Complications of Radiation Therapy to the Head and Neck

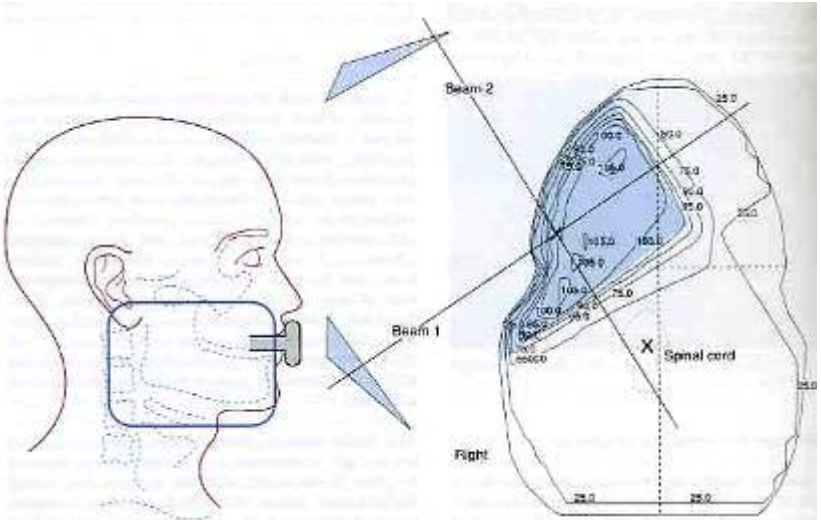
Donita Dyalram DDS, MD
Assistant Professor
Associate Program Director
Maxillofacial Oncology/Microvascular Surgery
Department of Oral Maxillofacial Surgery
University of Maryland

Lecture Goals

- Understand the use of Radiation in H&N
- Early effects
- Late effects
- Dental Implications
- Treatment protocol for:
  - Candidiasis
  - Xerostomia
  - Dental Extractions in irradiated Jaw
  - Implants in the irradiated Jaw

Radiotherapy

- Therapeutic radiation is delivered by 2 main methods:
  - Electromagnetic (photons): x-rays, gamma rays
  - Particulate radiation
    - Electrons
    - Protons
    - Neutrons
- Depth of penetration required is the main criterion used in choosing which energy to employ



Radiotherapy

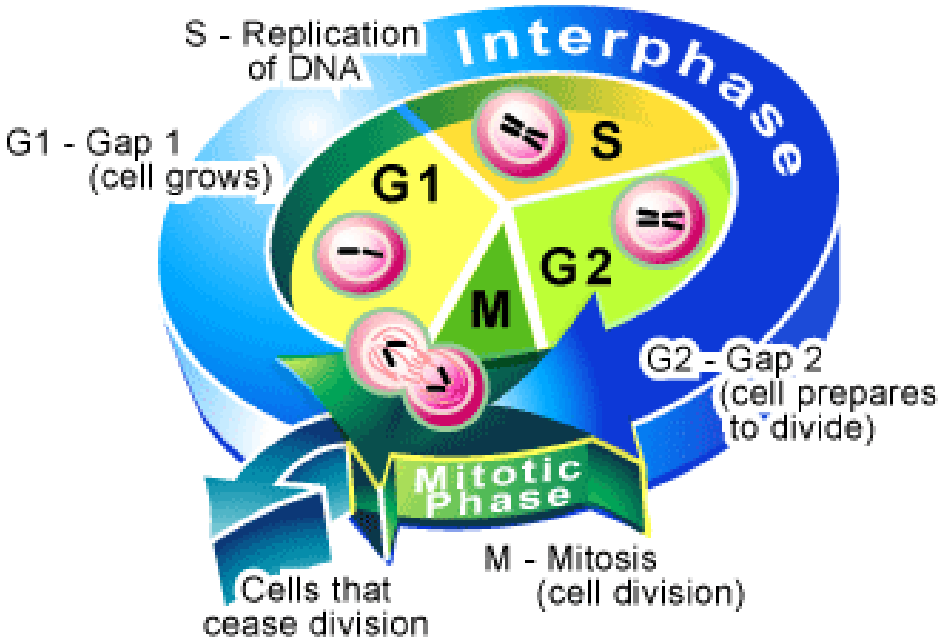
- Roentgen→measure of ionization in air
  - Used for radiation safety
- Gray (Gy)
  - Dose absorbed by the tissue (clinically relevant)
  - 1 Gy = the absorption of 1 joule/kg
  - 1 Gy = 100 cGy = 100 rad
- There is no absolute resistance to radiation
  - Normal tissue tolerance limits the dose

