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Changing Paradigm In Precision Radiation Technology(Title)

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Abstract(300 words)

There has been dramatic and rapid advancement in Radiation therapy (RT) in the past few decades. The list of advancement is endless ranging from CT imaging for planning, use of multileaf collimators, 3D Conformal treatment, Intensity modulated treatment (IMRT), Image guided treatment (IGRT). There has been innovations in physics dosimetry also. The result of these innovations is precision in dose delivery to the target and better sparing of critical organs. Precision radiotherapy targetsto deliver maximum possible dose to the tumour,at the same time sparing normal tissue. This has been achieved with the help of advances in technology involving newer imaging modalities, more powerful computers and software, and newer delivery systems.

Keywords – Radiotherapy, Conformal Radiation Oncology, IMRT, Tomotherapy, yberknife, IGRT.

Introduction

Advancement from Two to Three Dimensional Conformal Radiotherapy

Three Dimensional Conformal Radiotherapy (3DCRT)based on computed tomography (CT) imaging (which helps in volumetric delineation of the tumour and critical organ structures) has largely replaced Two Dimensional Radiotherapy (2D RT)which was based on plain X-ray imaging. Because of it better definitions of target volumes viz. gross tumour volume (GTV), clinical target volume (CTV), and planning target volume (PTV) is possible. Moreover, the development of MLC'S has provedto be an useful tool in for clinicians and physicists to conform the dose to above target volumes. Some organs are relatively more sensitive to radiation induced damage (like spinal cord, salivary glands, lungs, etc.) and these are specially considered during radiotherapy treatment planning. MLC’s based conformal shaping of the beam has made possible reduction in the amount of irradiated healthy tissue, and tissue outside the target volume receive lower dose through use of multiple beams. This treatment technique (known as 3DCRT)is a benchmark in evolution of precision therapy.

Intensity Modulated Radiotherapy (IMRT)

In IMRT irregular-shaped radiation fields are created that are not only conformal to the target volume but also avoid critical organs. IMRT uses inverse planning in which critical organs are given constraints to limit the dose. This is possible because ofvery advanced computer based treatment planning systems. IMRT involves: a) inverse planning software and b) multiple radiation beams which are computer-controlled intensity-modulated. Various machines are able to deliver IMRT like linear accelerators with static or dynamic multi-leaf collimators or tomotherapy machines using binary MLCs. Many studies have established that IMRT is superior to 3DCRT, mainly due to reduced dose to critical organs. So, IMRT has become treatment of choice for conformal radiation treatment.

Treatment planning algorithms

The smarter and faster algorithms have been developedwhich are capable of auto-contouring, smart segmentation and better dose calculation. They have both rigid and deformable registrations which play an important role in 3D and 4D planning. The commercially available TPS algorithms which compute volumetric doses are: pencil beam convolution (Eclipse PBC), analytical anisotropic algorithm (Eclipse AAA), AcurosXB (Eclipse AXB), FFT convolution (XiO Convolution), multigrid superposition (XiO Superposition), Collapsed cone convolution (Tomotherapy) and Monte Carlo photon (Monaco MC), etc.

Stereotactic Radiosurgery (SRS) / Stereotactic Radiotherapy (SRT)

Stereotactic radiotherapy/radiosurgery treatment are specifically useful for brain cases. Small field treatments with high dose per fraction are used in SRS/SRT. SpeciallySRS uses a single fraction high dose of around 12-18 Gy. For immobilization in SRS, stereotactic invasive frame is used. The accurate delivery of the SRS requires mechanically very precise machines. Contrary to it, non invasive specialized thermoplastic immobilization and fractionated treatment is used in SRT. For small fields with miniature MLCs or cones, the planning system commissioning need to be very accurate. With MLC, around 1-2 mm margin is used around PTV and same precision is expected from the machine. Special attention regarding quality assurance is neededfor DICOM transfer of the plan from treatment planning system to the machine. In order to increase localization, other imaging modalities MRI and Angiography are fused with CT. Nowadays, IGRT plays important role with use of frameless SRS/SRT.

