Current advances in radiotherapy of head and neck malignancies

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ABSTRACT

Necessity is the mother of all inventions. This is also true in case of cancer therapy. With increasing incidence of head and neck malignancies, remarkable developments have been made towards cancer development and treatment which continues to be a major challenge. Approximately fifty percent of all cancer patients receive radiotherapy which contributes towards forty percent of curative treatment for cancer. New developments in radiation oncology have helped to improve outlook for patients and find more effective treatment. With the advent of new technologies, radiotherapy seems to be promising in patients with head and neck malignancies these advancements include Altered fractionation, Three-dimensional conformal radiotherapy, Intensity-modulated radiotherapy, Image Guided Radiotherapy, Stereotactic radiation, Charged-particle radiotherapy, and Intraoperative radiotherapy.

Key Words: Head and neck malignancy, image guided radiotherapy, intensity-modulated radiotherapy, three - dimensional conformal radiotherapy.

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Introduction

Over the past few decades, conventional radiotherapy which used simpler rectangular treatment fields has changed significantly to conformal radiotherapy techniques which include three dimensional Conformal Radiotherapy and Intensity Modulated Radiotherapy. These have resulted to improve the dose delivered to the tumor bearing tissues which reduces the radiation to the organ at risk thus improving radiation therapy. The dose of radiation is administered over the planned target volume which includes gross tumor volume and the areas of microscopic spread in and around its margin that accounts for physiologic organ changes that may occur during treatment planning and radiation delivery.[1,2] Improved treatment outcomes with adequate evidence have been obtained from several tumor sites of head and neck malignancies with dose escalation and altered treatment fractions.[3-5] Three dimensional Conformal Radiotherapy results in significant reduction of dose to organs at risk. This can be brought about by using IMRT and IGRT which reduces the size of planned treatment volume and enables radiation dose escalation which results in improved treatment outcome. These promising therapies have been discussed below.

Particle Radiation therapy

It is a part of state of art which is expected to be an important part of radiation therapy which include proton and neutron therapy. Since the early 1990's proton therapy has been available on a limited scale.

Proton rays are made of protons which do not have any mass or charge when compared to x rays and gamma rays. Proton rays have an advantage of being able to conform to the shape of the tumor more precisely when compared to x rays. They consequently allow the delivery of higher radiation dose to the tumor site with minimal side effects and less injury to the surrounding tissues. Proton rays act by disrupting the atomic electron in the target cells.

The second promising type is neutron therapy which is composed of very high energy neutron rays which consists of neutrons that have particles with mass and no charge when compared to x rays, gamma rays and proton rays. Neutron rays act on target cells by acting on atomic nuclei rather than the electron. Conventional radiation is dependent on oxygen for its action, hence its effect on larger tumor is very minimal as the central part of these tumors are oxygen deficient but neutron radiation is effective in absence of oxygen by causing cellular damage, therefore beneficial in large tumors e.g. include inoperable salivary gland tumor and bone malignancies.[6-8]

Intra Operative Electron Radiation Therapy (or "IOERT")

IOERT excludes the irradiation of normal tissues and the critical structures in and around the target volume, hence called precision radiotherapy as the clinician views the tumor directly. As the dose falls off rapidly below the target site sparing the underlying healthy tissue, electron radiation can be applied directly on the tumor (residual tumor/tumor bed) which is vulnerable for destruction during intraoperative/ operative procedures. IOERT has proven to be beneficial when used in conjunction with endovascular brachytherapy which in-turn reduces integral dose and treatment time. [9, 10]

Stereotactic radiotherapy

This is an important new development in the treatment of brain tumors. Stereotactic radiation uses a single high dose of radiation sent into cancerous tissue with very narrow beam of radiation. This is a precise technique that is painless. An example of this technique is the Gamma Knife. It is a revolutionary type of surgery that uses highly targeted radiation to treat brain abnormalities which is Proven safe and effective, with good outcomes. Gamma Knife procedures offer new hope, less risk and quicker recovery. The data from Computed Tomography scans, Magnetic resonance imaging and arteriograms to pinpoint abnormal areas within the brain and destroy them using multiple beam of low dose gamma rays which converge to produce a high dose of radiation at the exact side, thus protecting the tissues along the route of the lesion which is safe and effective. This innovative type of surgery is currently used in treatment of intra-cranial oligometastases where the gamma knife "cuts" deep into the brain without using scalpel.[11]

Three-dimensional (3D) conformal radiation therapy

The possibility of "geographic miss." Which is bound in conventional radiotherapy where a small portion of tumor is excluded, results in treatment failure. With the advent of Three-dimensional (3D) conformal radiation therapy which uses reconstructed matched computed tomograms (CT) and magnetic resonance images (MRI) that are used during treatment plan reduces the risk of geographic miss and the distribution of the beam can be conformed to the tumor size and shape using customized showed dense block or by multileaf collimators. Aproximately 40 pairs of tungsten measuring 1cm in width, can be adjusted to define x-ray beam, thus reducing the dose of radiation to normal tissues upto 50% and this inturn reduced late damages.[6]

Intensity-modulated radiotherapy (IMRT)