Radiotherapy

- Brachytherapy
  - Radium
  - Cesium
  - iridium

Radiotherapy

- Mechanism of action
  - Interacts with atoms and molecules of the cells
  - Produces free radicals
  - Damages DNA
  - Affects all phases of the cell cycle but cells going mitosis are most affected



Radiation

- The sensitivity of cells to radiation is most pronounced shortly before and during mitosis; thus, the effect is greatest in rapidly dividing cells.

- Highly radiosensitive tissues are mucosa, skin, bone marrow, nerve, and muscle tissue.

- Of the bone cells, osteoblasts are more radiosensitive than are osteoclasts and osteocytes.

What orofacial tissues are affected by Radiation therapy?

- Oral mucosa
- Skin
- Subcutaneous tissue
- Cartilage
- Muscles of mastication
- Temporomandibular joint
- Teeth
- Oral flora
- Salivary glands
- Nasolacrimal drainage system
- Bone
- Thyroid and parathyroid glands
- Pituitary gland
- Peripheral and cranial nerves
- Lymphatics
- Paranasal sinuses

Tissue Effect – Early

- Acute skin reactions
- Hyperemia
- Reduced salivary gland function
- Mucositis
- Loss of taste

Tissue Effect – Long Term

- Seem not to occur when the tissues are exposed to less than about 45 Gy
- Chronic damage to skin, muscle, nerves, and bone

Mucositis

- A term given for widespread oral erythema, ulceration and soreness

Mucositis

- Presents with:
  - Pain
  - Erythema
  - Ulceration
  - Bleeding

Mucositis

World Health Organization Toxicity Grading

Grade	Clinical features
0	-
1	Soreness/erythema
2	Erythema, Ulcers but able to eat solids
3	Ulcers, but requires liquid diet
4	Oral alimentation not possible

Mucositis

- May be reduced by:
  - Minimizing doses of radiation
  - Using mucosa-sparing blocks
  - Using **Amifostine** before therapy
  - **Betamethasone** mouthwashes

Mucositis

- Opioids (MSO4 etc..)
- Avoiding irritants (smoking, spirits, or spicy foods)
- Good oral hygiene
- Oral cooling using ice chips
- Topical analgesics (especially before meals)
  - 2% lidocaine solution mouthwash
  - Magic Mouth Wash
    - Benadryl, Mylanta, and Carafate and viscous lidocaine in a 1:1:1:1

Mucositis

- The time to healing depends on the dose intensity and is usually complete within 3 weeks after the end of treatment.

Candidiasis

Candidiasis

- Infections by Candida albicans are commonly seen in irradiated patients

- Can be painful

Candidiasis

- Rinses
- Nystatin
- Amphotericin

- Clotrimazole (Mycelex) trouches
- Caution trouches contain sugars

- Oral/Systemic medications
- Diflucan

Xerostomia

Xerostomia

- Salivary Gland
  - Transient tenderness
  - Occasionally swelling
  - Occurs within a few hours after 1st dose
  - Decrease salivary flow noted within 24 hrs
  - May have ~50% decrease flow after 1st wk
  - Flow continues to decrease throughout treatment course and may become barely measurable at 6 wks.

Xerostomia

- Salivary changes
  - Increased viscosity
  - Decrease pH
  - Increased [Na], [Ca], [Mg]
  - Decreased [HCO3]
  - Decreased IgA

Xerostomia

- Persists for several months to year
- May not recover
- Depends on volume of radiated salivary glands, total dose, individual patient
- Causes difficulty with:
  - Swallowing
  - Chewing
  - Talking
  - Denture wear

Xerostomia

- Prevention
  - IMRT
  - Amifostine (Ethyol)
    - Cytoprotective agent
  - RTOG 0244
    - Phase II study of submandibular gland transfer to the submental space prior to therapy
  - RTOG 97-09
    - Phase II study to test the efficacy of the prophylactic use of oral pilocarpine to reduce hyposalivation and mucositis. Closed. No improvement in mucositis but improved salivation

