International Journal of Dental and Health Sciences
Volume 01,Issue 03

Review Article

RECENT TRENDS IN RADIATION THERAPY OF ORAL AND OROPHARYNGEAL CANCERS

Varun Salgotra[1], Sonam Kohli[2], Raghav Agrawal[1], Soumen Mandal[1]
1. Dept.of Oral and Maxillofacial Surgery, D.J. College of Dental Sciences and Research, India
2. Dept.of Oral Medicine and Radiology, D.J. College of Dental Sciences and Research, India

ABSTRACT:

Cancer, one of the most formidable disease affecting mankind today, has not spared any age group, nor has it left untouched any organ of the body. Cancer is a scourge that affects millions of the world population. Oral cancer is the sixth most common cancer worldwide. Radiation therapy has been used alone, or with the surgery or chemotherapy for the combined treatment modality. The major morbidities associated with radiation therapy are altered taste and permanent xerostomia. To overcome these limitations, new treatment regimens and a variety of new imaging modalities have been incorporated into the radiotherapy planning and delivery process. This paper provides an insight about the advances made in the field of radiation therapy for the management of oral and oropharyngeal cancer.

Key words: Radiation therapy, oral Cancer, Oropharyngeal cancer, image guided radiation therapy and intensity modulated radiation therapy

INTRODUCTION:

Oral cancers are the sixth most common cancer worldwide, accounting for an estimated 4% of all cancers. The incidence and mortality from oral cancers varies geographically; the highest age standardized rates of oral cancers are reported in parts of Europe (France, Hungary), Botswana and south central Asia (Sri Lanka, Pakistan, Bangladesh and India).[1] In a recent report prepared by National Institute of Health and Family Welfare (NIHFW), about 75,000 to 80,000 new cases of such cancers reported every year in India accounting 86 per cent of the total oral cancer figure across the world. Squamous cell carcinoma represents 95 percent of the malignant neoplasm of the head and neck cancer. Radiation therapy and surgery have been both used for decades to achieve locoregional control and have a well-established role in the management of oral and oropharyngeal cancers. Radiation therapy has been used alone, or with the surgery or chemotherapy for the combined treatment modality.

Over the past decade, new treatment regimens and a variety of new imaging modalities have been incorporated into the radiotherapy planning and delivery process. Modern radiotherapy has evolved from non-site-specific techniques using bony anatomy and hand-drawn

*Corresponding Author Address: Dr Varun Salgotra,Dept.of Oral and Maxillofacial Surgery, D.J. College of Dental Sciences and Research, India ,Email: varunsalgotra@yahoo.com

blocking toward specialized planning incorporating three-dimensional reconstructions of images and computer optimization algorithms. Corresponding to these changes, there has been specialization in the types of technology used for different cancer sites. For example, the obvious advantages associated with sparing the salivary glands have pushed intensity modulated radiation therapy (IMRT) in the standard treatment of head and neck cancer faster than other cancer sites.[2]

Intensity-modulated radiation therapy (IMRT)

Traditionally, Conventional external beam radiation therapy or 2D - radiotherapy consisted of a single beam delivered to the patient from one to four directions. 3-dimensional conformal radiation therapy (3D-CRT),or CT-based planning was a major advancement in which the profile of each radiation beam is shaped to fit the profile of the target from a beam's eye view (BEV) using a multileaf collimator (MLC) and a variable number of beams. When the treatment volume conforms to the shape of the tumor, the relative toxicity of radiation to the surrounding normal tissues is reduced, allowing a higher dose of radiation to be delivered to the tumor than conventional techniques would allow.[3] IMRT is the further advancement of 3D-CRT. It optimizes the delivery of irradiation to irregularly-shaped volumes and has the ability to produce concavities in radiation treatment volumes. Intensity-modulated radiation allows modulating the intensity of each radiation beam, so each field may have one or many areas of high intensity radiation and any number of lower intensity areas within the same field, thus allowing for greater control of the dose distribution with the target. By modulating both the number of fields and the intensity of radiation within each field, there are limitless possibilities to sculpt radiation dose.[2] IMRT can be delivered using linear accelerators with static multi-leaf collimators (MLC, step and shoot IMRT) or dynamic leaf MLCs or volumetric arc modulated therapy.[3,4]

