

RADIATION INDUCED DERMATITIS AND MUCOSITIS

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Faculty/Presenter Disclosure

- Faculty: **Dr Marc David**
- Relationships with commercial interests:
 - **NO commercial interest to disclose**

Disclosure of Commercial Support

- Potential for conflict(s) of interest:
 - NO conflict of interest to disclose

Mitigating Potential Bias

Practice Profile

- ▣ Radiation Oncologist in practice for 16 years
- ▣ Main sites treated are breast, esophagus prostate.
- ▣ Other main interest is palliative care
- ▣ More than 10 years participation in multidisciplinary Cancer Pain clinic

PLAN

- ▣ DEFINITIONS
- ▣ PATHO-PHYSIOLOGY OF RT DAMAGES
- ▣ PREDICTING FACTORS
- ▣ DERMATITIS
- ▣ UPPER GI MUCOSITIS/HEAD NECK
- ▣ PROCTITIS

DEFINITIONS

- ▣ ACUTE side effects of RT:
 - Side effects appearing during or shortly after RT. Commonly accepted period within 3 months (90days)
- ▣ LONG TERM side effects of RT:
 - Side effects appearing any time after 90 days and up to several years.

DEFINITIONS

- ▣ Commonly used scoring scale is used for uniformity, comparison and generalization
- ▣ NCI Common Toxicity Criteria Adverse Event
- ▣ Functional Assessment of Cancer Therapy
FACT-B/E/L/P
- ▣ Radiotherapy Oncology Group
RTOG/EuroORTC
- ▣ LENT-SOMA

PATHO-PHYSIOLOGY OF RT DAMAGES

▣ ACUTE INJURIES

■ Structural tissue damage

- ▣ Organ in series (spinal cord, GI)
- ▣ Organ in functional unit (lung, skin)
- ▣ RT generates free radicals causing double strand DNA breaks
- ▣ Initiation of secondary inflammatory response in basal layers of dermis or mucosa.

PATHO-PHYSIOLOGY OF RT DAMAGES

- ▣ LATE INJURIES OF RT
- ▣ Cascade of inflammatory responses causing apoptosis of clonogenic stem cells, upregulation and amplification of cytokines
- ▣ Results in full-thickness damages with ulceration and colonization of bacteria causing further inflammation.
- ▣ Stimulation of angiogenesis process with neovascularization and fibroblasts deposit excess collagen.

PREDICTING FACTORS

▣ PATIENT RELATED

- Hygiene, lifestyle (smoking, OH).
- Comorbidities such as Lupus, sclerodermia, RhAr are relative contra-indication to RT.
- Diabetes, COPD and peripheral vascular atherosclerotic patients have increased risk of complications with RT.
- Age and race are NOT predictor factors.

PREDICTING FACTORS

- ▣ TREATMENT RELATED
 - RT tolerance knowledge is derived from radiation exposure accidents, Nazi's experimentation and clinical experience.
- ▣ Organ radio sensitivity are often dose limiting.

PREDICTING FACTORS

- ▣ TREATMENT RELATED
- ▣ Most radiosensitive organ (<50Gy)
 - Skin, mucosa (GI,GU,Gyne), bone marrow, spinal cord, lenses
- ▣ Intermediate radiosensitive organ (<60-65Gy)
 - Heart, kidneys, bladder, brain
- ▣ Less radiosensitive (<70Gy)
 - Bones, great vessels

PREDICTING FACTORS

▣ TREATMENT RELATED

▣ Curative intent dose of RT

- ▣ Radical RT (head&neck, esophagus, prostate, anus, cervix, sarcoma, lung, brain)
 - ▣ Some cancers like Lymphoma, testis or pediatric are treated with radical intent but dose required is smaller.
- ▣ Adjuvant to surgery (breast, rectum, uterus)
- ▣ Concomitant use of chemotherapy may increase radio sensitivity

PREDICTING FACTORS

- ▣ TREATMENT RELATED

- ▣ Palliative intent

- ▣ Dose is less and rarely leads to acute dermatitis or mucositis.

Overall PS of patient is best predictor

- ▣ Concomitant use of new drugs in immunotherapy may have radio sensitizing effects (cetuximab, nivolumab)

PREDICTING FACTORS

- ▣ TREATMENT RELATED

- ▣ Palliative intent

- ▣ Re-irradiation in same localization is increasingly common since patients survive longer. Previous dose have to be taken into account to avoid accumulation of late side effects of RT.

