Review

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Unravelling the landscape of image-guided radiotherapy: a comprehensive overview

Abstract

Image-guided radiation therapy (IGRT) is essential to modern radiation therapy. It ensures precise radiation delivery to tumor targets, sparing healthy cells and tissues. IGRT techniques upgraded themselves to a level where the technology allows for tracking the real-time image of the tumor during treatment and significantly improves the accuracy and precision of radiation therapy. By integrating advanced imaging modalities such as cone beam computed tomography, magnetic resonance imaging, and positron emission tomography, clinicians can visualize the tumor and surrounding tissues in three dimensions. It also can account for intrafraction variations, such as organ motion and changes in tumor size or shape, which can occur throughout treatment. Using IGRT techniques, clinicians can adapt the treatment plan in real-time to ensure optimal radiation delivery to the tumor while sparing healthy tissues. Moreover, IGRT is crucial in managing systematic and random errors during radiation therapy. These errors could lead to underdosing of the tumor or overdosing of healthy tissues, compromising treatment efficacy and patient safety. To mitigate these errors, imaging and frequent verification of the treatment are necessary throughout the treatment. This review paper offers a comprehensive summary of IGRT, its diverse modalities, clinical integration, quality assurance tests performed, and the role of artificial intelligence (AI) in IGRT.

Palliat Med Pract 2024; 18, 4: 228–233

Keywords: image-guided radiation therapy, cone beam computed tomography, surface-guided radiation therapy, magnetic resonance linear accelerator, artificial intelligence

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Palliative Medicine in Practice 2024; 18, 4, 228–233

DOI: 10.5603/pmp.100218

Received: 12.04.2024 Accepted: 10.06.2024 Early publication date: 13.06.2024

Introduction

Accurate determination of the target volumes of radiotherapy is of utmost importance for improving local tumor control and minimizing toxicity. To achieve this, the set-up of a patient's anatomy concerning the treatment beams is used to enhance the accuracy of the set-up from the point of systematic and random error. Anisotropic margins expand the gross tumor volume (GTV) to a clinical target volume (CTV) [1]. The CTV is then enclosed by a planning target volume (PTV), which adds an extra margin to the CTV to consider positional and delineation uncertainties [2]. However, it is to be noted that, to manage less toxicity, smaller margins may underdose the CTV [3]. Therefore, advanced imaging techniques during image-guided radiation therapy (IGRT) are essential to enhance the accuracy and precision of treatment delivery.

Image-guided radiation therapy techniques, as is known, allow the user to confirm the set-up and match the target before treating the patient with high-energy radiation to deliver the dose precisely. These treatment modalities are especially beneficial in cases where the tumor is located near critical organs or structures, as they can shape the radiation beam to match the desired target contours of the tumor, minimizing radiation exposure to nearby sensitive tissues.

Several techniques are used for position verification, such as megavoltage electronic portal imaging device (MV-EPID) and megavoltage cone beam computed tomography (MV-CBCT). Imaging based on kilovoltage cone-beam computed tomography (kV-CBCT) is preferred as it provides additional anatomical information compared to EPID imaging [4]. Nowadays, linear accelerators (LINAC) have imaging devices that produce high-quality images, simplifying the set-up verification process. The set-up error is determined using sophisticated software by comparing the image taken immediately before or after the treatment session with the planned image [5].

Image-guided radiation therapy rationale and hypothesis

"Increasing the precision and accuracy of radiation delivery will reduce toxicity with potential for dose escalation and improve tumor control" is the basic hypothesis [6]. Hence, to significantly reduce set-up error, it is essential to use high-precision techniques to ensure that the daily anatomy and position of the patient match or surpass the treatment plan at every stage. In current clinical practice, verification is primarily employed to guide the radiation beam to a predefined limit by repositioning the patient correctly and eliminating the misalignment. By imaging before treatment, set-up errors and uncertainties in positioning can be reduced. Images acquired in between or along with the treatment provide information on positional changes due to organ motion during the treatment. This can increase confidence in the effectiveness of treatment and avoid potential mistargeting incidents [7].

