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Radiotherapy for Head and Neck cancers-a review

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Abstract

Radiotherapy still remains an enigma in the treatment of Head and Neck cancers. Radiotherapy treatment planning of Head and Neck cancers pose a challenge due to its proximity to critical adjacent organs. This article briefs the various types, uses, techniques of Radiotherapy.

Keywords: Radiotherapy, Van de Graff Generator, Linearaccelerator, Brachytherapy, Teletherapy.
Key Messages: Radiotherapy still remains an enigma in the treatment of Head and Neck cancers. Radiotherapy treatment planning of Head and Neck cancers pose a challenge due to its proximity to critical adjacent organs. This article briefs the evolution, various types, uses, techniques of Radiotherapy.

Introduction

The invention of xray by Wilhelm Conrad Roentgen and radioactivity by Henry Bequerel marked a history in the evolution of radiotherapy.(1) The various rays used in radiotherapy consists of electromagnetic (x rays and Gamma rays) and Particulate radiation (Electrons, Protons, Neutrons).

The first application of Radiotherapy in the field of Medicine was done by Emile Grubbe on 29th January, 1896 in Chicago for the treatment of breast carcinoma.(1) The Evolution of radiotherapy machines is shown in Table 1.

Table 1: Evolution of radiotherapy machines

Year	Evolution of radiotherapy machines
1900	Low voltage Teletherapy <150 KV
1919	Radium Teletherapy Machines
1920	Orthovoltage Xray Machines 200-500 KV
1922	Radium Howitzer
1939	Megavoltage Xray Machines > 1MV
1956	First Cobalt therapy machine (Eldorado A) at W.I.A cancer Institute, Chennai
1953	Linear Accelerator (LINAC) 8MV
1968	Gamma Knife
1976	First Linear Accelerator at Cancer Institute, Chennai
1980	Linac Based- Stereotactic Radiotherapy(SRT)
1993	Tomotherapy
1994	MiMIC Tomotherapy
1995	MLC Dynamic
1997	MLC Step and Shoot or MSF(Multi static field) First LINAC based Stereotactic Radiotherapy started in AIIMS(All India Institute of Medical sciences)
2002	Helical Tomotherapy
2013	Hybrid Linac MRI (linac-MR)

Radiotherapy has a wide range of applications in the treatment of tumors like Lymphoma, seminoma, Myeloma, Ewings sarcoma, Wilms tumor, Medulloblastoma-an exquisitely radiosensitive tumor and Kaposi Sarcoma occurring in AIDS, to palliate disease symptoms of bone pain from metastatic tumors, to prevent the development of leptomeningeal disease and brain metastases in acute leukemia and lung cancer, control of Brain metastases, reversal of spinal cord compression, superior vena cava obstruction, shrinkage of Painful masses.

Radiation therapy or Radiotherapy is the use of electromagnetic radiation like x-rays or gamma rays or particulate radiation like neutrons, protons, electrons to destroy or damage cancer cells.

The initially developed Co-60 teletherapy units that produce gamma rays failed to treat deep seated cancers. Hence to increase the depth of penetration of the charged Particle Accelerators are used.

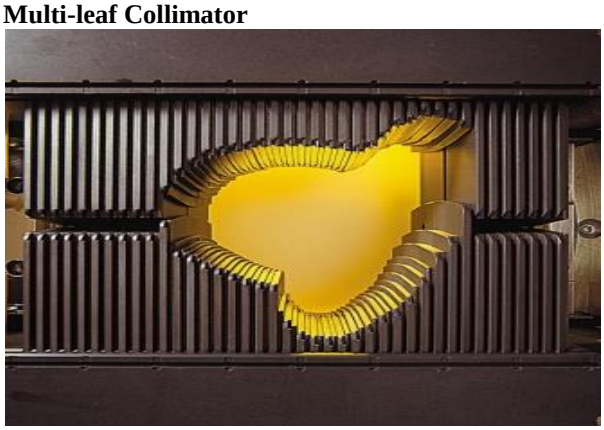
An accelerator is a device that accelerate charged particles using electromagnetic fields. There are two types of Particle accelerators-Electrostatic accelerators –those that require electric fields that do not change with time E.g. Linear accelerator invented by Rolf Wideroe (1927), Van De Graaff Accelerator by Robert Van De Graaff (1929), Cockcroft-Walton accelerator by John cockroft and Ernest Walton (1932) and oscillating field accelerators- those that require electric fields that change with time e.g., Cyclotron by Ernest Lawrence (1928), Betatron by Donald Kerst (1940), Microtron by Vladimir Veksler (1945), Synchrotron by Frank Goward and D Barnes.

Linear Accelerator: A linear Accelerator is a device that increases or accelerates the velocity of charged particle like Electron, Neutron, Proton when subjected to combined electric and magnetic field thereby

enhancing its penetration into tissues for Deep seated Tumors. A Linear (Particle) accelerator works on the principle of "resonant vibration "as proposed by Gutav Ising.