Xerostomia - Treatment

- Sialogogues
  - Pilocarpine (Salagen) 5 mg tid
  - Salivix (Malic acid)
- Salivary replacements
  - Glandosane
  - Luborant
  - Oralbalance
  - Salivace
  - Saliveze

Radiation Caries

- Circumferential cervical decay
- Incisal decay

- Related to:
  - Xerostomia
    - Change in oral flora
    - Pulpal death
    - Dentine dehydration
    - Enamel loss

Prevention of Radiation Caries

- Daily flouride application
- 0.4% stannous flouride gel
- 1.1% neutral sodium flouride
- Tray worn for 5-10 minutes
- Must cover cervical portion of teeth

Osteoradionecrosis
ORN

Pathophysiology of ORN

- Watson & Scarborough (1938)
- Meyer (1970)
  - Triad:
    - Radiation Therapy
    - Local trauma
    - Infection
- Marx's Theory
  - 3 H's
    - Hypovascular
    - Hypocellular
    - Hypoxic

What is the Incidence of ORN?

- Recent studies
  - 5% to 15%
  - overall incidence of 5.4%
  - Bimodal distribution
    - 12 months and 24-60 months

Incidence of Osteonecrosis according to radiation dose to bone

	Incidence of Osteonecrosis	
Dose to Bone (cGy)	Dentulous Pt.	Edentulous Pt.
<6500	0/36 (0%)	0/3 (0%)
6500-7500	8/29 (28%)	1/15 (7%)
>7500	11/13 (85%)	2/4 (50%)
Total	19/78 (24%)	3/22 (14%)

Data from Morrish et al., Cancer 1981

Osteoradionecrosis

- Almost all cases occur within the field of radiation
- Most cases associated with a dental extraction

