RECENT TREATMENT ADVANCEMENTS IN RADIATION THERAPY

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ABSTRACT

Radiation therapy is one of the fields of medicine that have seen a lot of technological advancements in the last few decades. The era of 2D treatments have evolved significantly to 3D and image guided treatment plannings and delivery. This recent developments have allowed us to deliver a highly conformal dose to the tumor while sparing the surrounding critical structures. Three-dimensional conformal radiotherapy (3DCRT), intensity-modulated radiotherapy (IMRT), volumetric-modulated arc therapy (VMAT), stereotactic body radiation therapy (SBRT) and image-guided radiation therapy (IGRT) have significantly improved target delineation and provided an accurate dose delivery to the target volumes. In addition, adaptive and artificial intelligence (AI) based IGRT have facilitated modification in the treatment plans in the best possible way even during treatment and augmented treatment planning with a flexible workflow respectively. Recently, particle beam therapy have come up with promising results but not without limitations which limits its widespread use. Major impact of these recent advances in radiation technology has been towards reduction of treatment toxicity, improvement in treatment-related morbidity and quality of life. Further research by use of these newer technologies are necessary for optimal utilization and effective management of cancers.

Keywords – 3DCRT, IMRT, VMAT, SBRT, IGRT, particle beam therapy

I . INTRODUCTION

Radiation therapy is a type of treatment modality used in treatment of cancer in which ionizing radiation (X-rays, gamma rays etc.) are used to deliver a tumoricidal dose to the tumor. A significant problem in the use of radiation for treatment lies in its delivery to tumors that are in the vicinity of normal tissues which limits a tumoricidal dose delivery to the tumor [1]. For this very reason, a lot of technological advancements in this field have come up in the last few decades that allows us to deliver a highly conformal dose to the tumor while sparing the nearby organs at risk (OARs). Radiation therapy can be delivered in the form of external beam radiation therapy (EBRT) or teletherapy, where the radiation source is placed outside the patient's body, or internal beam radiation therapy or Brachytherapy using internal radiation sources [2].

II . 3DCRT

3DCRT is a modified form of 2D EBRT that incorporates individualised 3D treatment planning based on 3D anatomic information obtained from imaging. Most common imaging modalities used are CT scan, MRI or PET images. Compared to 2D RT, 3DCRT conforms a high dose radiation delivery to the tumor areas while minimizing radiation to the normal tissues. 3DCRT is most commomly used for the treatment of brain tumors, head and neck cancers, breast cancer, gastrointestinal cancer, lung cancer, prostate, bladder and gynecologic malignancies. [3]. 3DCRT has been found to produce similar clinical outcomes (relapse and death) but associated with an increase in the frequency of toxicity compared to IMRT in the treatment of oropharyngeal cancers [4]. However there were no differences in the toxicity between 3DCRT and IMRT in the treatment of esophageal cancers although IMRT reported better survival outcomes [5].

3DCRT requires stringent evaluation in the treatment planning and dose optimization to achieve a highly conformal dose that will maximize the tumor control while minimizing normal tissue toxicity.

III . IMRT

IMRT is an advanced extension of 3D CRT. In IMRT, non-uniform beam intensities from multiple fields are delivered to a highly conformal target volume that maximizes an optimal dose distribution to the tumor while minimizing dose to the surrounding OARs [6]. Conventional treatment planning is forward planned where the beam parameters and beam configurations are first defined and the treatment plan is optimized to get the desired dose distribution. In contrast, IMRT incorporates the principle of 'inverse planning' in which tumor dose and normal tissue dose limits are first specified and by means of a computerized treatment planning, beam parameters and intensities are modified to get the best desired plan [7].

As the name suggests, intensity modulation allows delivery of different levels of dose to different parts of the tumor which is of particular value in tumors located near critical structures such that IMRT can maximize normal tissue sparing. But the use of multiple beams of different intensities, a larger volume of normal tissues are exposed to low radiation doses and is expected to increase the risk of development of second malignancies although the risk is not as high as theoretically expected in cases of adults. However, relative risk in children treated with this technique may be higher [8]. IMRT is used in the treatment of head and neck cancers, breast cancers, gastrointestinal and prostate cancers. In the treatment of esophageal cancer, IMRT reported an improved overall survival (OS) but without any significant difference in the incidence of radiation toxicities [9]. In head and neck cancers, compared to 3DCRT, IMRT significantly reduces the incidence of moderate to severe xerostomia and submucous fibrosis without significant differences in 10 year disease related outcomes for locoregional control of disease [10]. IMRT is generally preferred over 3DCRT in the treatment of prostate cancer for dose escalation (>70 Gy) which is dose limiting to bladder and rectum. This dose escalation to the tumor target while sparing bladder and rectum effectively translates to an increase in disease specific survival [11].

IMRT using simultaneous integrated boost (SIB) approach allows simultaneous delivery of different levels of dose to different target volumes within a single fraction as a form of accelerated fractionation.

IV. VMAT

VMAT was introduced in 2007 and is increasingly being utilized to give simultaneous highly conformal dose distribution by continuous modulation of field shaping multileaf collimators (MLCs). Radiation is delivered by means of a continuously rotating arc, either single or multi arc treatment and during each rotation, the beam is continuously modulated by the MLCs and the treatment is further optimized by regulating the dose rate. Compared to IMRT, VMAT significantly improved dosimetric treatment efficiency and reduced the treatment time.VMAT is being increasingly used for treatment of head and neck cancers, breast cancer, lung cancers, genitourinary and gynaecologic malignancies. in head and neck cancers, IMRT and VMAT have shown comparable tumor control outcomes and survival. However, in breast cancer, although VMAT reported an enhanced dosimetric coverage and conformity, it increases low dose baths to heart and lungs, which possibly explains the preference of tangential IMRT fields [12].