Modern Linacs have multileaf collimator made of tungsten that is incorporated into the head of the machine designed in such a way that they destroy the cancer cells while sparing the surrounding normal tissue.(Sparing effect).

Multi-leaf Collimator



The Linear accelerator has the capability to deliver therapeutic radiation at multiple angles and also permits a homogenised dose to a given treatment volume.

Linear Accelerator (LINAC)

The differences between Co-60 Teletherapy and Linear Accelerator are described in Table 2.

Table 2: Differences between CO-60 Teletherapy and linear accelerator

	CO-60 Teletherapy	Linear Accelerator
Dose Rate	Decays with time	constant
Penumbra Effect	Higher	Lesser
Deep seated Tumors	Not effective	Better
Field size	Cannot treat field size less than 5 x 5 cm	5 x 5cm
Precision of radiation	Dose delivered cannot be recorded	Dose delivered is continuously monitored and recorded
Dose rate /Min	constant	variable
Motorized Wedges	Not Possible	Possible
Multileaf collimator	Absent	Present
Portal vision attachment	Not Possible	Allows to view actual tumor during treatment
Stereotactic attachment	Not Possible	Possible. Provides wider range of Applications

Therapeutic radiation is delivered in three ways:

1. Teletherapy –in which beams of radiation generated at a distance and aimed at the tumor within the Patient.
2. Brachytherapy – in which encapsulated sources of radiation implanted directly into or adjacent to a site of tumor.
3. Systemic therapy-in which radionuclides are targeted in some fashion to a tumor site.

Types of Radiotherapy

Brachytherapy: A type of radiation therapy in which radioactive materials are placed in direct contact with the tissue being treated. In Intracavitary treatment, containers that hold radioactive sources are put into the body cavities that are in or near the tumor (e.g. Intrauterine, vagina). Sometimes Brachytherapy is done in conjunction with External Beam radiotherapy. The External beam radiation destroys cancerous cells in a large area surrounding the tumor. Brachytherapy delivers a boost or Higher dose of radiation, to help destroy the main mass of tumor cells. Some Brachytherapy sources are described in Table 3.

Table 3: Brachytherapy Sources

Radionuclide	Radiation Emitted	Energy	Half-Life	Form
Radium-226	Gamma rays	1 MeV	1620 Years	Needles, Tubes
Caesium-137	Gamma rays	0.66 MeV	30 Years	Tubes, Needles, Pellets
Cobalt-60	Gamma rays	1.25MeV	5.26 Years	Rods
Iridium-192	Gamma rays	0.4 MeV	74 days	Wires
Gold-198	Gamma rays	0.41 MeV	2.7 days	Seeds
Strontium-90	Beta rays	2.27 MeV max	28.1 Years	Pellets
Ytrrium-90	Beta rays	2.27 MeV max	64 Hours	Rods

Table 4: Therapeutic radiation dosage for various anatomical regions of head and neck

Anatomical Region	Therapeutic Dosage
Oral Cavity	45 Gy
Brain Stem	50 Gy
Spinal cord	48 Gy
Mandible	30 Gy
Parotid gland (right or Left)	30 Gy
Larynx	45 Gy
Oesophagus	45 Gy

Brachytherapy- 5 Types

1. External Applicator or molds
2. Interstitial Brachytherapy – Gatrointestinal carcinoma, Carcinoma Prostate
3. Intracavitary Brachytherapy – Cancer of the cervix and Rectum.
4. Intraluminal Brachytherapy - Cancer of the Lung.
5. Intravascular Brachytherapy

Radiotherapy administered inside arteries after angioplasty, stent insertion or bypass grafts to prevent coronary restenosis after stent insertion. The first study of intracoronary brachytherapy in humans was initiated in July 1994 by Condado and his colleagues in Caracas, Venezuela.[17]

Laird et al has reported that neointimal hyperplasia could be inhibited in the short term by the application of a ^{32}P impregnated stent. These stents had activities in the range of 0.14 mCi and delivered doses to tissue of approximately 280 cGy.[19]

Interstitial Brachytherapy: In Interstitial Brachytherapy radioactive sources are placed directly into or adjacent to the tumor (e.g., in the form of needles). Iridium 192 is used in the form of needles or wires. The Iridium wires can be inserted through the tumor bearing tissue or the bed of the tumor, following surgical removal or radiotherapy. Gold(Au)-198 can also be used in the form of grains for cancer of the tongue.[16]

In interstitial Brachytherapy radioactive sources are placed directly into the tumor (e.g., in the form of needles). These radioactive sources may stay in the patient permanently. Sometimes the radioactive sources are removed from the patient after several days. This technique is helpful in treating cancers of the cervix, uterus, vagina and certain head and neck cancers, breast cancer, brain, skin, esophageal, soft tissue, lung, bladder and Prostate cancer.

