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Oral and Mandibular Toxicities of Radiotherapy

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Introduction

- **EARLY EFFECTS**
  - Xerostomia →
    - Dental caries →
    - Infection →
  - Taste changes
  - Mucositis

- **LATE EFFECTS**
  - Radiation Fibrosis
  - Trismus
  - Swallowing (KH)
  - Osteoradionecrosis
Xerostomia

- Major salivary gland
  - Parotid
    - Stimulated/serous
  - Submandibular
    - Unstimulated/Mixed
  - Sublingual
    - Mucous

- Minor salivary gl.
  - Mucous
Xerostomia

- Introduction
- Xerostomia
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- 30-40 Gy irreversible salivary gland damage
- Standard dose for H & N ca. 60-70Gy
Salivary Flow Rates
Parallel opposed/ Anterior neck fields

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*Fig—Mean flow rates of stimulated whole saliva in 42 patients with cancer before, during, and after radiotherapy.*
Xerostomia
Intensity Modulated Radiation Therapy (IMRT)

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Xerostomia - IMRT

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T3 N2c M0 SCC Lt. BOT
Proton Therapy

- Multifield optimization intensity modulated proton therapy (MFO-IMPT)
- New generation of proton therapy delivery
- Theoretical advantages of reduced dose to:
  - Spinal cord
  - Parotid gl.
  - Brain stem
Xerostomia

Dreizen’s Data

- Stimulated saliva (rubber bands)
- Starting flow rate: 1.10ml/min
- End of year: 0.12ml/min
- 2 year: 0.10ml/min
- 3 year: 0.05ml/min
- 87.5% reduction in saliva flow at 1 year

Current Data

- Stimulated saliva (citric acid)
- Starting flow rate: 1.13ml/min
- End of year: 0.49ml/min
- 2 year: 0.44ml/min
- 56.7% reduction in stimulated saliva flow at 1 year

*Data suggests some sparing of salivary function with IMRT*
Xerostomia

- Increased number of caries forming bacteria
- Loss of buffering capacity
- Lowered salivary pH
- Elimination of mechanical flushing
- Decreased production of saliva immunoglobulins, lysosomes and peroxidases
Xerostomia Management

- Increase oral moisturizing
  - Water or sugar-free liquids
  - Saliva substitutes may provide symptomatic relief
  - Stimulate saliva production with sugar-free Xylitol gum

- Avoid alcohol and phenol containing mouth rinses

- **Pilocarpine** and **Cevimeline** are cholinergic agonists that stimulate exocrine glands
  - **Pilocarpine** 5-10mg tid (duration of 3 hr)
  - **Cevimeline** 30-60mg tid (duration of 5 hr)

- Acupuncture
Caries
Xerostomia effect of Microflora

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Caries

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Effect of Radiotherapy on the DEJ

- Delamination of enamel from dentin is rare
- Distinctive pattern of dentition breakdown with radiation
- Shear fracture of enamel

Hypothesis: DEJ Matrix interface is destabilized by direct or indirect radiation damage

- Retrospective analysis of 93 patients treated with XRT
- XRT dose to individual teeth compared to dental deterioration severity

**Results**
- < 30 Gy minimal damage
- 30-60 Gy had a 2-3 times greater risk for tooth deterioration
- > 60Gy had a 10 fold increase in tooth deterioration (delamination)
Caries Prevention

- Avoid moistening mouth with sugar containing, acidic or carbonated liquids
- Avoid sugar containing mints/gums
- Avoid frequent sugary between meal snacks
- Brush teeth after every meal or snack
- Use soft toothbrush and floss & fluoride toothpaste (1100ppm)
- 3 mo. dental recall
- Use topical fluoride gel daily (10 min.)
Caries Prevention

Fluoride therapy (topical):
(0.4% Stannous Fl or 1.1% Sodium Fl)
- Decreases post XRT dentinal sensitivity
- Remineralize cavitated enamel
- Inhibits caries-forming organisms
Daily fluoride Treatment

1. Floss all teeth.

2. Brush with fluoride toothpaste for three minutes.

3. Rinse with baking soda and water mixture. (½ tsp. baking soda in 1 cup water)

4. Fill trays ⅓ full with fluoride gel and insert over teeth. After 10 minutes remove trays and spit out excess fluoride.

5. NPO for 30 min. (Life long therapy)

0.120 Soft clear mouthguard material
Caries Management

- Class 1 or 2 direct restorations
  - Amalgam or microhybrid composite
- Class 3 direct restorations
  - Microhybrid composite or resin modified GI
- Class 5 direct restorations
  - Amalgam, microhybrid composite or resin modified GI
- Enamel white spots or non-cavitated dentin
  - Apply fluoride varnish 2-3x/wk, SDF, MI paste
  - Daily topical fluoride gel in trays
Caries: Non-restorable tooth

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Radiographs courtesy of Drs. Terry Ott & Claudia Holt
Oral Infection

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Oral Infection

- Fungal
  - Fluconazole 100mg
    2 tablets on day one then 1 tab. for 6-13 day
  - Clotrimazole
    Dissolve 1 troche 5X daily for 14 days
  - Nystatin suspension QID x 14d

- Bacterial
  - Prescribe antibiotics based on the culture results

- Viral
  - Acyclovir 400mg TID X7 days
  - Famciclovir 500mg BID X7 days

Multi-resistant bacteria / Exotic fungal infection → ID specialist
Taste changes

- Tongue chemoreceptors have reduced activity due to xerostomia.
- Atrophy of tongue mucosa ↓ taste bud activity.
- Mucinous saliva is a barrier to dietary, thermal and mechanical stimulation.