C. Nutting et al in a phase III multicenter randomized controlled trial compared intensity modulated and conventional radiotherapy (RT) in head and neck cancer. They found no differences between the overall survival and locoregional control rates, in acute mucositis or pain scores and in other late toxicities. However, there was statistical significant reduction in the incidence of xerostomia in IMRT group.[5] T Gupta et al in a randomized controlled trial, compared the 3D-CRT and IMRT in squamous cell carcinoma of the head and neck and concluded that IMRT significantly reduces the incidence and severity of xerostomia compared to 3D-CRT in curative-intent irradiation of head and neck squamous cell carcinoma (HNSCC).[6] Rathod S et al reported improved Quality-of-life (QOL) scores in patients with head and neck squamous cell carcinoma (HNSCC) treated with IMRT compared to 3D-CRT.[7] Few studies have investigated the impact of IMRT on swallow function and the impact on

everyday life. Initial studies have reported potential benefits but are limited in terms of study design and outcome data.[8] CM Nutting et al and Chen WC et al reported the reduction in the incidence of xerostomia and improvements in associated Quality of Life with IMRT for head and neck cancer.[9,10]

For oral cavity tumors, IMRT as an adjuvant treatment after surgical resection is feasible and effective, with promising results and acceptable toxicity.[11] Oropharyngeal cancer treated with IMRT have excellent disease control. Locoregional recurrence was uncommon, and most often occurred in the high dose volumes. Parotid sparing was accomplished without compromising tumor coverage.[12] IMRT for locoregional Head and Neck Cancer (HNC) is feasible not only as a single modality but also after surgery, after induction chemotherapy and concurrently with chemotherapy.[13]

Image Guide Radiation therapy (IGRT)

Image-guided radiation therapy is the process of frequent two and three-dimensional imaging, during a course of radiation treatment, used to direct radiation therapy utilizing the imaging coordinates of the actual radiation treatment plan. Image-guided radiotherapy by combining the steep dose gradient of IMRT and daily imaging may potentially improve further the toxicity of head and neck irradiation because of the possibility of safe Packed Tumor Volume (PTV) reduction given the reduced inter-fraction movement through daily imaging. Positron-emission tomography (PET) scan or PET-computed tomography (PET-CT) allows accurate delineation of the tumor and cervical lymph nodes that can be incorporated into the planning CT. PET-CT is superior to CT for tumor imaging because of its ability to detect the tumor metabolic activity in addition to its anatomic location. Although PET-CT is the diagnostic imaging of choice for head and neck cancer IGRT, magnetic resonance imaging (MRI) also plays a critical role when there is suspicion of nerves infiltration, base of skull or parapharyngeal space invasion by the tumor given its better soft tissue discrimination compared to CT. For patients with nasopharyngeal cancer, MRI is complementary to PET-CT because of the tumor location with high risks for intracranial invasion through the skull base foramen and parapharyngeal extension.[14]

The use of IGRT has improved the Quality of Life and preservation of the parotid gland function with treatment toxicity at acceptable level.[15,16] 'The prevalence of osteoradionecrosis ranges from 5 to 7% in head and neck cancer patients treated with the conventional fractionation (1.8–2 Gy/fraction) and 3D-CRT. The risk of radionecrosis may be reduced with IMRT because of the sharp dose gradient allowing for reduction of the volume of normal bone radiated to a high dose. The reported prevalence of osteoradionecrosis ranges from 1 to 5% depending on the anatomic site of the cancer as cancers of the oral cavity usually require treating a large of volume of the mandible to a high radiation dose. The

IGRT technique may further decrease radiation dose to the mandible and thus the risk of radionecrosis. In a study of 83 head and neck cancer patients of various anatomic sites treated with IMRT and IGRT, only one patient developed radionecrosis. Thus, IGRT may be a promising technique for mandibular preservation in future clinical trials'.[14]