Osteoradionecrosis

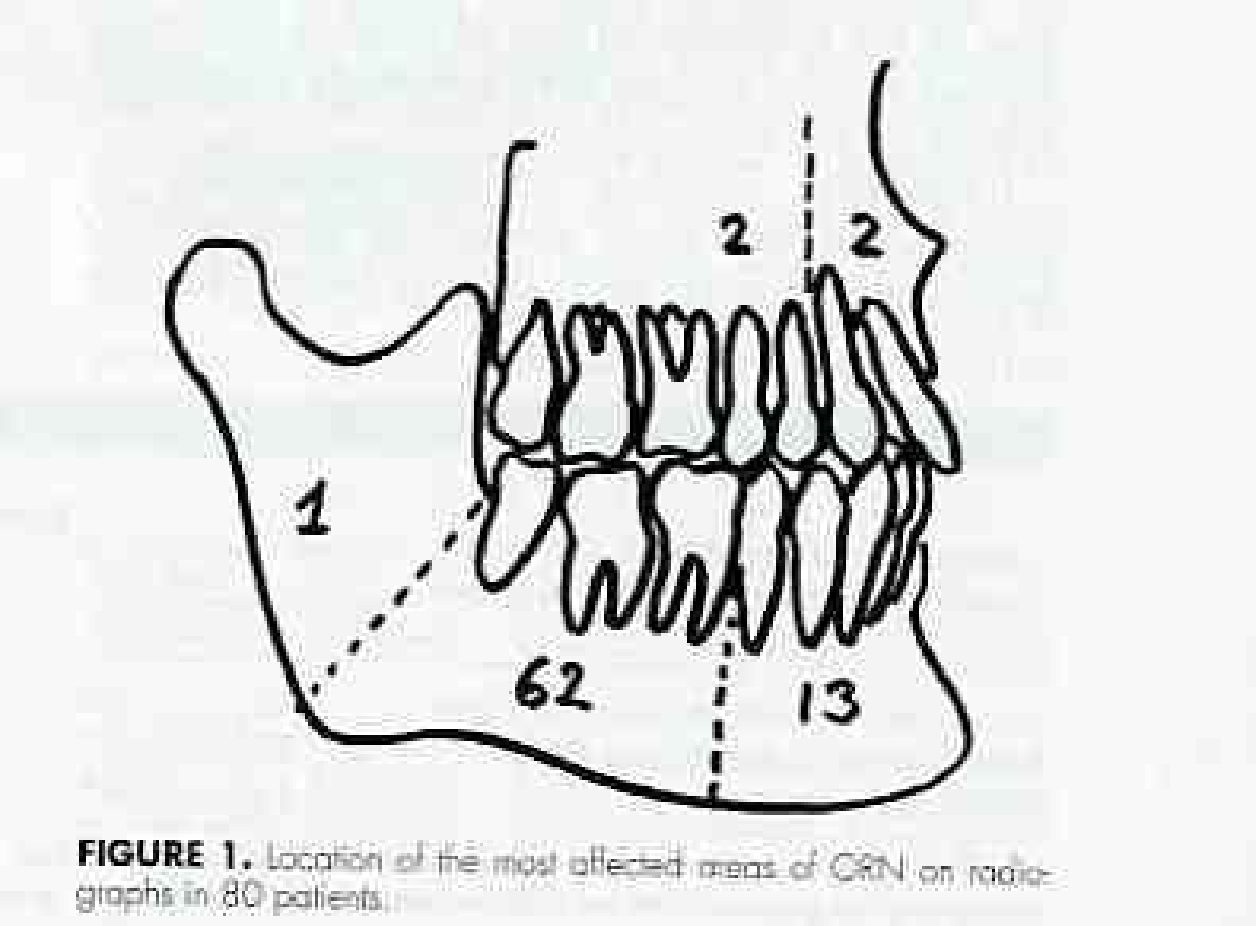


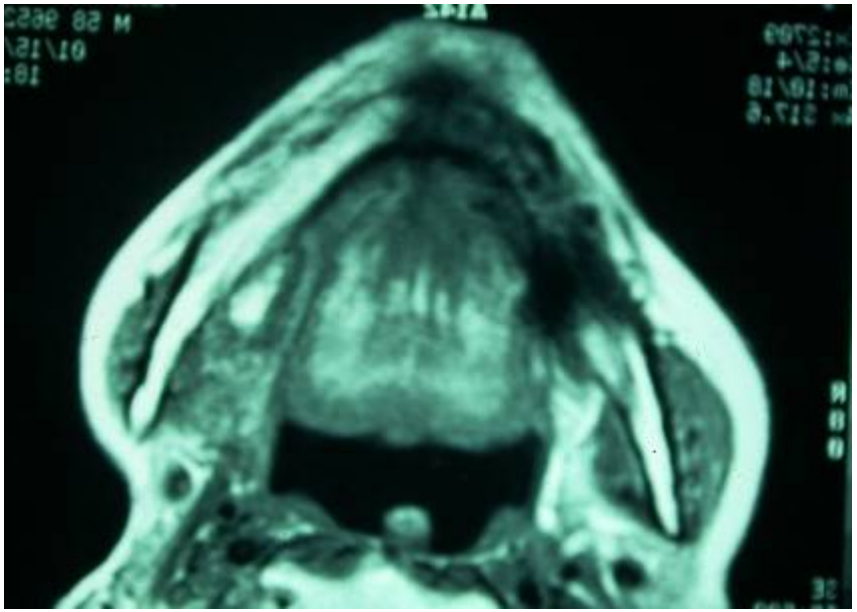
FIGURE 1. Location of the most affected areas of ORN on radiographs in 80 patients.

Clinical Features of ORN

- Exposed bone, loss of soft tissue and bone
- Pain and dysphasia/anesthesia
- Soft tissue necrosis
- Trismus
- Pathologic fracture and orocutaneous fistula

Radiographic Features of ORN

- Diffuse radiolucency without sclerotic demarcation
- CT / MRI to evaluate extent of ORN
- Must Biopsy to rule out tumor recurrence



Conservative Management of ORN

- Daily local irrigation (saline, NaHCO3, Chlorhexidine)
- Systemic antibiotics
- Avoidance of irritants
- Good oral hygiene instructions
- Gentle removal of sequestrum

HBO

- Administration of 100% oxygen in a special chamber at 2.4 atmosphere absolute pressure for 90 minutes each session.
- Delivered once a day, 5 times per week

What is the Mechanism of HBO

- Improve tissue healing by:
  - Angiogenesis
  - Inducing fibroplasia and neocellularity
  - Promoting survival of osteoprogenitor cells
  - Promoting the formation of functional periosteum

Controversies regarding use of HBO in ORN

- Hyperbaric Oxygen Therapy for Radionecrosis of the Jaw: a randomized, placebo-controlled, double-blind trial from the ORN96 study group.
- Annane D, Depondt J, Aubert P, Villart M, Gehanno P, Gajdos P, Chevret S
- J Clin Oncol 2004 Dec 15; 22(24): 4893-900