Permanent Interstitial Implants: They are used when the tumor to be treated is inaccessible making the removal of radioisotope impossible or impractical.

These implants usually have short half lifes mainly used to treat deep seated cancers of Pelvis, Abdomen, Lung, Colon, Rectum.

Isotope Used: Pallodium 103, Iodine 105, Gold 198.

Use: Deep seated tumours in Pelvis, Abdomen, Lung, Colon, Rectum.

Temporary (Removable) Interstitial Implants

Temporary removable implants are used in anatomic areas where there is no body cavity or orifice to accept radioactive sources. Radioiostope commonly used are Iridium-192, Caesium-137.

Such Implants are used for breast and chest wall irradiation, anterior, lateral and posterior wall of vagina.

Teletherapy: Teletherapy or External Beam Therapy involves delivering a beam of ionizing radiation to the tumor volume from a radioactive source kept 80 – 100 cms away from the skin of the subject.

Radical/ Curative Radiotherapy: When there is Severe impairment of function or cosmesis with surgery or when Surgery has high morbidity or has poor results.

Palliative Radiotherapy: Aims to relieve the symptoms of the disease without attempting to cure the patient or causing new symptoms from acute normal tissue reaction.

Palliative Radiotherapy is indicated in incurable disease with short life expectancy, to relieve bleeding or pressure symptoms caused by the bulk of the tumour.

Sites which tolerate Palliative Radiotherapy poorly are the oral cavity(soreness and dysphagia), upper abdomen (sensitivity of the stomach and duodenum), and Perineum(Painful skin and Vaginal reaction).

The Differences between Radical and Palliative Radiotherapy is mentioned in Table 5.

Table 5: Differences between Radical radiotherapy and Palliative radiotherapy

Radical Radiotherapy	Palliative Radiotherapy
Homogeneity of Dose distribution across the target tumour volume is important to achieve Maximum tumour kill	Homogeneity of Dose distribution is much less important
Wedge fields are needed	Wedge fields not needed Single or Parallel opposed fields suffice
Computerised Planning is needed	Computerised Planning is not needed.

Table 6: Differences between conventional and stereotactic radiotherapy

Conventional Radiotherapy	Stereotactic Radiotherapy
Coplanar setup of radiation field	Non coplanar setup of radiation field
Helps in treating Large volumes of tumor	Helps in treating small target /treatment volumes of tumor
Uses Less number of treatment fields	Uses more number of treatment fields
Coplanar setup	Non coplanar setup
Positional Accuracy +/- 5mm	Positional Accuracy + / - 1 mm
Markings necessary on Patients skin before treatment planning	No markings necessary on Patients skin before treatment planning
Less conformality of radiation Dose	More conformality of Radiation Dose
Sensitive structures such as Brain stem, optic chiasma, salivary gland need not be protected	Sensitive structures such as Brain stem, optic chiasma, salivary gland must be protected

Adjuvant Radiotherapy: Radiotherapy in conjunction with surgery or chemotherapy is called Adjuvant radiotherapy.

Adaptive Radiotherapy: Adaptive radiotherapy means changing the radiotherapy plan after treatment has started.

Pre Operative Radiotherapy: Indicated in large tumor volume at primary site or neck.

Post Operative Radiotherapy: Indicated in large primary tumours – T3 or T4 with soft tissue infiltration, Close or positive margins of excision, Lymphovascular & perineuralinvasion. Bulky nodal disease. Extra nodal extension and multiple level involvement.

Steps in Radiotherapy Treatment Planning

1. Volume Definition.
2. Immobilisation Devices
3. Patient data acquisition and Simulation
4. Verification.
5. Treatment Planning system
6. Selection of Field
7. Weekly evaluation of tumor response and Tolerance
8. Followup.

Volume Definition: The following volumes have been defined as principal volumes related to 3D treatment planning: Gross tumour volume, Clinical target volume, Internal target volume, and Planning target volume.[7]

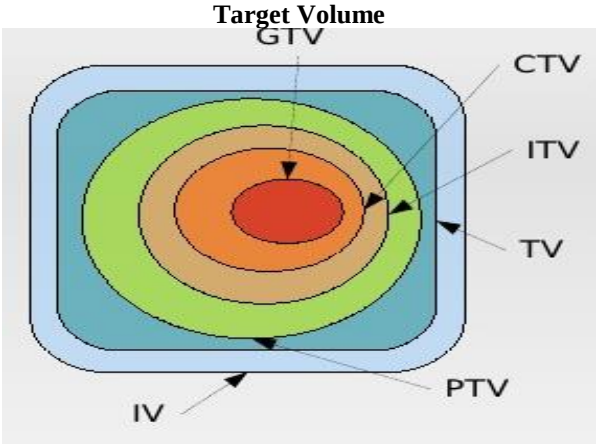
The Gross Tumour Volume: "The Gross Tumour Volume (GTV) is the gross palpable or visible/demonstrable extent and location of malignant growth". The GTV is usually based on information obtained from a combination of imaging modalities(CT, MRI, ultrasound, etc.), diagnostic modalities (pathology and histological reports, etc.) and clinical examination.[7]