IGRT systems include gantry-based systems and robotic arm-based systems. Radiation is on while gantry or robotic arm is rotating with multileaf collimator leaf moving continuously. Intensity modulation is created by overlapping arcs. In gantry-based systems, a gantry rotates the therapeutic radiation source around an axis passing through the isocenter. Gantry-based systems include C-arm gantries, in which the therapeutic radiation source is mounted, in a cantilever-like manner, over and rotates about the axis passing through the isocenter. Gantry-based systems further include ring gantries having generally toroidal shapes in which the patient's body extends through a bore of the ring/toroid, and the therapeutic radiation source is mounted on the perimeter of the ring and rotates about the axis passing through the isocenter. Traditional gantry systems (ring or C-arm) deliver therapeutic radiation in single plane (i.e., co-planar) defined by the rotational trajectory of the radiation source. Examples of C-arm systems are manufactured by Siemens of Germany and Varian Medical Systems of California. In robotic arm-based systems, the therapeutic radiation source is mounted on an articulated robotic arm that extends over and around the patient, the robotic arm being configured to provide at least five degrees of freedom. Robotic arm-based systems provide the capability to deliver therapeutic radiation from multiple out-of-plane directions, i.e., is capable of non-coplanar delivery. In comparison to IMRT these systems are fast, safe and accurate.[17] They are superior to step and shoot IMRT plans and the treatment delivery time is shortened by fifty percent.[18]

Altered fractionation radiation therapy

There is no absolute standard time dose fractionation scheme for the treatment of head and neck cancer. Most commonly used schedule is 2 Gy in a single fraction per day, five days a week, for seven weeks. However, alternative radiotherapy regimens to reduce the total treatment time for head and neck cancers have been assessed. 'Acceleration' of the treatment (delivering the same total dose in a shorter time) should reduce the regrowth of the tumor between sessions, resulting in improved local control of the disease. In 'hyperfractionated' regimens, two to three fractions are delivered each day, with a reduced dose per fraction equal to 1.1 to 1.2 Gy. The reduction of the dose per fraction may reduce the risk of late toxicity, despite an increased total dose. Acceleration and hyperfractionation can be combined, in particular for regimens in which overall treatment time is reduced. The radiobiological principles explaining why fractionation allows for tumor control without local necrosis are the four "R's"

i.e. repair, reoxygenation, repopulation and redistribution.

A systemic review for head and neck cancer by Baujat B et al reported that 'altered fractionation radiotherapy confers greater benefit than conventional radiotherapy in tumor control and survival. The effect was greater for the primary tumor than for nodal disease. The effect was also more pronounced in younger patients and in those with good performance status. Hyperfractionation seemed to yield a more consistent advantage for survival than accelerated radiotherapy. However, there was more diversity in accelerated fractionation regimens than in hyperfractionated regimens, and some of these regimens might be associated with higher non-cancer related death, off-setting their benefit in improving tumor control'.[19] Similarly, Glenny AM et al in a systemic review concluded that the altered fractionation radiotherapy is associated with an improvement in overall survival and locoregional control in patients with oral cavity and oropharyngeal cancers.[20]

CONCLUSION:

The present volume of evidence seems to suggest that the Intensity Modulated Radiation Therapy (IMRT) reduces the incidences of Xerostomia and improves the quality of life in patient treated for oral and oropharyngeal cancer. The Image Guided Radiation Therapy (IGRT) is a further improvement of IMRT. IGRT is fast, accurate and reduces the treatment time by half. The altered fractionation radiotherapy in comparison to conventional radiotherapy is associated with an improvement in overall survival and locoregional control in patients with oral cavity and oropharyngeal cancers and the hyperfractionation provides the greatest benefit.