Hypofractionated Radiotherapy/ Stereotactic Body Radiotherapy (SBRT)

In Stereotactic body radiation therapy (SBRT) ultra-high doses of radiation with few fractions (usually 4-8) to a target volume using very advanced technology is used.It has emerged as a novel treatment modality for cancer. SBRT is specially more important at two conditions—in oligometastaticdisease andin early primary cancer. It has shown good results in the treatment of early-stage non-small-cell lung cancer, renal-cell carcinoma, liver cancer, prostate cancer, and for treatment of oligometastases in the lung, liver, and spine. The use of a single high dose of radiation (like Gamma Knife technology in cases of brain malignancies) in place of multiple smaller doses can be especially beneficial for patients with painful spine metastasis.

Image Guided Radiotherapy (IGRT)

IGRT is a technique, where, geometric accuracy of radiation beam deliveryis improved through imaging being performed, prior to radiotherapy, within the treatment room itself. It is particularly useful for delivery of highly conformal dose through techniques such as IMRT, hypofractionated SRT, and charged particle therapy. The combination of accurate daily targeting of the tumor and highly conformal dose distribution, results in the dose escalation while decreasing the radiation related morbidity. IGRT has proved to have both geometric and dosimetric benefits in a variety of disease sites including the prostate, head and neck, lung and liver.

Techniques of IGRT: Previouslyskin and surface marks were used to direct the radiation beams.After that, portal imaging was used for this purpose. However, with the availability of 3D imaging, it is possible to have wide range of techniques that may be used for IGRT.

Cone-Beam Computed Tomography (CBCT): It is the most commonly used IGRT technique in which onboard kilovoltage systems is currently available with the linear accelerators. Through improved flat-panel technology, CBCT has got superior image quality.Plus radiographic or fluoroscopic monitoring throughout the treatment process is also possible. Usually, many projections over the entire volume of interest is required in cone beam CT in each projection. The 2D projections are reconstructed into a 3D volume analogous using the reconstruction algorithm to the CT planning dataset.

Megavoltage Cone Beam CT (MVCT): In this technique megavoltage beam of accelerator is usedto get images just before treatment. Earlier accelerator models had been usingit and now it is used in Tomotherapy, in which 3MV energy is used to get MV images.

Ultrasound: US is specifically useful for soft tissue visualization like in breast and prostate cancer patients.

Optical tracking: In Optical tracking a camera is used to define information related to position of objects within its inherent coordinate system through a subset of the electromagnetic spectrum of wavelengths ranging from ultra-violet, visible, to infrared light. Optically tracked tools help to define the positions of patient reference set-up points and then they are compared to their location within the planning CT coordinate system. These two sets of coordinates are used for computation based on least-squares methodology to determine a treatment couch translation that will lead to the alignment of the patient's planned isocenter with that of the treatment set up.

MRI based IGRT systems: A patient's internal anatomy can be seen in real-time MRI-guided radiation therapy using continual soft-tissue imaging. It is especially useful when the tumor is movingand allows to keep the radiation beams on target during treatment.

Electromagnetic transponders: Electromagnetic transponder not only have the same clinical function as CBCT or kV X-ray, but also provide a more temporally continuous analysis of setup error which is analogous to that of the opticaltracking strategies.

Correction Strategies:To determine the optimum patient position and beam structure, two basic correction strategies used: on-line and off-line mode. Both have different function in the clinical setting, and have their own advantages. To get the optimum result, both strategies are employed in combination. Often, on-line strategies are used during the first radiation fraction and subsequent adjustments off-line during check film rounds.

On-line: The On-line strategy makes adjustment to patient and beam position during the treatment process, based on continuously updated information throughout the procedure. The advantage of this strategy is a reduction in both systematic and random errors. Gold markers are implanted into the prostate to provide a surrogate position of the gland. Prior to each day's treatment, portal imaging system results are returned.