- Example: treated for prostate 10 years ago with 70Gy in 35 fractions now has bone mets in the acetabulum

Isodoses (Gy)

8.64

8.40

8.00

7.60

7.20

6.80

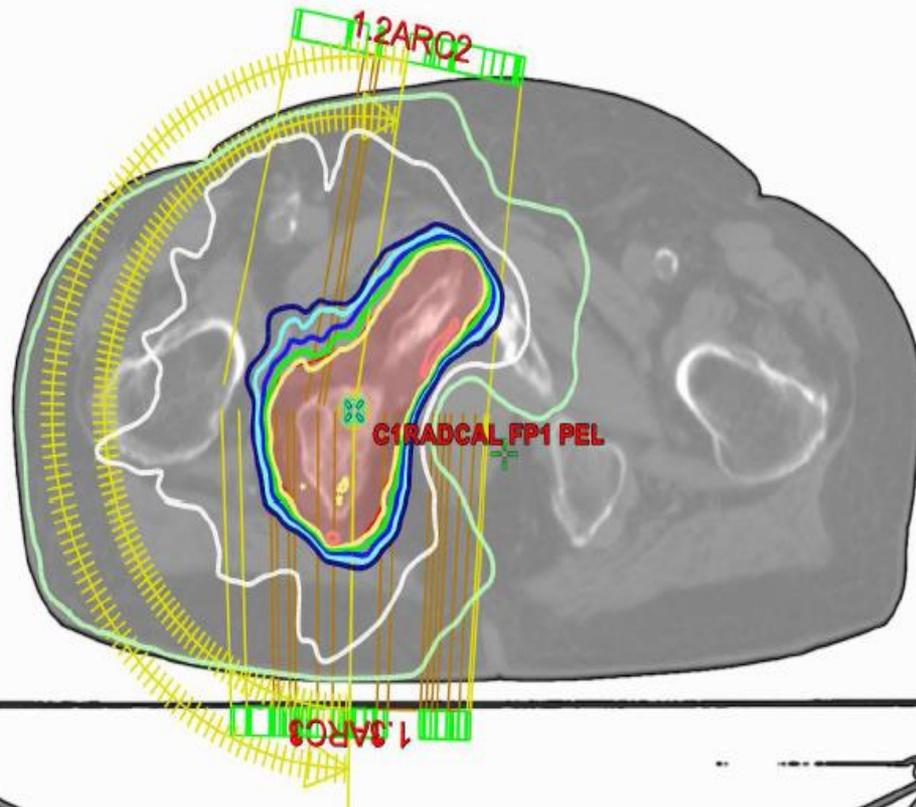
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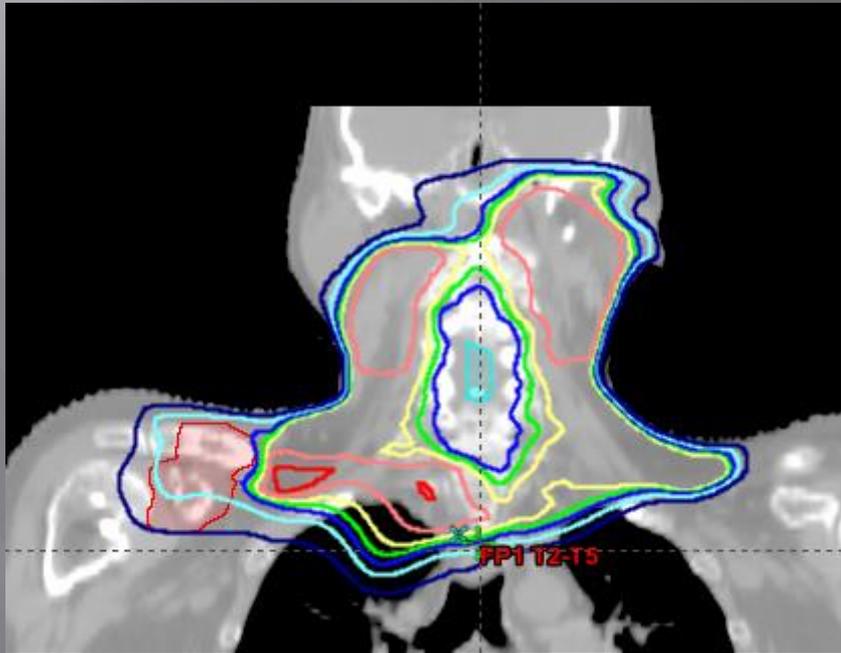
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2.00

R

A





PREDICTING FACTORS

- ▣ TREATMENT RELATED
- ▣ Field size
- ▣ Total dose (# of fractions)
- ▣ Dose per fraction
- ▣ Radio sensitizers
- ▣ RT technique delivery
 - 3D planning using CT simulation now standard
 - IMRT (Intensity Modulated) is use in most centers in radical curative intent



PREDICTING FACTORS

- ▣ TREATMENT RELATED
- ▣ IMRT is multiplying #fields to distribute dose and avoid hot spots
- ▣ IMRT requires greater resources for planning, better immobilization and longer sessions on the machine.

DERMATITIS

- ▣ Clinical symptoms:
- ▣ Redness
- ▣ Itchiness/pruritus
- ▣ Burning/soariness/tightness
- ▣ Swelling
- ▣ Pain

TREATMENT OF DERMATITIS

NCI CTCAE v 4.02

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Dermatitis	No change noted	Faint erythema or dry desquamation	Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema	Moist desquamation other than skin folds and creases; bleeding induced by minor trauma or abrasion	Skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site; skin graft indicated	Death

TREATMENT OF DERMATITIS



Treatment of dermatitis

- ▣ Hygiene myth:
 - Washing with soap → ■ Yes proven by RCT₁
 - Deodorant → ■ No, conflicting literature₂
 - Shaving → ■ No, but no trial
 - Sun exposure → ■ No
 - Corn starch → ■ No, increases risk of infection

Treatment of dermatitis

PROPHYLAXIS

All clinical trials have small samples (10-100)

- ▣ Comparing 2-3 agents or cream vs water+soap
- ▣ Results often are not significant and defy “departmental” culture.