V. SBRT

SBRT is a radiation procedure that delivers high doses of radiation per fraction in a hypofractionated manner to small targets (maximum cross-sectional diameter of 5 cm or less) . As high dose radiation are delivered in a short period of time, SBRT requires a precise delivery of highly conformal dose to the target volume while minimizing radiation exposure to the surrounding OARs through steep dose gradients. SBRT is typically used to treat early-stage lung cancer, hepatocellular carcinoma (HCC),, renal cell carcinoma, prostate cancer and metastasis (lung, liver or spine). In early- stage NSCLC, OS rates associated with SBRT were similar to those observed with surgery without increasing toxicity [13]. In HCC, SBRT offer advantage in patients with deranged liver functions who may not tolerate transarterial chemoembolization (TACE) or radiofrequency ablation (RFA) procedures [14].

Cyberknife is one of several available SBRT/ stereotactic radiosurgery (SRS) systems that delivers highly conformal radiation using a small linear accelerator mounted on a robotic arm. This robotic arm moves around the patient, localizes the target and adjusts the radiation precisely to the target even when the target moves.

VI. IGRT

IGRT is a radiation technique that uses image guidance from treatment planning throughout the treatment procedure to improve the accuracy and precision of the treatment. Image guidance improves geometrical accuracy by adjusting the inter- and intra-fraction motion. Target localization is done for each treatment fraction by several methods including implanted fiducial markers or by imaging using fluoroscopy, X-ray imaging , USG, KV or MV CT or MRI. Cone beam CT (CBCT) is one of the most widely used IGRT technique. Newer techniques like 4D gating and real-time-tumor tracking systems help in management of organ motion [15]. In addition to improving the accuracy and precision of treatment, it also helps track the shape and size of the tumor volume throughput the treatment (tumor regression) so that treatment plans can be modified accordingly to protect OARs. It is being widely used for treatment of head and neck cancers, lung cancer, and prostate cancers.

A. Adaptive IGRT

Adaptive RT has been implemented to further refine the treatment target volumes based on anatomical information provided by IGRT acquired over the course of treatment. Adaptive RT enables the treatment plan to be modified or adapted to account for changes in the anatomy (tumor response, weight loss,) and also modification of the treatment strategy based on early tumor response (addition of CT). There has been several advances in the tools needed for adaptive RT including autosegmentation, deformable image regiatration (DIR) and automated planning. Autosegmentation of CBCT allows assessment of daily dose and adaptation of treatment based on dosimetric information. DIR allow accumulation of dose over the course of treatment and adaptation based on accumulated dose and calculation of final delivered dose. Another emerging sophistication in adaptive RT is additional evaluation of functional changes in the patient and automated planning systems.

Development/ emergence of integrated MRI-guided radiation therapy systems makes it possible to adapt the treatment plan using MRI. In addition to providing excellent soft tissue visualization, it also helps identify movements without delivering any additional dose of radiation [16]

B. AI-based IGRT

AI has been an ongoing topic of interest nowadays. AI based approaches has seen tremendous development recently with major contribution from advancements in deep learning approaches. Focus on AI based approaches has helped to augment better target localization and motion management but with a simplified and flexible workflow. AI based IGRT algorithms has provided more accurate tumor localization and better tracking of tumor changes thereby eliminating fiducial implantation requirements. It also enhances the probability that the prescribed dose is actually delivered to the target volume which increases probability of tumor control. A limitation of AI based approach is that they are data driven and relies on training data distribution. The predictive model yields results based on the training data distribution. AI algorithms can also simplify commissioning procedures and reduce the required manpower. But before widespread commercial use AI algorithms needs continuous review, surveillance and monitoring [17].

VII. Particle therapy

Particle therapy using proton and cardon ions have recently come up with promising results in radiation oncology. Proton therapy offers a substantial clinical advantage compared with conventional radiation because of its unique depth dose characteristic (Bragg peak) where there is a sharp fall-off in dose distribution outside the target. This allows maximal normal tissue sparing. Proton therapy has found particular use in younger patients and children in whom integral dose reduction is of paramount importance. Particle beam therapy has found clinical use in tumors near sensitive organs like skull base tumors (chordoma, chordosarcoma), meningiomas, spinal tumors, head and neck cancers, lung cancer, genitourinary cancers etc. Carbon ion therapy (CIRT) has a higher radiobiological effectiveness compared to protons and photons but is limited to only a few centres worldwide. CIRT has higher biologic effectiveness and is particularly useful in relatively radioresistant tumors like sarcomas, melanomas, glioblastomas and RCCs [18].Despite evidence of promising results with particle therapy, its high cost and logistic requirements are limitations for its widespread use [19].

VIII. Conclusion

Radiation therapy is a rapidly evolving field and significant advancements have been made in the last few decades that allow precise radiation delivery. Major impact of modern advances of radiation technology has been towards reduction of treatment toxicity, improvement in treatment related morbidity and quality of life. Further research by use of these newer technologies are necessary for optimal utilization and effective management of cancers.

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