The recent advancements in imaging and treatment delivery provide accurate tumor localization and repositioning of patients. The concept of IGRT has dramatically improved the management of geometric uncertainties, thus providing precise information on the patient and tumor position, allowing for verification of planned and actual treatment geometry, resulting in improved dose delivery. However, it must be addressed that IGRT delivers an extra dose in addition to the treatment dose, though it helps to reduce toxicity and allows improved tumor control [8].

IGRT is an imaging tool used in radiotherapy to correct geometrical mismatch, delineate target volumes and organ-at-risk (OARs), determine biological attributes, *etc.* It is commonly known as image-based radiotherapy, more focused on imaging with radiation treatment, improving the precision of radiotherapy for advanced techniques like 3D-CRT, IMRT, and stereotactic radiosurgery/radiotherapy (SRS/SRT) [9].

Definition and different IGRT modalities

IGRT is a radiotherapy procedure that uses image guidance in various stages [10]. It is the central pillar in advancing radiotherapy, and imaging information has been adopted and integrated to facilitate various treatment modalities. The following are the different technologies used in radiation therapy.

Planar

Two-dimensional (2D) images, both kV and MV, generated from modern accelerators, are produced by two sets of imaging systems. The kV image is obtained from a conventional X-ray tube mounted orthogonally to the MV radiation gantry and opposes a flat panel detector. In contrast, the second detector that opposes the gantry, the so-called electronic portable imaging device (EPID), to obtain 2D MV images is the other type. The flat-panel detectors are matrices of solid-state amorphous silicon photodiodes. KV-KV, MV-MV, or KV-MV image acquisition methods acquire the images [11]. EPID is generally used when image quality is not a factor. An EPID image in the prostate may be an example where corrections are made based on the bony anatomy and radio-opaque fiducials [12].

Another type of room-mounted planar imaging system is a two-unit system. Two units from different directions define the target. Such a system uses fiducial markers, bony anatomy, or direct visualization for accuracy and localization [13]. Notably, ExacTrac [14], Cyberknife [15], and Vero [16] are some examples of such systems.

The application of a planar imaging system offers multiple picture-matching options. After converting the 3D CT simulation image to a 2D (digital radiographic reconstruction) image, the matching X-ray images acquired before, during, or after the treatment are compared with these DRRs to determine their maximum resemblance to the relevant X–ray images. The patient is then set up according to the manual match and DRR to eliminate rotational errors. Finally, the algorithm decides the region of interest to fuse and filters out structures that provide more ambiguity to the fused image [14].

Cone beam computed tomography system

The imaging system's flat panels produce orthogonal planar projections, are suitable for fluoroscopy, and can complement 3D and 4D images. CBCT plays a vital role in IGRT by providing high-quality, three-dimensional imaging of the treatment area. CBCT allows for accurate visualization of the target volume and surrounding structures, enabling precise alignment and positioning of the patient before each treatment session. This technology helps detect anatomical changes, such as tumor size and shape, bladder and rectum fillings, and allows for immediate adjustments to the treatment plan, ensuring optimal dose delivery [17].

Radiotherapy planning done in a three-dimensional platform is a new concept and is growing rapidly, although the techniques of CBCT existed long ago. Besides verifying the patient's position in 3D, CBCT has potential benefits for dose verification and adaptive planning in the future. CBCT systems are available in the MV and kV range, and the choice depends on several factors, including the extra dose the patient receives depending on the frequency of its use [17].

Elekta's X–ray volume imaging (XVI) and Varian's On-Board Imager (OBI) are the kV–CBCT imagers mounted orthogonally to the MV treatment beam, used as an IGRT system that uses a kV X-ray source composed of an amorphous silicon flat panel detector. Amorphous silicon flat-panel detectors are well suited to mount on the linear accelerator because of their low optical scattering and high-resolution properties [18].