Conclusion: Patients with overt mandibular osteoradionecrosis did not benefit from hyperbaric oxygenation

HBO and Osteoradionecrosis

- The influence of HBO on the outcome of patients treated for osteoradionecrosis:8 year study

- 23 patients
- HBO group – 12.5% cure rate
- Non-HBO group – 86% cure rate

- D’Souza et al. IJOMS 2007

ORN – Fibrosis Theory

- Damage to bone caused by radiation induced fibrosis

- Bone cells damaged by free radicals , acute inflammation and chronic activation of fibroblasts

Lyons A, Ghazali N Br J Oral Maxillofac Surg 2008

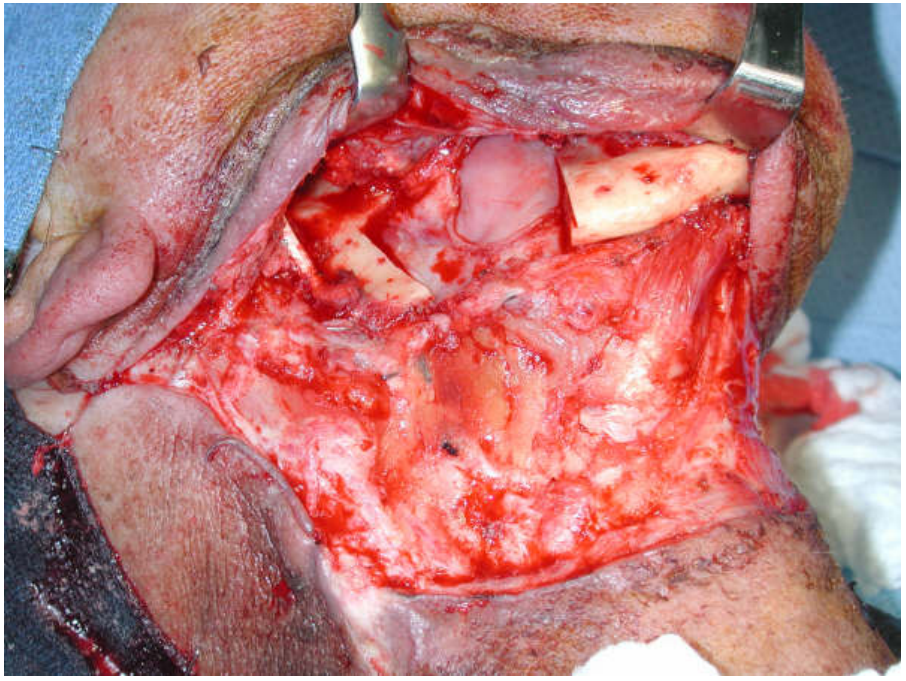
Treatment ORN– Fibroblast Activation Theory

- Pentoxifyline
  - Vasodilator
  - Anti -TNFα
  - Inhibits dermal fibroblasts

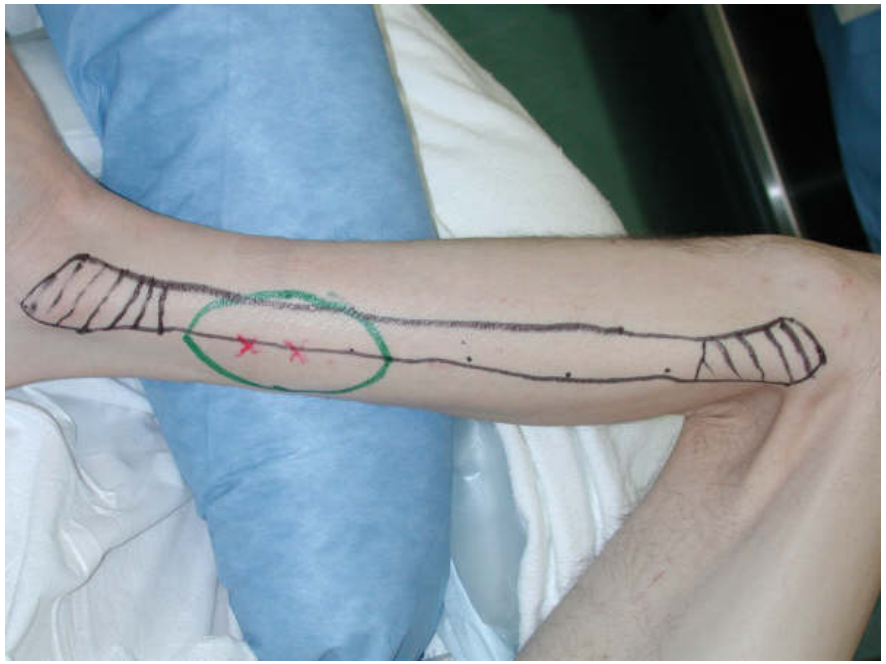
- Vitamin E
  - Anti-oxidant
  - Reduce free radical damage