Treatment of dermatitis

- ▣ PROPHYLAXIS
- ▣ Only agent that has a significant effect in reducing from 37% to 11% symptoms and a trend in reducing severity of acute reaction is topical corticosteroids. ³
- ▣ Mometasone 0.1% was used
- ▣ 4 other RCT.

Treatment of dermatitis

- ▣ PROPHYLAXIS
- ▣ All other creams did not reach recommendation level in consensus review.⁴
- ▣ Trolamine (biafine)⁵, hyaluronic acid-based, aloe vera gel, silver sulfazidine (flamazine)
- ▣ Neither any oral agent such as sucralfate, proteolytic enzymes or medicated dressing (silver dressing, hydrocolloid, GM-CSF)⁴

Treatment of dermatitis

- ▣ TREATMENT OF ACUTE DERMATITIS
- ▣ Symptoms oriented and goal is to prevent infection which would worsened reaction.
- ▣ Use of sulfazidine cream (Flamazine 1%) bid-tid is recommended.
- ▣ For patient allergic to sulfa drugs, alternative exist: Calendula ointment, topical antibiotic cream, non adherent dressing .

Treatment of dermatitis

- ▣ TIME IS THE GREATEST MEDICATION
- ▣ Acute dermatitis usually heals in 2-4 weeks depending on severity.
- ▣ Patients need reassurance, support and after RT skin care advise.
- ▣ Keep regular habit to apply moisturizing cream and avoid sun exposure of treated area.

Treatment of dermatitis

- ▣ RECALL DERMATITIS
- ▣ Dermatitis in previously radiated area.
- ▣ Can be triggered by chemo (adriamycin) or immunotherapy (cetoxumab, nivolumab).
- ▣ Often no obvious cause
- ▣ Same treatment as acute dermatitis

RECALL DERMATITIS



Treatment of dermatitis

- ▣ Long term/ Late dermatitis
- ▣ No known predictor factor
- ▣ Symptoms are often cosmetic but can also cause:
 - ▣ Tightness feeling
 - ▣ Reduce range of arm motion (breast or limb)
 - ▣ Pain
 - ▣ Telangiectasia

Treatment of dermatitis

- ▣ Long term/ Late dermatitis
- ▣ Pentoxifylline which increases blood flow has receive attention but no formal recommendation.⁶
- ▣ Requires several weeks or months to have response.
- ▣ Dominant side effects is nausea.

Treatment of dermatitis



Treatment of dermatitis

- ▣ Long term/ Late dermatitis
- ▣ Hyperbaric O₂ chambers can be used in refractory ulceration.
- ▣ Requires daily treatment 5-6 weeks.
Accessibility issues.
- ▣ In failed conservative measures, surgical debridement with/without skin graft is to be considered.



UPPER GI MUCOSITIS/HEAD NECK

- ▣ In head neck tumors, RT is used in curative intent.
- ▣ Often concomitant chemo.
- ▣ Combined and synergistic toxicity.
- ▣ Both skin of neck/face and oral or upper GI mucosa are affected.
- ▣ Systemic pain medication and nutritional support is necessary.

UPPER GI MUCOSITIS/HEAD NECK

- ▣ Pre treatment Dentist assessment.
- ▣ Oral hygiene education.
- ▣ Prophylaxis:
 - Gentle rinse with salty water or baking soda qid
 - Several agents and rinse have failed to demonstrate significant difference. ⁷
 - Ex: amifostine, benzidamine(tantum), Magic Mouth Wash.

PROCTITIS

- ▣ Can occur in 5-20% patient treated for rectal, anal, GYN and prostate.
- ▣ Symptoms are:
 - ▣ Diarrhea with/without mucus discharge
 - ▣ Tenesmus
 - ▣ Urgency
 - ▣ Bleeding
- ▣ Acute and initial late proctitis have same symptoms.

ACUTE PROCTITIS

- ▣ In acute proctitis, stool cultures to rule out c.diff or other treatable infections.
- ▣ Nutritional support and antidiarrheatic medications.
- ▣ Other treatment for acute symptoms are corticosteroids enema, sucralfate enema or ASA enema. IR devices can induce trauma to friable mucosa.

telangiectasia



LATE PROCTITIS

- ▣ Often presents with rectal bleeding.
- ▣ Should rule out other cause such as other malignancy by referring for endoscopy.
- ▣ Endoscopic therapy with laser, argon or cryoablation according to your GI's experience.
- ▣ Several session are required (median of 4).
Response rates varies 30-90%.⁷

LATE PROCTITIS

- ▣ 5-20% of patients with late proctitis progress to Obstruction or fistula.
- ▣ MRI pelvis is imaging tool for fistula.
- ▣ Requires immediate surgical management.

THANK YOU

QUESTIONS?

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