Intensity-modulated radiotherapy delivers planned, specified dose of radiation directly to the tumor cells at the target site, thus sparing the surrounding healthy tissue. This is also known as tomotherapy. The principle remains the same, but the technology of IMRT is that it is an advanced form of three dimensional conformal radiotherapy, where IMRT is delivered using linear accelerators with static or multi-leaf collimators, or volumetric arc modulated therapy. A powerful computer program optimizes a treatment plan based on clinician's dose instruction, and information about tumor size, shape and location in the body. Linear accelerator is the key system with multi leaf collimator that shapes the radiation beam, delivers the radiation in accordance with the treatment plan, which can be adjusted in the most favourable angles in the tumor to kill the cells. The equipment can be rotated around the patient where the beams are moved in dozens or hundreds of times that may vary with intensity, resulting in radiation sculpted in three dimensions. This boosts the IMRT doses that are delivered at various target sites in a single phase and obviates the need for field matching and the use of electrons, thus minimizing dosimetric uncertainties.

When IMRT is applied in the management of head and neck malignancies, IMRT provides an advantage of sparing the important vital structures such as salivary gland, digestive tract mucosa, optic nerves, cochlea, pharyngeal constrictors, brain stem and spinal cord.[12-14] In an IMRT multi centered study which compared parotid gland sparing with conventional radiotherapy of phyreangealcancer (oral and pharyngeal) has shown significant reduction of xerostomia (40%) in one year post radiotherapy.[15] IMRT also spares the oral and hypopharyngeal muscles which helps in normal deglutition hence reduces radiation induced dysphagia. The ability of IMRT to spare cochlea reduces the incidence of radiation induced loss of hearing.[2] the burden of in IMRT when compared to conventional radiotherapy is reduced, this permit dose escalation to improve treatment outcome.

Image Guided Radiotherapy (IGRT)

IMRT system includes image acquisition software, treatment software, treatment stimula- lator, platinum medical linear accelerator, dynamic multileaf collimators, which deliver sharp radiation dose gradient in accordance with the treatment plan which in turn leads to geographic miss of the tumor and a consequent over dose to the organ at risk.

Optimal IMRT relies on accurate image guidance. IGRT can be a useful tool that can detect and correct the geographic miss that can occur in treatment delivery. Currently more advanced IGRT technique are available for patient orientation and target positioning. Image guidance can be used for improved tumor delineation and to correct intra and inter fraction movement during radiotherapy. Computerized tomograms with image guidance provide three dimensional view of tumor and normal anatomy. However CT scans are inferior to MRI scan in detailed definition of soft tissues, hence CT and MRI fusion should be considered for radiotherapy planning in treating head and neck malignancies. Dental implant and amalgam restorations should be considered during treatment planning as they can cause Artifacts.

Positron emission tomography is a nuclear medicine technique that enables biological imaging of tumors. The proliferating areas of tumor can be highlighted by using fluoro-2-deoxy-D-glucose positron emission tomography which aids in delineation of gross tumor volume and Positron emission tomography guided dose escalation using IMRT.[16] Radioactive tracers, namely fluorine-18-labelled fluoromisonidazole and copper (II)-diacetyl-bis(N(4)-methylthiosemicarbazone highlight the hypoxic areas of tumors which are radioresistant and increasing the radiation dose might help overcome radioresistance with pet guided dose using IMRT.[17-22] feasibility of this approach in terms of acute toxicity have to be considered.[21,22] However, follow-up data for treatment outcomes and toxicity should be evaluated before this approach is used in standard clinical practice.[23]

Thermo radiotherapy (hyperthermia)

It involves the application of localized high temperature at the tumor site which is said to improve the radiation treatment outcome. Currently scientific research as been conducted on this treatment modality.[6]

Radioimmunotherapy

Radioimmunotherapy is a form of radiotherapy where cytotoxic radionuclides such as Yttrium 90, Iodine-131 are linked to antibodies in order to deliver toxins directly to the tumor targets. It is also known as Targeted Radiotherapy. The efficiency of their radioisotopes is that it has longer path length and thus large tumors may receive a higher dose of radiation to a greater depth. Another important factor is that conjugation or the chemicals linkage to the radioisotope to the tumor antibody, which allows the therapy to be delivered to the tumor cell. Radioimmunotherapy has proved to be effective for treatment of lymphomas. Whereas its application in oral cancer has been reported to be under clinical trials using monoclonal antibodies.

The Advantage of radioimmunotherapy is that each cell does not have to be bound by the antibody to receive cytotoxic radiation. Thus the adjacent tumor cells though do not receive antigenic determinants, can be destroyed by radiation. Hence is it not mandatory that each tumor cell should receive antigen determinants as in conventional immunotherapy. Thus the evidence of immunogenicity of oral cancer may help in the success of Immunotherapies.[6, 24]

Conclusion

Radiotherapy is one of the important treatment modality for head and neck malignancies. Continual assessment and monitoring of patients undergoing radiotherapy are necessary for effective treatment outcome, improve quality of life, increase the life span of cancer patients and minimize the radiotherapy related toxicities. The advents of new technology have improved sparing normal cells/tissues through dose fractionation, conformal radiation techniques, IMRT, IGRT. However further research on treatment outcomes and related toxicity are required before these approaches can be used in standard clinical practice.

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