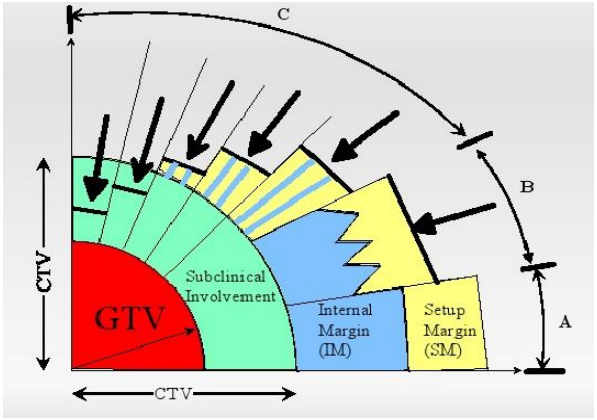
The Clinical Target Volume: "The Clinical target volume (CTV) is the tissue volume that contains a demonstrable GTV and/or sub-clinical microscopic malignant disease, which has to be eliminated. This volume thus has to be treated adequately in order to achieve the aim of therapy, cure or palliation.[7]

Planning Target Volume: "The Planning target volume is a geometrical concept, and it is defined to select appropriate beam arrangements, taking into consideration the net effect of all possible geometrical variations, in order to ensure that the prescribed dose is actually absorbed in the CTV".

The PTV depends on the precision of such tools as immobilization devices and lasers, but does NOT include a margin for dosimetric characteristics of the radiation beam (i.e., penumbral areas and build-up region) as these will require an additional margin during treatment planning and shielding design.[7]

Target Volume





GTV – Gross Palpable or Visible Tumor
CTV – GTV + Sub clinical microscopic malignant disease
PTV – CTV + Margin for geometric uncertainties
TV – (Treated Volume) – Volume of the tumour and surrounding normal tissue that is included in the isodose surface representing the irradiation dose proposed for treatment (V_{95})
ITV (Irradiated Tumour volume) – Volume included in isodose surface with a possible biological impact on the normal tissue encompassed in this volume.

Immobilisation Devices: Immobilisation devices have two fundamental roles:

1. To immobilise the patient during radiotherapy treatment.
2. To provide a reliable means of reproducing the patient position from simulation to treatment, and from one treatment to another.

The simplest immobilisation means include masking tape, velcro belts, or elastic bands.

The basic immobilisation device used in radiotherapy is the head rest, shaped to fit snugly under the patient's head and neck area, allowing the patient to lie comfortably on the treatment couch.

Head: Aquaplastic Mask. Cutout over eyes and mouth, Bolus when needed. The bolus is a thermoplastic material, sufficiently flexible to conform to the patient surface, should be tissue equivalent and durable.

Bolus often used when treating uneven areas of a patient, such as tumours at the nose or ears, to make up for missing tissue, or to provide build-up of dose to the skin surface.

Patients to be treated in the head and neck or brain areas are usually immobilised with an Aqua plastic mask which, when heated, can be moulded to the patient's contour. The mask is affixed directly onto the treatment couch or to a plastic plate that lies under the patient thereby preventing movement.

Chin: Biteblock and Mouthpiece. Biteblock maintains the position of the chin and moves the tongue away from treatment area.

Neck: Neck rest is used for stabilising neck while performing radiotherapy.

Clavicle: Aquaplastic Mask, Shoulder restraining

Limbs and Trunk: Thermoplastic Moulds, Velco straps, Belts.

For Stereotactic Radiotherapy –Gill Thomas Cosman (GTS) Frame is used

Patient Data Acquisition: Patient data acquisition is an important part of the simulation process, since reliable data is required for treatment planning purposes and allows for a treatment plan to be properly carried out.

Simulation: Patient simulation was initially developed to ensure that the beams used for treatment were correctly chosen and properly aimed at the intended target.

Presently, treatment simulation has a more expanded role in the treatment of patients consisting of:

- Determination of patient treatment position and selection of immobilisation devices.
- Identification of the target volumes and organs at risk.
- Determination and verification of treatment field geometry.
- Generation of simulation radiographs for each treatment beam for comparison with treatment port films.
- Acquisition of patient data for treatment planning.

The simplest form of simulation involves the use of port films obtained on the treatment machines prior to treatment in order to establish the treatment beam geometry. However, it is neither efficient nor practical to perform simulations on treatment units. Firstly, these machines operate in the megavoltage range of energies and therefore do not provide adequate quality radiographs for a proper treatment simulation, and secondly, there is a heavy demand for the use of these machines for actual patient treatment, so using them for simulation is often considered an inefficient use of resources.