Off-line: The Off-line strategy determines the best patient position through accumulated data gathered during treatment sessions, almost always initial treatments. However, the use of off-line strategies does reduce the risk of systematic error. The risk of random error may still persist.

Motion Management: Radiotherapy in the presence of intra-fraction organ motion causes blurring of the static dose distribution over the path of the motion. This displacement results in a deviation between the intended and delivered dose distributions. There are various methods to account for respiratory motion in radiotherapy. Slow CT acquisition, Inhale and exhale breath-hold CT, Four dimensional or respiration-correlated CT.

Respiratory gating methods: The motion can be managed by means of gated delivery. Respiratory gating involves the administration of radiation, during both imaging and treatment delivery within a particular portion of the patient's breathing cycle. The position and width of the gate within a respiratory cycle are determined by monitoring the patient's respiratory motion, using either an external respiration signal or internal fiducial markers. Since the beam is not continuously delivered, gated procedures are longer than non-gated procedures. Gating using an external respiratory signal This device uses external markers for gating the radiation beam however, it has x-ray imaging capabilities for determining the internal anatomy position and for verifyingthe reproducibility of the internal anatomy during treatment.

Gating using internal fiducial markers: The fiducials are implanted in or near the tumour using a percutaneous or bronchoscopic implanting technique. Fiducial position is tracked in all three dimensions several times a second using a pair of stereotactic kilovoltage x-ray imaging systems in combination with automatic detection software. When each fiducial is within an acceptable range of the desired (simulation) position for both stereotactic x-ray cameras, the linear accelerator delivers radiation.

Gated IMRT: In this method, an arc (conventional gantry system) or continuous rotation (ring gantry system) is repeated while gating the accelerator until the correct number of pulses is delivered from each beam angle. The couch is stationary until all beam pulses are delivered, then indexed to the next position. The same technique can also be used with helical delivery: the treatment helix would need to be repeated until all of the pulses for each angle had been delivered. The ability to quickly start and stop gantry rotation or patient breathing irregularity and other uncertainties are still to be resolved.

Volumetric Modulated Arc Therapy (VMAT)

Despite the obvious benefits of IMRT, there are still some disadvantages. IMRT plans use a larger number of monitor units compared with conventional plans leading to an increase in the amount of low dose radiation to the rest of the body. The increase in MU and subsequent increase in low dose radiation has led to concerns of increased risk of secondary radiation-induced malignancies, which is of particular relevance in paediatric patients or patients with long life expectancies. VMAT is a new radiation technique that combines the ability to achieve highly conformal dose distributions with highly efficient treatment delivery. VMAT allowed the simultaneous variation of three parameters during treatment delivery, i.e. gantry rotation speed, treatment aperture shape via movement of MLC leaves and dose rate. The basic concept of VMAT is the delivery of radiation from a continuous rotation of the radiation source and allows the patient to be treated from a full 360° beam angle.

Helical Tomotherapy (HT)

As a modality for delivering rotational therapy, HT offers dosimetric advantages by combining a continuously rotating gantry with a binary multileaf collimator. HT, delivers intensity-modulated fan beams in a helical pattern using binary multileaf collimator leaves while the couch is translated through the gantry. For precise irradiation and possible treatment adaptation, the fully integrated on-board image-guidance system provides online volumetric images of patient anatomy using 3.5-MV x-ray beams and the xenon computed tomography detectors system.

CyberKnife

The CyberKnife(CK) system uses the combination of a robotics and image guidance to deliver concentrated and accurate beams of radiation to intracranial and extracranial targets, many of which are inoperable with sub- millimeter accuracy. The robotic arm is highly flexible, allowing access to tumors in difficult-to-reach locations. The CyberKnife, unlike other stereotactic radiosurgery systems, is able to locate and track the position of the tumor without the use of an invasive stereotactic head frame or stereotactic body frame. The system compensates for the patient's respirations and movement during treatment, constantly ensuring accurate targeting for the delivery of radiation beams.

