Radiation
Radiation

- Principles of radiation therapy
- Indications of radiation therapy & ttt planning
- Oral effects of radiation
- ORN
- Dental management of irradiated patient
- Prosthetic management of irradiated patient
Principles of radiation therapy
Radiation Therapy: Therapeutic Use of ionizing radiation
• W.L. < 1 Å and called **Photons**
• No Mass - no Charge
• Energy is Measured in KeV or MeV
• Include X-rays and Gamma Rays
• Identical in nature but differ in the way of production.
• **X-rays** are produced by electric devices.
• **Gamma Rays** produced by radioactive disintegration of unstable radioisotopes

• They have a mass and have a charge.
• **Protons** (+), **Electrons** (-), **Neutrons** (no Charge).
• Electrons can be accelerated to high energy level by electric devices such as in production of x-rays.
Protons (+), Electrons (-)
Charged particulate have sufficient energy to disrupt the atomic structure by producing chemical and biologic changes.

Photons, Neutrons
They give out their energy to produce fast moving particles
By Photoelectric Effect
Compton effect
Pair production
Biologic Effects of radiation

• Nucleus is 100-1000 times more affected by radiation than the cytoplasm.

• Most of the Damage is confined to DNA and mitotic apparatus.

• Effect on individual cells depends on the position the cell occupies in the cell cycle since cells are relatively radio resistant during early and end of DNA synthesis.
Immediate cell death

May lead to cell death or repair of this sublethal damage according to time of cell division.

6 hours interval
Biologic Effects May be Direct or Indirect

**Direct**

- Secondary particles (protons/electrons) interacting with the target molecules

**Indirect**

- Interaction with water to produce free radicals (hydroxyl and hydrogen) which in turn interact with target molecules

Overall, amount of DNA is far less than the amount of water in the cells, so most of the interactions are of INDIRECT effect.
• However, These interactions are dependent on the oxygenation level of the tissues.

**Role of Oxygen:**

• Reacts with organic free radicals to form non-restorable organic peroxides, leaving more hydroxyl free radicals which interact with more target molecules.

• So, absence of oxygen would allow the hydroxyl group to react with the hydrogen radical forming the inactive molecules of water.
Anoxic tissues: may be 3 times more radio resistant than they would be under normal oxygenation.

• Therefore treatment of Hypoxic tumors by radiation therapy requires treatment strategies that increase oxygen transport to the tissues. (re-oxygenation)
Radiation Therapy is delivered in a series of treatments or fractions.

- **Advantages of fractionation:**
  1. Allows reoxygenation of cells.
  2. Allows affection of more tumor cells during radiosensitive phase of their cell cycle.
  3. Normal Cells seem to recover more completely between fractions from sub lethal damage.
Fractionation

Conventional Fractionation

Altered Fractionation
• Conventional Fractionation:
  Total Dose of 65-72 Gray
  Daily Fraction of 1.8-2 Gray

Final total dose is limited to tolerance of critical normal tissues.
Altered Fractionation:
Advances aim towards increasing the dose to the tumor and decreasing it to the surrounding normal tissues.

There are 4 basic radiation plans of altered fractionation:
1) Conventional fractionation
2) Hypo fractionation
3) Hyper fractionation
4) Accelerated fractionation
Modalities

Radiation Delivery

External Source

CT

IMRT

Surgically implanted material

Brachytherapy
A “seed” is placed into the lung where it lets off radiation, killing local cancer cells
• **Conventional Radiation Therapy: (CT)**
  Involves the use of an **external source** of radiation.
  It deals with tumor as a point on which opposed parallel fields of radiation are being directed.

• **Intensity Modulated radiation therapy: (IMRT)**
  - The delivered doses of radiation are defined for volumes as opposed to points.
  - These volumes are drawn by the use of digital CT and software (planning target volumes)
Planning target volume:
1. Gross tumor volume
2. Safety margins
3. Uncertainties
• **Brachytherapy**

It is a Method of radiation delivery in which sealed radioactive sources containing radioisotopes are used to deliver the dose a short distance.

either by :

1. Interstitial (direct insertion into the tissue)
2. Intracavitary (Placement within a cavity)
3. Surface application (molds)
• Advantages
  1. More local control while maintaining structure and function

• Disadvantages
  1. Inhomogeneity of the dose throughout the volume. This may lead to hot spots if sources placed too close or cold spots if sources placed too far apart.
  2. The need for general anesthesia and hospitalization.
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Indications & ttt planning
Majority of Malignant neoplasms of the mucosa of head and neck are squamous cell carcinomas of various degrees of differentiation and radio sensitivity.