For the above reasons, dedicated equipment for radiotherapy simulation has been developed. Conventional simulation systems are based on treatment unit geometry in conjunction with diagnostic radiography and fluoroscopy systems.

Modern simulation systems are based on computed tomography (CT) or magnetic resonance (MR) imagers and are referred to as CT-simulators or MR-simulators.

The clinical aspects of treatment simulation, be it with a conventional or CT-simulator rely on the positioning and immobilization of the patient as well as on the data acquisition and beam geometry determination.

Fields Used in Radiotherapy

Wedge Fields: Wedge fields were first developed by Miller at Sheffield in 1944.Wedge fields can be used for therapeutic x-ray radiations more than 250 Kv. Wedge field is achieved by placing in the beam of absorbing metal such as copper which gives much

lower radiation intensity on the side of the radiation beam with greater thickness of copper than on the other side.

Wedge fields are of great value in treating tumours in corner sites, e.g. in the head, when two fields at right angles on the corner give a uniform dose distribution to the tumour, while irradiating very little normal tissue. Wedges can be used to compensate for a sloping surface, as for example, in nasopharyngeal treatments where wedges are used to compensate for decreased thickness anteriorly.

Parallel Opposed Fields: Indicated for large tumors or when a tumor is located near or close to midline such as Mediastinal Masses.

Advantages

- Simplicity and reproducibility
- Homogeneous dose distribution
- Less chance of Geometric Miss.

Disadvantage

- Excessive dose to normal tissues and critical organs above and below the tumor.

Wedged –Pair Field: Wedged Pair field allows a therapeutic dose to unilateral disease while sparing a high dose to opposite side.

Lateral Field: The Lateral field irradiates only the neck region of the Patient.

Antero-Posterior Field: This field mainly irradiates the supraclavicular regions on both the sides.

Three-Field Technique: The three-field technique consists of 2 opposed lateral fields to irradiate the primary tumor and cervical lymph nodes in the upper and lower neck, and a third anterior field to irradiate the supraclavicular lymph nodes.

Mantle Field: The name Mantle technique is derived from the word "Mantle", which is a type of cloak. It has been so named because the areas included in this radiation field technique resembles a person wearing a cloak. It has been used traditionally for radiotherapeutic treatment of Hodgkins Lymphoma. It is a type of extended field radiation technique and includes multiple involved and uninvolved lymph nodes. When the multiple sites are involved above the diaphragm, then the field is known as Mantle field. It includes the following group of lymphnodes: Bilateral cervical, Bilateral supraclavicular, Bilateral Infraclavicular, Bilateral Axillary, Bilateral Hilar, Bilateral Mediastinal.

Modifications of Mantle Field Technique

Minimantle: In this Minimantle field of radiotherapy, the Hilar and Mediastinal Lymphnodes are not included.

Modified Mantle: In this Modified Mantle field of radiotherapy, the region of Axillary Lymph nodes are not included.

Involved – Node Radiotherapy (INRT): Involved-node radiation therapy (INRT) is a term used for delivering radiotherapy to only those areas of the body below the subdiaphragmmatic level. Radiotherapy consists of 30-40 Gy in 15-20 Fractions for treating early aggressive Non-Hodgkins Lymphoma.

Simulation: Simulation is done with the help of conventional radiographic techniques or three dimensional radiographic techniques like CT or MRI. Is a precise mock-up of a patient's treatment with radiographic documentation of the treatment portals simulators that provide the ability to mimic most treatment geometries and helps to visualise the resulting treatment fields on radiographs and to visualize the resulting treatment fields on radiographs or under fluoroscopic examination of the patient.

They consist of a gantry and couch arrangement similar to that found on isocentric megavoltage treatment units, with the exception that the radiation source in a simulator is a diagnostic quality x-ray tube rather than a high-energy linac or a cobalt source.

For the vast majority of sites, the tumour is not visible on the simulator radiographs and can be determined only with respect to anatomical landmarks visible on the radiographs (usually bony structures or lead wire clinically placed on the surface of the patient).

Verification: Verification simulation is a final check that each of the planned treatment beams covers the tumor or target volume and does not irradiate critical normal structures. It is the second part of a two-step process on the simulator.

It involves taking radiographic images or portal images of each of the treatment beams using external marks and other immobilization devices

Isodose Curves: Isodose curves are the lines joining the points of equal Percentage Depth dose (PDD), a quotient expressed as a percentage of absorbed dose at any depth (d) to absorbed dose at dmax along the central axis of the therapeutic beam radiation.

Isodose curves are used to evaluate treatment plans along a single plane or over several planes in the patient. The isodose covering the periphery of the target is compared to the isodose at the isocentre. If the ratio is within a desired range (e.g., 95-100%) then the plan may be acceptable provided critical organ doses are not exceeded.