Flattening Filter Free (FFF) beams

Flattening Filter Free (FFF) X-ray beam has been in clinical use for quite some time. However, not until recently, these FFF beams are used in limited, small field sizes, for example, in Tomotherapy and CyberKnife machines, However, FFF X-ray beams in conventional linacs have up to 40 X 40 cm field sizes for both 6 and 10 MV X-rays. For large treatment fields, the dose uniformity within an irradiated treatment field will need to be modulated by MLC movements to cut down the higher beam intensity near the central portion of the FFF X-ray beam. Thus, larger MUs are required compared with a conventional (flattened) X-ray beam. Or, MLC movements (IMRT) are now being used to "flatten" the FFF X-rays to provide dose uniformity within those large PTVs. The high dose rates from the FFF X-rays are now being off-set by the larger MUs requirements. Therefore, FFF X-rays can bring clinical advantages over conventional X-rays when used with small field sizes, such as in SBRT and/or SRS applications. The primary purpose of the FFF X-rays is to provide much higher dose rates available for treatments. Commercially available FFF dose rates are 1400 MU/minute for 6 MV X-rays and 2400 MU/ minutes for 10 MV X-rays. Higher dose rates have definite clinical benefits in organ motion management. In SRS or SBRT treatments, large MUs are often required and FFF X-ray beams can deliver these large MUs in much shorter"beam-on" time. With shorten treatment time, these FFF X-rays improve patient comfort and dose delivery accuracy. FFF X-ray beams may become one of the necessary equipment configurations for SBRT and/or SRS treatments, in the future.

Brachytherapy

The brachytherapy has evolved tremendously over past few decades. With development of various manual and after-loaded applicators and different Radium substitutes like Cs-137, Co-60, Ir-192 large potential of brachytherapy were evident. High Dose Rate (HDR) remote after-loading coupled with advances in treatment planning systems has ensured well defined protocols and methods for brachytherapy dose analysis. Recently use of imaging techniques for 3-D data acquisition for brachytherapy application, contouring and treatment planning has made significant contribution for precise brachytherapy dose delivery. Conventional Simulator radiographs had been basic tools for TPS to input brachytherapy applicator & source data. Recently CT-Simulator has been used to input the applicator data and 3-D reconstruction through direct images transfer by DICOM network. The CT & MRI are also being used for contouring various volumes like target & clinical organs which coupled with 3-D planningalgorithms gives direct doses to critical organs with volume analysis. In case of intracavitary application MRI gives better visualization of soft tissue so that we can more clearly see the critical organs like bladder & rectum. American Brachytherapy Society (ABS) Image guided Brachytherapy working group (IGBWG) have provided guidelines in reporting the image based brachytherapy, which recommends the prescription of dose to a volume rather than a point. Later GEC ESTRO published guidelines for the practice and reporting of image based ICA, which has been widely accepted so that a unified approach is formed among the users of image based brachytherapy.

Hadron Therapy

The new and exciting development is use hadrons such as protons and heavy ions (carbon) for radiotherapy. Proton beam therapy has the advantage that the proton beam gives up its maximum energy at end of its range in a small area known as the Bragg peak. This has advantages in terms of normal tissue sparing, better dose homogeneity. The Carbon ions have advantage of greater Relative Biological Effectiveness (RBE), which is very important characteristics. Intensity modulated proton therapy (IMPT) allows for the modulation of the fluence and the position of the Bragg peak, permitting three-dimensional dose distributions.

Dosimetry and Quality Assurance

The advances in physics dosimetry include, advance softwares in radiation field analyzers, detector arrays (ion chamber based and diode based), in-vivo dosimetry systems (diodes, MOSFETs, Gel dosimeters, optically stimulated luminescence dosimeters (OSLD) etc). The developments in film dosimetry led to more recent and instant readout from the Radiochromic films. Electronic portal imaging has played its important role in IGRT and dosimetry as well. EPID based dosimetry is used for patient specific dosimetry in IMRT and volumetric modulated arcs.

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