Lymphomas are radiosensitive

Adenocarcinomas are less predictable.

Sarcomas and Melanomas require surgeries with wide margins.

Radiation supplemented with chemotherapy is generally the ttt of choice for carcinomas arising from the nasopharynx, soft palate and base of tongue.
• Tumors exhibiting deep invasion of soft tissue or extension into bone or cartilage are far less likely to be controlled with radiation alone, and a combined approach with surgery followed by radiotherapy is advised.

• Smaller carcinomas of the border of the tongue and free portion of the epiglottis and floor of the mouth without tongue infiltration or mandible should be controlled by radiation in 60 to 80 % of patients.
The intent of radiation oncologist is to deliver a curative dose to the tumor while limiting the dose to the normal structures to a level that is within their tolerance.

The physician must first determine the extent of disease and the tumor volume to be treated by:

- Complete physical examination
- Appropriate laboratory tests
- Radiographic assessment (CT, MRI,..)

Radiotherapy treatment is given to the tumor site mainly and also to areas at high risk for direct spread and lymph nodes involvements.
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Oral effects of radiation therapy
• Any tumor can be destroyed by radiation if the dose delivered is sufficient.

• **The limiting factor** is the amount of radiation the surrounding and adjacent normal tissue will tolerate.

• Tissues which exhibit *rapid* turnover rates (mucosa) are more readily affected. Healing is equally rapid if the dose is not excessive.

• The tissues with *slower* turnover rates (muscles), damage may not be evident for months or years after therapy.
Oral effects of radiation

Acute
- Mucositis
- Fungal infections
- Taste apparatus

Late
- Mucous membrane
- Muscle
- Skin
- Edema
- Trismus
Early changes in mucosa

Erythema → ulceration

Severity dependent upon:
- Clinical treatment volume, dose and fractionation.
- Sites: The less keratinized the mucosa the more severe the mucosal reactions.
- More severe in patients presenting with chronic alcoholism and liver cirrhosis.
- More severe in patients with insulin dependent diabetes.
- Severity may be lessened by a reduction of oral bacterial loads.

Mucositis is more severe in patients receiving concomitant chemotherapy.
Oral mucositis begins as an erythematous reaction associated with the tumor site generally after about 7-10 days of the therapy. This erythema is accompanied by soreness and a burning sensation.
 Changes in the oral flora during therapy are thought to intensify radiation mucositis (Ramirez-Amador et al, 1997).

 Colonization by gram negative bacilli (Spijkervet, 1991) appear to induce more severe mucosal reactions such as the reaction in this patient.
- Taste gradually returns to normal levels after therapy is completed.
- Some patients with severe xerostomia may never have normal taste acuity.

Taste Apparatus

- Taste acuity is readily affected by tumoricidal doses of radiation (Sandow et al, 2006; Mirza et al, 2008).
- Dramatically affects the quality of life (Redda and Allis, 2006).
- Changes in taste cells and buds are due to both the direct and indirect effects of irradiation (Yamashita et al, 2006).
Olfaction

- Since the olfactory epithelium is high in the nasal passage and often not within the clinical treatment volume smell is less affected
Late changes
Clinical significance

- Easily traumatized mucosa or ulcerated
- Slow healing for ulcers (due to reduced vascularity & fibrosis of c.t.)
- Intolerance to dentures

- Scarring and fibrosis of lamina propria
- Telangiectasia – dilation and coalescence of small venules close to the surface of the epithelium
- Epithelial layer is thinner and less keratinized
Talangiectasias

In most patients scarring and telangiectasia are confined to the tumor site (arrow).
Scarring at the tumor site

This patient would be a good candidate for complete dentures. She is compliant and the scarring and telangiectasia is confined to the tumor site. **However, overextension of the lingual flange in this region could result in a mucosal perforation and lead to an osteoradionecrosis.**
In patients treated for pharyngeal, soft palate and base of tongue tumors, fibrosis and muscle wasting of the muscles of pharyngeal wall and the soft palate responsible for velopharyngeal closure leads to velopharyngeal insufficiency. These changes are more common in patients treated with chemo-radiation and many patients are unable to swallow after completion of radiation therapy.
Edema