Preparation of Isodose Charts

An Isodose chart consists of a family of isodose curves usually drawn at regular intervals of PDD. For SSD Setups, all isodose values are normalized to 100% at point of dose maximum on the central beam axis. For SAD(Source At Distance) Setups, the isodose values are normalized to 100% at the isocentre.

The various factors affecting the isodose curves are Source size. Field size, Beam quality, Beam Collimation, Source-skin Distance, Source-collimator distance.

Radiotherapy Treatment Planning

For Most epithelial malignancies such as squamous cell carcinoma of the oral cavity, radiation is commonly delivered in 1.8-2.2 Gy per fraction for 6-8 weeks. Total Dose 6500-7500 cGy.

The maximum therapeutic dosage given for various anatomical regions of Head and Neck is shown in Table 4.

Fractionation: The Delivery of radiation therapy as a number of small discrete doses is referred to as Fractionation. Fractionation helps in Repair of sublethal damage of cells that are subjected to radiotherapy, allows for Redistribution of tumor cell population, Regeneration of damaged normal cells and also reoxygenation of normal cells adjacent to tumor cells. Fractionation helps to increase the differential effect of the radiation on the tumor compared with the normal tissues.

Conventional Regimen

Curative - 1.8 – 2 Gy / day given amounting to 66 – 70 Gy in 33 fractions over 6 ½ weeks.

Palliative - 3 Gy/day is given i.e., 30 Gy in 10 fractions over 2 weeks.

Altered Fractionation

Hyper fractionation – increase in the number with reduction in size of fraction.

1.5 Gy twice daily to a total dose of 80.5 Gy over 7 weeks.

Hyperfractionation (Accelerated fractionation)(Concominant Boost Technique): Instead of treating once a day, the number of daily fractions can be increased, in practice rarely to more than three. This approach has been explored in tumors where conventional fractionated radiotherapy has often failed to cure tumors. e.g. Cerebral gliomas and advanced lung and head and neck cancer – shortening of Rx time with no change in number, size of dose / fraction and total dose.

Newer Regimen:

Continous Hyper Fractionated Accelerated Radiation Therapy (CHART) – 54 Gy in 36 fractions – 1.5 Gy T.I.D. over 12 consecutive days.

Hypofractionation

Hypofractionation refers to the practice of giving less than the conventional five daily fractions per week. This approach is illogical for treating most tumor sites since long gaps between fractions may allow tumor repopulation. Hypofractionation is more logical in treating tumors with a higher capacity for repair, e.g. Melanomas and soft tissue sarcomas and in Palliative radiotherapy. In Palliative radiotherapy single fractions of 4-15 Gy for bone metastases are in general as effective as multiple fractions to total doses of 20-40 Gy. As good and Prompt pain relief can be achieved by a single fraction of 8 Gy as by 30 Gy in 10 daily fractions. Two fractions of 8.5 Gy given a week apart are as effective in relieving the symptoms of Non-small cell lung cancer as 30 Gy in 10 daily fractions.

With the advent of 3-D imaging modalities like CT,MRI, Fusion Imaging (which is a combination of CT and MRI image of a particular anatomical region)PET,SPECT,CBCT three dimensional conformal radiotherapy is possible now for Head and Neck cancers in which the therapeutic radiation is precisely targeted at the tumor volume without affecting the adjacent vital structures such as in the treatment of carcinoma of the maxillary sinus can now be treated by IMRT without affecting the adjacent vital structure such as the orbit. Conformal 3-D Treatment Planning permits delivery of high doses of radiation to target volume without increasing complications in transit volume.

IMRT (Intensity Modulated Radiotherapy)

Technological and computer treatment planning advances led to the development of IMRT.[16,18]

IMRT is defined as a radiation therapy technique in which non-uniform fluence is delivered to the patient from any given position of the treatment beam to optimize the composite dose distribution. Fluence refers to the number of particles incident on a unit area. The fluence beams are electronically transmitted to the linear accelerator, which is computer controlled to deliver intensity modulated beams as calculated.

The technique of IMRT is more complex and resource-intensive than 3DCRT. It uses a CT-based inverse-planning process to deliver ionizing radiation conformally to the target tumour volume but also conforms low dose to the adjacent sensitive tissues by altering the beam intensity using tungsten-based multileaf collimators

IMRT theoretically reduces radiation dose to adjacent organs or tissues at risk (e.g., the parotid glands. However, with IMRT a larger volume of uninvolved adjacent tissues may be exposed to ionizing radiation than 3DCRT.

Currently, IMRT is being used most extensively to treat cancers of the head and neck, Prostate gland tumors and central nervous system, pediatric malignancies.

IMRT has also been used in limited situations to treat breast, thyroid, lung, as well as in gastrointestinal, gynaecologic malignancies and certain types of sarcomas.