Delanian S et al. Int J Radiat Oncol Biol Phys 2010

ORN treatment failure



Fibula Osteocutaneous Free Flap



ORN treatment failure

Dental Management
Pre-Radiation

Dental Management Prior to Radiation

- Complete oral/dental examination and treatment plan
- Any necessary extraction and surgery
- Maintenance of teeth and caries control
- Restoration of restorable teeth
- Prothetic examination to prevent postradiation trauma from ill-fitting dentures

Dental Management Prior to Radiation

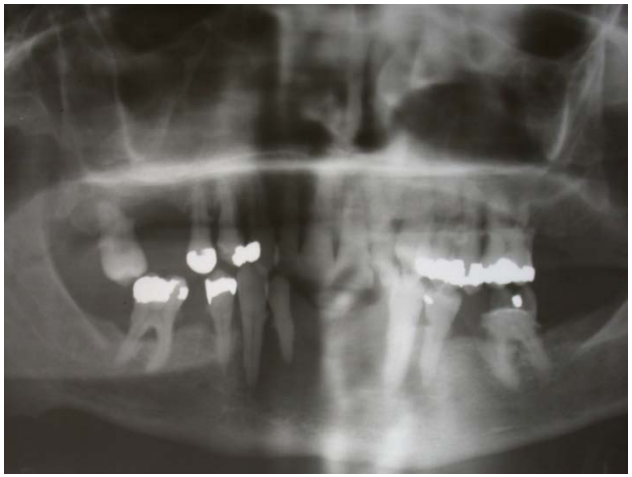
- Consider:
  - Condition of the dentition
  - Level of oral hygiene and patient attitude
  - Age of the patient
  - Radiation field and dose
  - Urgency of radiation treatment

Dental Management Prior to Radiation

- Caries control
  - Prophylactic care before and at the end of therapy
  - Oral hygiene instructions
  - Daily administration of fluoride
  - Weekly follow-up during therapy and every 3-4 weeks afterward

Guideline for Extraction Prior to Radiation

- All carious teeth in the field of xrt (>60 Gy) should be extracted except in patients with excellent oral hygiene and dentition
- All questionable teeth should be extracted
- Full bony impacted teeth can be left in place
- Optimal time for extraction is 21 days before beginning xrt



Extractions

- Atraumatic extractions
- perform an alveolectomy
- smooth the bone
- Perform a primary closure
- Allow a minimum of 1 week to 10 days for healing prior to beginning XRT
- Preferable to allow 14 to 21 days

Dental Management Post-Radiation

Management of patient post radiation

- Obtain records of radiation fields and dose
- Recall for prophylaxis q 3 months
- Daily fluoride treatment for life
- Wait for mucositis to resolve prior to prosthesis placement
- Avoid invasive procedure involving irradiated bone
- HBO vs. Pentoxifylline & Vitamin E

Implants in Irradiated Jaw

- 48 patients
- 271 implants placed
- Implant survival
  - 1 year (99%)
  - 10 year (72%)
- Higher incidence of implant failures
  - Maxilla
  - Posterior oral cavity
- Conclusion
  - Dental implants placed into irradiated bone have a higher failure rate than non-irradiated bone

Buddha A. et al. Clin Implant Dent Relat Res 2010

- HBO for irradiated patients who require dental implants: a Cochrane review of randomised clinical trials

- 1 trial found
- 26 patients HBO vs. non-HBO

- Conclusion – no evidence for or against effectiveness of HBO for improving dental implant outcomes

Coulthard P et al. Eur J Oral Implantol 2008

Radiation induced Malignancies

Radiation induced Malignancies

- Soft tissue Sarcomas
- Thyroid Carcinoma


THANK
YOU!