↓ Salivary gland stimulation
↓ Dietary intake and weight loss
Mucositis

- Common morbidity
- Oral mucosa sensitive to XRT
- Severity varies with:
  - Total dose
  - Size of fraction
  - Volume of irradiated tissue
  - Associated infection
- Increased with chemo + XRT
- Pain, ↑ mucous production, dysphagia, odynophagia
- 90% of XRT patients
  - 39% having grade 3 and 4
Mucositis - management

- Supportive and symptomatic
  - Neutral rinses (½ tsp baking soda + 8 oz. H₂O)
  - Topical analgesics (2% viscous lidocaine)
  - Systemic analgesics (Oral/ Transdermal)
  - Limited use of removable prostheses
  - Eliminate use of alcohol and tobacco
  - Soft and bland foods/ nutrition drinks
  - Culture non-healing mucositis and Rx
  - G tube for severe dysphagia (hydration and nutrition)
Trismus

- Reduced or restricted mouth opening <35mm (Normal 40-50mm)
- Radiation fibrosis of muscles of mastication and TMJ
- ↑ radiation dose to TMJ/pterygoid and masseter mus. ↓ maximal vertical opening (Inverse relationship)
- Increased trismus
  - Tumors of RMT, masseter/pterygoid mus, buccal mucosa, and post. pharyngeal wall
  - Greater tumor size
  - Post radiation surgery
  - Concomitant chemotherapy
Trismus challenges

- Nutrition and chewing efficiency
- Interferes with oral health and access for dental procedures
- Interfere with oncologic follow-up
- Speech disruption and pain
- Reduces QOL.
Principles of Stretching

- Principles of stretching techniques include 4 components:
  1. Properly stabilized
  2. Apply force in the exact direction to produce tension to appropriate tissues
  3. Prolonged, low force stretch produces the greatest permanent elongation
  4. Pain tolerance should not be exceeded
     - Barrett et al. JPD 1988

ACTIVE VS. PASSIVE STRETCHING
Trismus-Active Stretching

- Actively stretch/separate the maxilla from the mandible.

- Disadvantages
  - Unilateral force only
  - Potential to luxate anterior teeth or injuring soft tissue
  - Tolerated for short periods of time
Hand strength engages the device

Bilateral

Lightweight and easy use

Follow natural hinge opening of the jaw
Trismus-Passive Stretching

- Low load, prolonged duration stretch can elongate a scar with more pliability
- Reproducible, calibrated tension
- Custom bite plates produce bilateral tension
Osteoradionecrosis (ORN)

- Three “H” principle (hypovascular, hypocellular, hypoxic)
- Bone is hypocellular, devoid of fibroblasts, osteoblasts and osteocompetent cells
- Tissue breakdown > tissue repair.
- Trauma can hasten process.
- Inflammation and endarteritis leads to thrombosis of vessels, cell death

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Osteoradionecrosis
Contributing Factors

- Mandible > Maxilla
- Total dosage > 60 Gy have greater incidence
- Post RT trauma, extractions, oral surgery.
- Poor oral hygiene
- Continued use of tobacco and alcohol
- Premature use of dental prosthesis
- Proximity of tumor to adjacent bone
Osteoradionecrosis

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Osteoradionecrosis

- 61 yr. old male
- T4 N0 M0 NPC Chemo and XRT 70 Gy
- Dental deterioration with bilateral molar extractions
- Bilateral ORN
- Left marginal mandibulectomy
- Infection/ pathologic fracture/ orocutaneous fistula
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Photo courtesy of Dr. Matthew Hanasono

Total mandibulectomy with fibula flap reconstruction
ORN Treatment Algorithm

- ORN (Superficial)
  - Pain/ infection
    - Persistent/ progressive
      - Pathologic fracture
        - Fistula

- CHX rinse, conservative debridement (CD)
- CHX rinse, Culture + ABX, CD
- CHX, Culture + ABX, CD, HBO (NED), PENTOCLO
- Surgical debridement, Reconstruction, +/- HBO

HEALING
Conclusions

- Multiple late and early morbidities of radiotherapy
- Toxicities are related to dose, volume and structures involved with the radiation
- Significant challenge to patient QOL
- Dental team has significant role in care of post XRT patients
- Customize oral supportive care intervention based on morbidities
- Promote realistic outcomes expectations
- New treatment modalities and research