Delivery Techniques in IMRT

Step and Shoot: Done by superimposing a number of different beam shapes with the same gantry orientations, known as segments. Segments are created by differing MLC arrangements where the target is differentially blocked.

Dynamic/Sliding Window: The Multileaf collimators sweeps across the field with different speeds and duration to create the segments.

Head and neck IMRT planning techniques include the split-field and the extended-field IMRT techniques.[6-9]

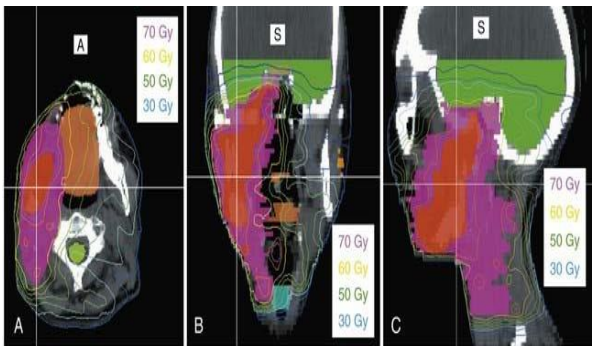
Split Field IMRT Technique: In this technique the primary and the upper neck above the vocal cords are treated with IMRT, and the lower neck and the supraclavicular fossae are treated with the conventional anterior field. The IMRT fields are matched with the anterior field at the isocenter with a half-beam block technique. The main disadvantage of the split-field technique is that there is possible under dosage of the tumor at the field junction.[30]

Extended Field IMRT Technique: Extended-field IMRT treats all tumor volumes of the Head and neck simultaneously with different prescription doses to the primary tumor and the regional lymph nodes. This technique can increase the dose to the larynx if a special dose constraint is not applied to protect the larynx or to any involved lymph nodes in the lower neck and supraclavicular region.(30)

Advantages of IMRT

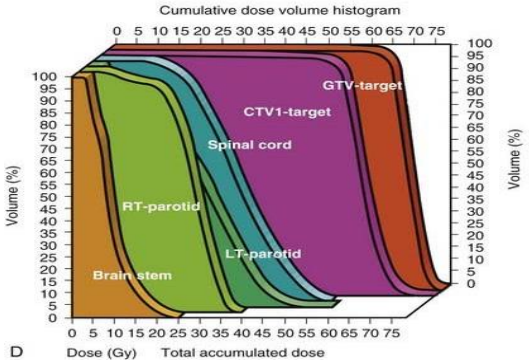
1. Superior Planned Tumour volume conformality
2. Better normal tissue sparing e.g. Superior Parotid gland sparing in treating salivary gland tumors.
3. Fewer fractions needed.
4. Lesser number of treatment days required.

Isodose Chart Prepared for a Planned IMRT



Dose-Volume Histogram (DVH): Dose volume histograms (DVHs) summarize the information contained in the 3-D dose distribution and are extremely powerful tools for quantitative evaluation of IMRT, IGRT or VMAT treatment plans. All cumulative DVH plots start at 100% of the volume for 0 Gy, since all of the volume receives at least no dose. Dose Volume Histogram summarises entire dose distribution in a single curve for each anatomical structure of interest.

A Cumulative Dose-Volume Histogram

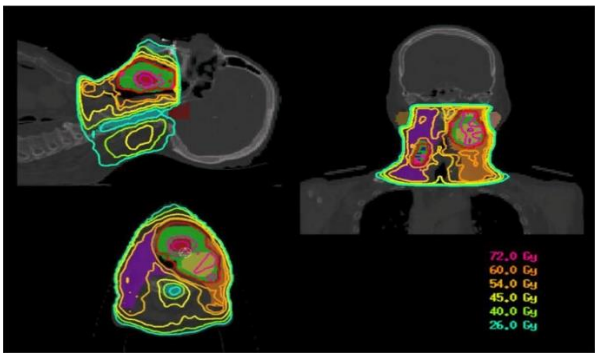


IGRT: (Image Guided Radiotherapy):(5) IGRT is a technique in which Fiducial markers such as a small metal (typically gold) spheres, coils or cylinders about the size of a grain of rice that are placed in or near a tumor with the help of an interventional radiologist to help guide the placement of radiation beams during treatment.

The markers help pinpoint the tumor's location with greater accuracy and allow the treatment team to deliver the maximum radiation dose to the tumor while sparing healthy tissue.

Volumetric Modulated Arc Therapy (VMAT): VMAT or Rapid-Arc is a newer technique of delivering IMRT. VMAT delivers highly precise sculpted 3-D therapeutic radiation dose in a single rotation of the gantry, varying the gantry speed and dose rate during delivery, in contrast to standard IMRT, which uses fixed gantry beams.(6)

Isodose Curves for a Planned VMAT



Stereotactic Radiotherapy: The word Stereotactic (Stereo+ taxis derived from Greek word meaning orientation in space)was first performed by Lars Leksell. He built the first isotope radiation machine, the Gamma knife in 1968.The stereotactic radiotherapy with LINAC (Linear accelerator) was first started in early 1980s by swedish Physicist Larsson. In India, All India Institute of Medical Sciences (AIIMS) started SRT on 27th May 1997. The differences between conventional and stereotactic radiotherapy is mentioned in Table 6.

