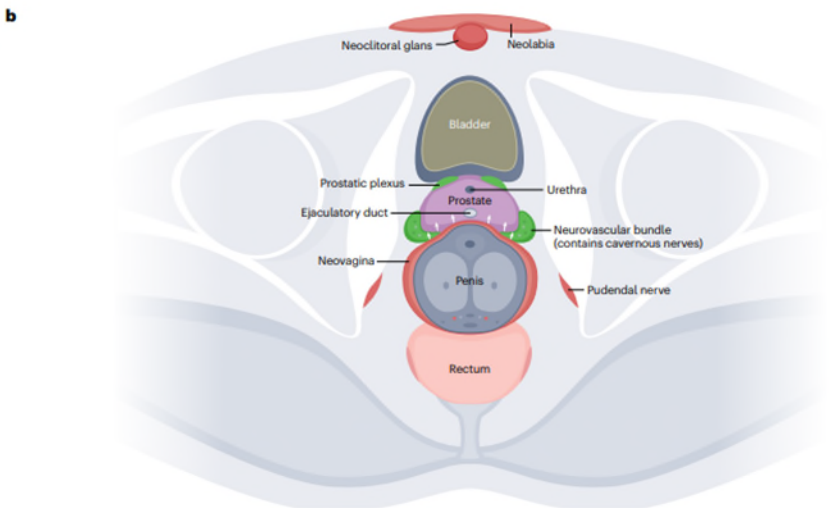
- Emerging research for sexual and gender minorities

Review article

Sexual health and treatment-related sexual dysfunction in sexual and gender minorities with prostate cancer

Daniel R. Dickstein[1], Collin R. Edwards[2], Eric J. Lehrer[1], Elizabeth S. Tarras[3], Matthew Gallitto[4], John Sfakianos[5], Matthew D. Galsky[6], Richard Stock[1], Joshua D. Safer[7], B. R. Simon Rosser[8] & Deborah C. Marshall[1,9]

Nature Reviews Urology | Volume 20 | June 2023 | 332–355



Radiation Fatigue

- Common side effect
- Generalized weakness, diminished mental concentration; typically begins in 2nd week of treatment
    - Typically is not debilitating
- If patient altered or not responding, that is an emergency and unlikely a result of radiation
- Evaluate other causes of fatigue
    - Pain
    - Polypharmacy
    - Blood counts
- Otherwise patient should be counseled that this is normal

Other Radiation Side Effects

- Bone Marrow Suppression (worse with large pelvis or spine fields)
- Lymphedema (breast cancer receiving nodal irradiation, inguinal nodal irradiation, limb sarcoma)
- Peripheral nerve plexopathy (high dose radiation to sacral regions, brachial plexus)
- Cataract formation
- Alopecia (brain radation – much less common with SRS)
- Pneumonitis

Conclusions

- Radiation induced side effects vary considerably based on which part of the body is being treated and to what dose
- An awareness of the potential side effects of radiotherapy is important in the multidisciplinary management of cancer patients
- Patient quality of life is optimized with early intervention of radiotherapy induced side effects
- Do not ever hesitate if needed to contact the radiation oncologist after hours or weekends (resident and/or attending) if the patient is experiencing a radiation related side effect
- When possible, for patients who are undergoing radiation treatment who need urgent care, have them **come to ETC** if possible – patients who get admitted to an outside hospital cannot continue radiation
    - Breaks in radiation treatment can lead to worse cancer outcomes
    - 911 or local ER if unsafe to have patient come to ETC

Questions?