Fan beam

Helical tomotherapy can best explain fan beam radiotherapy. The basic idea of helical tomotherapy is to integrate a linear accelerator or other radiation-emitting device into a CT-like ring gantry configuration that can be used for both imaging and delivering therapeutic radiation. The machine is designed to treat the patient in slices, and the couch moves in the cranio-caudal direction of a CT [19]. The treatment unit includes a radiation detector system at the beam exit side, which is generally a Xenon-filled ionization chamber used for easy and fast acquisition of MVCT scans of the patient in the treatment position [20]. The main advantage of tomotherapy is that it uses the same beam for treatment and imaging. The image acquired from a fan beam CT has an advantage in its properties and has better image qualities with low artifacts and noise. It has a better spatial and contrast resolution than CBCT [21].

Non-ionizing visualization systems

All the imaging modalities mentioned above use ionizing radiation for imaging purposes. Such modalities incorporate an extra dose to the treatment dose. Imaging modalities like magnetic resonance imaging (MRI), ultrasonography, and surface-guided radiation therapy (SGRT) can eliminate these excess doses because they do not contribute to the treatment plan and use non-ionizing radiation, a non-harmful, real-time imaging technology [22].

In situations where the visualization of soft tissue was required, ultrasonography was found to be a handy and attractive tool for IGRT [24]. Imaging modalities like kV or MV X-ray imaging provide excellent localization for bony structures but lack adequate soft-tissue contrast to visualize organs such as the prostate. Ultrasonography imaging is a less expensive, real-time imaging modality that enables the visualization of soft tissue structures and can be used as a complementary imaging modality to other imaging systems. Ultrasonography uses high-frequency sound waves with a frequency above the audible level of human hearing; used for imaging in diagnostic radiology for a long time and is considered one of the safest methods in diagnostic imaging [18].

Magnetic resonance imaging is another non-ionizing visualizing tool used in IGRT. This technology has recently integrated with a linear accelerator and has been categorized as MR-LINAC. It can acquire an image the same as a kV-CBCT. The main advantage of MR-guided over kV-CBCT-guided is that it has better visualization ability of soft tissue and can help improve target localization and organ at risk (OAR) delineation [23] for several sites, such as the brain, prostate, and pelvis, thus reducing the possibility of geographical miss and enabling dose escalation [24]. MR images are often registered with CT images for treatment planning in radiotherapy to provide precise delineation of target volumes and OARs due to their superior soft-tissue contrast [25]. Changes in the shape and size of the tumor during the treatment can be further visualized using real-time tracking. Elekta Unity and ViewRay MRIdian are two examples of MRI LINAC used [26]. These two units facilitate rapid adaptive planning and treatment delivery by integrating MRI and LINAC.

Optical surface scanning or SGRT is another non-ionizing image-guided radiotherapy tool effective in intra-fractional motion, respiratory gating techniques, and patient positioning with the help of a light projector and a few camera units to register the real-time 3D surface of the patient [22]. It is an effective tool for patient positioning as it considerably reduces overall set-up time, and no radiation dose is involved [27]. Three systems are commercially available for surface guidance and to enhance system accuracy. The AlignRT (VisionRT) SGRT system, The Catalyst/Sentinel system of C-RAD, and the Identify system now acquired by Varian are in clinical use. These SGRT systems use multiple structured light projections, which are detected by cameras placed in different positions to obtain an image of the patient's surface [28].

Image-guided radiation therapy workflow

The set-up deviation is calculated by comparing and correcting the positional mismatch of the treatment with the reference image acquired at the time of simulation with the help of the image. It accounts for both random and systematic deviations. Systematic deviations refer to the differences between the planned set-up on the simulator and the actual set-up during treatment. These deviations may occur due to daily variations in the movement of skin marks about bones. On the other hand, random errors can result from various sources, including the simulator itself. To minimize geometric uncertainties, IGRT helps to adjust the patient's position or modifies the treatment plan based on anatomical changes. The image of the patient acquired immediately before a treatment offers opportunities for a more precise set-up [29].

IGRT follows two methods for image registration, *i.e.* online and offline. Online methods are known to be more effective than offline methods in reducing geometric uncertainties, but they require more work, longer treatment times, and higher radiation doses. Online approaches are generally preferred for cases where the high-dose area is close to critical anatomical structures, for dose-escalation programs, or hypo-fractionated treatments. However, recent studies have shown that offline procedures can achieve similar effectiveness [30]. Consequently, the radiation oncologist in charge of the patient must evaluate each case individually and determine the best method for correcting the target area. Regardless of the chosen method, a tolerance margin needs to be established for each disease and target location, considering factors such as the priority of PTV coverage, the importance of organs at risk, organ motion, and patient characteristics [5]. Patient immobilization and positioning in IGRT are essential factors in its success. Various immobilization devices, such as thermoplastic masks or customized body VacLok, ensure patients are in the correct position during treatment. These devices restrict the patient's movement and ensure optimal target volume throughout treatment.