A Stereotactic frame is attached to the patients head using Pins under local or General anesthesia following which an MRI and CT scan of the Brain is taken to determine the precise location of the tumor or angiography is done in case of AV malformation within the Brain. The various stereotactic frames used in stereotactic radiotherapy are Latinen frame, Gill Thomas cosman frame, Leksell frame, Hiedelberg frame, Body fix frame, Brown Robert well frame, Elekta Body frame. The diameter of the irradiated beam in stereotactic radiotherapy is regulated by circular collimator that varies in diameter between 1 and 35 mm and Micro multileaf collimators which have decreased leaf width (3.5 mm at centre, 4.5 mm intermediate leaves, 5.5 mm outside leaves) with maximum field size of 10 x 10 cm and hence optimal resolution between 1 and 3 mm, thereby provide greater PTV conformity and surrounding tissue sparing.

By performing multiple exposures and by readjusting the helmet and head position, different radiation shapes can be achieved.[15]

Uses

1. **Intracranial Tumors:** Stereotactic radiotherapy may be used for the treatment of Primary bone tumors such as Meningiomas, Pituitaryadenomas, Pinealtumors, Acousticneuromas, craniopharyngiomas and cancerous tumors that arise from brain cells such as Anaplastic astrocytomas or Glioblastomas. Tumors that travel to the brain from other parts of the body such as the cancer from the lung, Breast or skin may also be treated by this technique.
2. In the treatment of ablation of Arterio-venous malformations(AVM) of the Brain. The main aim is to thicken the blood vessels and create clots that helps in shrinkage of AV Malformations. Small AVMs (<3 cm) have an 80% success rate. Larger AVMs (>5cm) may require multiple stereotactic radiotherapy treatments.
3. In the treatment of Trigeminal neuralgia who have not experience any relief from medication and cannot be treated with surgery or any neuroablative therapy.
4. In the treatment of Ocular melanomas.
5. In the treatment of Parkinsons disease.

Radioembolisation: Radioembolization is based on the administration of ^{90}Y-loaded microspheres in the arterial vasculature of the liver. Currently, two types of microspheres are Food and Drug Administration–approved and commercially available: resin microspheres (SIR-spheres; Sir Tex Medical) and glass microspheres (Thera Spheres; BTG International Ltd.). Because of preferential arterial flow, the microspheres occlude small tumor arterioles, thus selectively irradiating tumors. An established treatment modality for chemoresistant, unresectable hepatic malignancies and also as a palliative therapy for primary and secondary hepatic malignancies.[12]

Auger Therapy (AT)

Auger therapy (AT) makes use of a very high dose of ionizing radiation in situ that provides molecular modifications at an atomic scale. AT differs from conventional radiation therapy in several aspects; it neither relies upon radioactive nuclei to cause cellular radiation damage at a cellular dimension, nor engages multiple external pencil-beams from different directions to zero-in to deliver a dose to the targeted area with reduced dose outside the targeted tissue/organ locations. Instead, the in situ delivery of a very high dose at the molecular level using AT aims for in situ molecular modifications involving molecular breakages and molecular re-arrangements such as a change of stacking structures as well as cellular metabolic functions related to the said molecule structures.[8]

Neutron Beam Therapy

Neutron Beam Therapy is used for surgically unresectable salivary gland tumors < 4 cm in diameter.[14]

Fast Neutron Therapy

Fast neutron therapy utilizes high energy neutrons typically between 50 and 70 MeV to treat cancer. Most fast neutron therapy beams are produced by reactors, cyclotrons by directing fast moving protons with 50.5Mev onto a Beryllium Target and linear accelerators. The Main advantage of Neutron Beam Therapy is its shorter treatment cycle. To kill the same number of cancerous cells, neutrons require one third the effective dose as protons.[9,14]

Fast neutron therapy has been applied successfully against salivary gland tumors like Adenoid cystic carcinomas, High Grade Gliomas and Osteosarcomas.[11]

Respiratory Gating

A four dimensional (4-D) radiotherapy technique in which the source of radiation moves as the tumor moves on respiration. It Permits breathing synchronized fluoroscopy on a treatment simulator which consists of a charge coupled Device (CCD), video camera attached to an infrared illuminator that tracks patients respiratory motion. It consists of retrospectively reconstruct CT slices at different phases of the breathing cycle allowing to measure residual movements and to choose the optimal patient's breathing phase where tumor movements are lower.[18]

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