- Secondary to obliteration of small lymphatic channels and worsened by scarring and fibrosis (Engerset, 1964; Sherman and O’ Brien, 1967).
- Clinically significant when it effects the tongue and buccal mucosa
- Generally most prominent in the submental and submandibular areas
- Radical neck dissection potentiates the effects and increases the edema
Edema

Both patients present with edema of oral cavity structures, one involving the tongue, the other the buccal mucosa. These two patients are susceptible to tongue and cheek biting.

Prevention: Accomplished by use of a prosthetic stent designed to displace the buccal mucosa or tongue away from the interocclusal surfaces.

In edentulous patients the enlargement of the tongue has negative effects on the floor of the mouth contour and adversely affects the lingual extension and the patients ability to tolerate and control the lower denture.
- Occurs mainly when TMJ and muscles of mastication are in the field of radiation as in nasopharyngeal, palatal, parotid tumors.

- Fibrosis of muscles of mastication usually after 3-6 months of radiation.

- The higher the dose, the greater the trismus.
Problem

Impairing the mastication and preventing convenient oral access for a bolus of food.

Compromises the use of complete dentures, obturator prostheses.

*Dramatically worsened by concomitant chemotherapy*

*Maximum opening may be reduced to 5-15 mm*

*In patients with combined radiation and surgery, early initiation of an exercise program before the fibrosis sets in provides the best results.*
Dynamic bite openers are the most effective form of treatment (Dijkstra, 2004)

- Patient is instructed to stretch with the device for 30 minute sessions three times per day.
- Requires a high level of patient cooperation because of the discomfort associated with the required manipulation.
- Tongue blades, taped together and used as a lever have been less effective in increasing mouth opening.
Major salivary glands are affected when lesions in the retromolar area, tonsillar area, soft palate and nasopharynx, in which all the major salivary glands are in the field of radiation.

(1) Changes in volume, viscosity, PH occur after irradiation of major salivary glands. (increase viscosity & decrease flow)

These changes predispose the patient to:
- Taste impairment
- Difficult swallowing
- Caries
- PDL disease
- Poor tolerance to prosthetic restorations
• (2) The epithelium of the salivary glands is relatively radioresistant but the changes observed in the parenchymal epithelium after radiation are secondary to compromise of the fine vasculature.

The viscous nature of saliva after radiation is due to

Serous acinar cells are more radiosensitive than mucous acinar cells (parotid is serous, submandibular is mixed while sublingual is mucous gland)

The sublingual gland is partially out of the radiation field in posterior superior lesions
• Many attempts to stimulate salivary activity after radiation therapy have been carried out.

• **Pilocarpine** has been partially successful in stimulating salivary secretion. It can be used as a mouth wash or in tablet form.

• Mouth rinses based on **carboxymethyl cellulose, glycerin, and mucin** have been used as salivary substitutes.
Bone

- Bone is 1.8 times as dense as soft tissues. **So** it absorbs a larger proportion of radiation than does a comparable volume of soft tissue.

- The **mandible** absorbs more radiation than maxilla because of its increased density.

- The higher incidence of ORN in the mandible than the maxilla is due to:
  - 1) It absorbs higher radiation than maxilla.
  - 2) Reduced vascularity of mandible as compared to maxilla.
What happens in bone after cancericidal doses of radiation?

**Early changes**

- Significant aberrations occur in the fine vasculature
- Progressive occlusion & obliteration of small vessels
  - Reduction of number of cells
  - Disorganization of the remodeling apparatus
  - Progressive fibrosis

**Late changes**

- The marrow exhibits marked a cellularity and a vascularity
- Significant fibrosis and fatty degeneration
• **The periosteum** demonstrates significant fibrosis with a similar loss of remodeling elements. Such bone exhibits a poor response to trauma and infection.

• These tissue changes profoundly affect the remodeling capability of bone.

