Advances in Radiotherapy for oral cancer
- A Review

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The sixth most common malignancy is oral cancer according to WHO, many a times they go undetected and untreated in developing countries or they will be detected in the later stages where the treatment will be of palliative mode.

Though basically there are three modes of treatment procedures such as surgery, chemotherapy& radiotherapy, the origin of therapeutic use of ionizing radiation has been started in the 19th century following the discovery of radium by Marie & Pierre Curie.[1]

Radiotherapy as the primary treatment allows for organ conservation. Radiotherapy techniques have been developed to enhance the therapeutic radiation though the biological factors do influence the response of tumors such as reparative capacity, repopulation of the tissue, oxygenated cells, which might influence and get implicated for recruitment, redistribution and re oxygenation of reparative tissue during the fractionated cycles of radiotherapy.[2]

Conventional therapy has been implicated like

- External beam therapy
- Brachytherapy

In the conventional therapy there will be constant intensity throughout the field of therapy. In external beam radiotherapy radiation is delivered in daily fraction of 1-2grays per day for 5 days a week for a period of 2 months with a total dose of 50-60 grays (Time-Dose Fraction). Nominal standard dose (NSD) will influence the tolerance of vascular and connective tissue to radiation, which in turn influences both the success of tumor control and the development of treatment complications. These could be short term complications as mucositis, taste disorders which might end up in altered nutritional status. Later long term complications such as fibrosis, trismus, xerostomia, dental caries and osteoradionecrosis are encountered.

When the tumor size is of T_1 & T_2 brachytherapy also called as interstitial therapy is indicated where the radiation is administered in the vicinity or into the tissue by implanting radio isotopes such as cesium, iridium, gold and iodine.[3]

In order to reduce the unwanted radiation exposure and complications related to conventional radiation therapy following advances have been introduced.[2,4,5]

1. **Conformal Intensity Modulated Radiation Therapy (IMRT)**
2. **Convergent beam irradiation**
3. **Chemo radiotherapy**
4. **Radio immunotherapy**

1. Conformal Intensity Modulated Radiation Therapy (IMRT)

One of the more recent adaptation of radiotherapy involves the use of IMRT, in IMRT, multiple shaped radiation beams are modulated to produce highly conformal dose distribution, this increases the radiation to the tumor tissues which limits the dose delivered to defined normal structures such as salivary glands, auditory and optic apparatus.[2]

The concept of IMRT was described as early as 1978 , started to be used widely from 1990s, the beam intensity pattern of IMRT so complex that a different type treatment planning algorithm was designed , called inverse planning.[6]

2. Convergent beam irradiation

Conceptually in conformal radiation therapy the target and dose limiting surrounding $5cm^3$ are delineated three dimensionally and amount of radiation delivered is better assessed in comparison to 2D RT. 3D- CRT maximizes and minimizes the amount of radiation reaching the target and important structures respectively, this will be achieved by changing the shape of the incident beam to conform to the projection of the target for a set of fixed beam directions or during rotational therapy. Convergent beam radiation using the machines like Linac, Gamma knife or Cyber Knife is usually given as single treatment. The optimal volume limit is approximately 5 cm^3 for Gamma knife and about $25cm^3$ for the Linac. Larger volumes are treated with multiple isocenters with increasing radiation dose.[7]

3. Chemo radiotherapy

Radiation combined with targeted therapies such as cetuximab or cis-platinum. Cetuximab is an IgG monoclonal antibody (MAb) that specifically targets the epidermal growth factor receptors (EGFR) with high affinity and competitively inhibits endogenous ligand binding.[5]

4. Radio immunotherapy

Angiogenesis is one of the hallmarks of malignancy. Radiotherapy aims at the neutralization of the growth factors and other angiogenic mediators in endothelial cell migration and proliferation. The neutralizing anti vascular endothelial growth factors (VEGF) acts either by capturing the growth factor it self or by blockage of its receptor.

Recently, a human recombinant ScFv fragment directed against a target of angiogenesis is the extra domain B (ED- B) of fibronectin. Fibronectin is an extracellular matrix component that is widely expressed in a variety of normal tissues and body fluids. A human recombinant ScFv fragment is designated as L19 in association with small immunoprotien (SIP). A radiolabelled L19- SIP has been used for squamous cell carcinoma of head and neck.[8]

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