REFERENCES:

1. Bessell A, Glenny AM, Furness S, Clarkson JE, Oliver R, Conway DI, Macluskey M, Pavitt S, Sloan P, Worthington HV. Interventions for the treatment of oral and oropharyngeal cancers: surgical treatment. Cochrane Database of Systematic Reviews 2011;9
2. A Bevan, M Roach, MK Bucci. Advances in Radiation Therapy: Conventional to 3D, to IMRT, to 4D, and Beyond. CA Cancer J Clin 2005;55:117–134
3. Camphausen KA, Lawrence RC. "Principles of Radiation Therapy" in Pazdur R, Wagman LD, Camphausen KA, Hoskins WJ (Eds) Cancer Management: A Multidisciplinary Approach. 11 ed. 2008.
4. Bhide and Nutting M. advances in radiotherapy. BMC Medicine 2010; 8(25)
5. C. Nutting et al. First results of a phase III multicenter randomized controlled trial of intensity modulated versus conventional

radiotherapy (RT) in head and neck cancer. J Clin Oncol 27:18s, 2009

6. Gupta T et al. Three-dimensional conformal radiotherapy (3D-CRT) versus intensity modulated radiation therapy (IMRT) in squamous cell carcinoma of the head and neck: a randomized controlled trial. Radiother Oncol. 2012 Sep;104(3):343-8
7. Rathod S et al. Quality-of-life (QOL) outcomes in patients with head and neck squamous cell carcinoma (HNSCC) treated with intensity-modulated radiation therapy (IMRT) compared to three-dimensional conformal radiotherapy (3D-CRT): evidence from a prospective randomized study. Oral Oncol. 2013;49(6):634-42
8. Justin W.G. Roea. Swallowing outcomes following Intensity Modulated Radiation Therapy (IMRT) for head & neck cancer – A systematic review. Oral Oncology. 2010; 46(10):727–73
9. CM Nutting et al. Parotid-sparing intensity modulated versus conventional radiotherapy in head and neck cancer: a phase 3 multicentre randomised controlled trial. The Lancet Oncology.2011;12(2): 127 - 136,
10. Chen WC et al. Scintigraphic assessment of salivary function after intensity-modulated radiotherapy for head and neck cancer: correlations with parotid dose and quality of life. Oral Oncol. 2013;49(1):42-8
11. Gomez DR et al. Intensity-modulated radiotherapy in postoperative treatment of oral cavity cancers. Int J Radiat Oncol Biol Phys. 2009 Mar 15;73(4)I
12. Garden AS et al. Patterns of disease recurrence following treatment of oropharyngeal cancer with intensity modulated radiation therapy. Int J Radiat Oncol Biol Phys. 2013 Mar 15;85(4):941
13. DV Gestel, DVD Weyngaert, D Schrijvers, J Weyler and JB Vermorken. Intensity-modulated radiotherapy in patients with head and neck cancer: a European single-centre experience. The British Journal of Radiology, 2011;84:367–374
14. NP Nguyen et al. Image-Guided Radiotherapy for Locally Advanced Head and Neck Cancer. Frontiers in Oncology. 2013 July;3(172):1-4
15. Voordeckers M et al.Parotid gland sparing with helical tomotherapy in head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2012 Oct 1;84(2):443-8
16. Chen-Hsi Hsieh et al. Image-guided intensity modulated radiotherapy with helical tomotherapy for postoperative treatment of high-risk oral cavity cancer. BMC Cancer 2011, 11:37
17. Wilko F.A.R. Verbakel et al. Volumetric Intensity-Modulated Arc Therapy Vs. Conventional IMRT in Head-and-Neck Cancer: A Comparative Planning and Dosimetric Study. International Journal of

Radiation Oncology Volume 74, Issue 1, 1 May 2009, Pages 252–259

18. Andrea Holt et al. Multi-institutional comparison of volumetric modulated arc therapy vs. intensity-modulated radiation therapy for head-and-neck cancer: a planning study Radiat Oncol. 2013; 8
19. Baujat B et al Hyperfractionated or accelerated radiotherapy for head and neck cancer. Cochrane Database of Systematic Reviews 2010, Issue 12.
20. Glenny AM et al Interventions for the treatment of oral cavity and oropharyngeal cancer: radiotherapy. Cochrane Database of Systematic Reviews 2010, Issue 12