• The surgeon must smoothly contour the alveolar ridge at the time of pre-radiation dental extractions. If this is not performed, the resulting alveolar ridge will not readily remodel. So construction and wear of mandibular denture on such an irregular bony base is quite risky in an irradiated patient. It may lead to an exposed bone and then ORN.
Periodontium & teeth

- The PDL exhibits changes that predispose to infection.
- It thickens and its fibers become disoriented.
- It exhibits decreased cellularity and vascularity.
- Cementum demonstrates changes similar to those seen in bone.
- Its capacity for repair and degeneration is severely compromised.
- Irradiated teeth decalcify more readily than non irradiated teeth.
- Significant changes in pulp tissues, it shows a decrease in vascular elements with accompanying fibrosis and atrophy.
- Pulp response to infection, trauma and various dental procedures appear compromised.
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Osteoradionecrosis
ORN
It is a complication (bone necrosis) resection of part of mandible

Types

**Spontaneous**…due to inability of hard and soft tissues to sustain cell turnover and collagen synthesis following irradiation.

This type occurs when large volumes of mandible are exposed to radiation

- high dose of radiation (70 GY and greater with CT),
- positioning of implant sources adjacent to bone,
- neutron beam therapy
- and concomitant chemo-radiation.

**Trauma induce**…..due to compromised wound healing when tissues become fibrotic and hypovascular.

Example, when the patient develops a peridontal or periapical infection or requires postradiation extractions, the compromised healing capacity may lead to bone necrosis.
Osteoradionecrosis involving the mandible
Common site

Most bone necroses occur in the mandible which particularly at risk when large volume of mandible are exposed to tumoricidal doses.

-Most patient that develop ORN are dentulous at the time of tumor diagnosis, fewer than 5% of all ORN occur in edentulous patient.
Osteoradionecrosis
# Contributing factors:

1. **Diseased teeth** present within the radiation treatment volume prior to radiation are the prime initiator of trauma-induced ORN.

2. **Periodontal infections** associated with mandibular teeth left within the gross tumor volume.

3. **Postradiation extraction** of teeth (esp.; mandibular) within the gross tumor volume lead to bone necrosis.

**So**

An aggressive policy of removal of diseased mandibular teeth within the radiation gross tumor volume, will minimize the incidence of bone necrosis.
4- When the dose in the area exceeds 65 Gy, post-radiation extraction of diseased teeth within the radiation treatment volume predisposes the bone to high risk of ORN if extraction is not accompanied by a course of HBO.

5- when the primary tumor is adjacent to or overlying bone, the risk of bone necrosis is increased. The greater the body of mandible that is included within the gross tumor volume, the greater the risk of ORN.
6-Bone necrosis are rare due to the use of removable partial denture or complete denture but when they do occur most resolve with conservative treatment measures.

-Radiation-induced xerostomia, saliva is an important lubricant for mandibular complete dentures and its absence leads to friction at the denture-mucosa interface.

7- placement of implants in irradiated bone.
#Treatment option:

1) Conservative measures.
2) HBO.
3) Vascularized free flaps.
Conservative measure:

- If the dose to the affected area is less than 70Gy, can be controlled with local irrigation of saline and chlorhexidine and also iodoform gauze packing impregnated with tincture of benzoin.

- Sharp bony projections can traumatize adjacent soft tissues or contribute to plaque accumulation and should be smoothed.

- If the necrosis remains limited to the local area and if pain and swelling of the adjacent soft tissues are not evidence, conservative method can be continued, periodic radiographs are recommended.

- Antibiotics are necessary only to control local acute infections.
(2) **Hyperbaric oxygen therapy:**

- Promotes neovascular proliferation in marginally necrotic tissues
- Enhance fibroblastic proliferation,
- Enhance the bactericidal activity of WBCs
- Increase the production of bone matrix.

Patient with bone necrosis were exposed to 2 atm of oxygen in a hyperbaric chamber for 2 hour per session.
Resection and immediate reconstruction with a free flap are recommended when patients present with:

- Advanced, diffuse ORN in which the full thickness of bone is necrotic,
- Pathologic fracture of the mandible,
- ORN associated with concomitant chemo-radiation therapy.
Soft Tissues Necrosis:

It is non-neoplastic mucosal ulceration that does not expose bone, occur most often following treatment with interstitial implant and per-oral cone modalities.

- Most of these necrosis occur within 1 year after completion radiation therapy.

Treatment
- Proper diagnosis and follow up (with local irrigation)
- Surgical excision and primary closure of soft tissue wound
- In severe cases may need HBO course
Thank you