Quality assurance

The introduction of the IGRT system in radiotherapy has improved the accuracy of treatment delivery. However, the components used in IGRT also ensure safety, geometric accuracy, and image quality. Thus, a rigorous quality assurance (QA) program should be conducted before clinical implementation to provide confidence that the imaging system is operating within acceptable limits.

Advanced IGRT technologies need to perform a QA program to ensure the system's performance is established at the time of commissioning [31]. The QA program concerning IGRT has three major components, *viz.* safety, geometry, and image quality, and these three components are applicable for radiographic and tomographic image guidance. The evaluation of geometric accuracy for repositioning patients before, during, or after treatment is the major test in IGRT [32]. Quality assurance of IGRT includes geometric accuracy tests, image quality checks, scale and distance accuracy, low contrast resolution, spatial resolution, uniformity and noise, image dose, accuracy in CT numbers, image registration, accuracy in remote control couches, and daily operational issues [33].

Artificial intelligence in image-guided radiation therapy

Artificial intelligence (AI) has the potential to optimize radiotherapeutic procedures, resulting in an improvement in the quality, safety, accuracy, and timeliness of radiotherapy. Recently, AI can contour organs and targets previously done by the oncologist manually, making their work easy. With the help of AI, the treatment target accuracy and minimal harm to the normal tissue have become easier, as well as quality assurance [34]. AI-based IGRT techniques can monitor tumor motion, reduce treatment uncertainty, and improve precision. Advanced techniques like intensity-modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT), and stereotactic ablative radiotherapy (SABR) require comparatively more precision; AI in IGRT can ensure a precise distribution of the radiation dose around the tumor volume, detects the change in position or shrinking of the tumor, thereby creating adaptive plans, minimizing the amount of healthy tissue irradiated. Advancements and upgrades in machine and deep learning have significantly impacted radiotherapy workflow and have the potential to provide high–quality treatment for cancer patients, which has grown exponentially in recent years [35].

Varian Ethos is an example that utilizes an intelligent optimization engine (IOE) designed for plan automation. This system adjusts radiotherapy treatment plans daily according to the anatomical changes. The system creates an adapted plan using artificial intelligence, thus speeding up the workflow [36]. The new feature IOE and its innovative workflow in generating the reference plan is designed to streamline the treatment planning process by automating the insertion of optimization parameters based on the physician's planning directives. It supervises modifying inputted goals and priority ranks before the final plan generation. The physicians or physicists are not able to control the optimizer. Instead, they set "clinical goals" to guide the IOE indirectly. It was found that utilizing an advanced AI-guided approach produces superior plan quality in the Varian Ethos IOE system [37].

Conclusions

The evolution of radiotherapy is advancing day by day to a new scenario, and IGRT plays an essential role in this field. IGRT is a vital tool in radiotherapy for verification and delivering a more conformal dose to the target. The technological advancements in IGRT have improved the delivery by integrating different imaging modalities in the treatment room to minimize the geometrical uncertainties. This tool verifies the consistency of planned and actual geometry, resulting in better dose administration. One of the issues with the IGRT is the extra dose a patient receives for imaging. On the other hand, however, more precision and accuracy of radiation administration are predicted to reduce toxicity.

Article information and declarations

Acknowledgments

The author acknowledges all the staff of the Department of Radiation Oncology, AIIMS Guwahati, for their support and guidance.

Author contributions

Conception, design, critical review — GS; manuscript preparation, literature review — HK; literature review, supervision — PPM; manuscript preparation, data collection — RK; design, manuscript preparation, data collection, literature review — DL.

Conflict of interest

The authors declare no conflicts of interest.

Funding

None.

Supplementary material

None.

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