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Developments in radiation therapy: image guided radiation therapy

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Abstract

Radiation therapy has been used in the management of cancer for more than a century. Its goal is to deliver a high therapeutic dose of radiation to a tumour whilst sparing healthy normal tissue. In order to achieve this continuous developments and innovations in the planning and delivery of radiation therapy treatment are made. Technological advances in radiation therapy have resulted in significant improvement in the planning and delivery of this cancer treatment, yielding decreased normal tissue toxicity, increased tumour control and good patient quality of life.

One of the arguably greatest developments in radiation therapy is the introduction of image guided radiation therapy (IGRT), which allows for imaging in the radiation therapy treatment room with adjustments per individual patient to account for geometric deviations. Reviewed literature from January 2012 to August 2016 was sourced to discuss and critically evaluate the different technological developments in radiation therapy.

Keywords imaging, developments, electronic portal imaging device (EPID), database searching, hand searching, Boolean search

INTRODUCTION

Radiation therapy (RT) has been used in the management of cancer for more than a century;[1] approximately 50% of all cancer patients undergo radiation therapy. Furthermore, RT contributes to 40% of curative cancer treatment.[2] Its goal is to deliver a high therapeutic radiation dose to a tumour whilst sparing healthy normal tissue.[3,4] In order to achieve this continuous developments and innovations in the planning and delivery of RT treatment are made. Technological advances in RT have resulted in significant improvement in the planning and delivery of this cancer treatment, yielding decreased normal tissue toxicity, increased tumour control thus improved patient quality of life.[1,3,5]

Technological developments in RT have led to the innovation and inception of new advanced techniques such as the intensity modulated radiation therapy (IMRT), charged particle therapy (currently available in proton beam and carbon ions), stereotactic radiosurgery/radiation therapy, and image guided radiation therapy (IGRT), to mention a few.[3] All play a role in pursuing the achievement of the goal of RT.

IMRT delivers an intensity modulated beam of radiation with a tight focus, consequently treating irregular targets with high conformity and greater normal tissue sparing effect.[3,5,6] Proton beam therapy allows for effective treatment of tumours located at difficult-to-access sites such as the base of skull. This is due to its capacity to deliver high doses of radiation more precisely and with less toxicity to normal tissue than photon beams. Stereotactic radiation is an alternative to surgery for patients who are not operable; it is non-invasive, safe and effective.[5]

Nonetheless, the major challenge of early RT technologies and techniques is the inability to adjust treatment to account for patient set-up errors and a compromise on precision owing to patient movement and organ motion. The endeavours to address this challenge have led to the inception of image guided radiation therapy (IGRT), which allows for imaging in the radiation therapy treatment room with adjustments per individual patient to account for geometric deviations. This technique, enabled by new technological imaging modalities, also addresses errors that arise owing to the motion of the target volume and surrounding structures; this includes inter-fraction and intra-fraction motions.[1,5,7] This paper discusses and critically evaluates a number of image guided radiation therapy techniques.

DESIGN AND METHODOLOGY

Research questions

1. What recent technological developments in imaging modalities inform image guided techniques in radiation therapy?
2. What are the advantages and disadvantages of these techniques?

Research design

This was a literature review study; the existing body of academic literature was used to address the identified research question(s). Keywords were used to search for relevant journal articles in databases. The sourced material was grouped into themes; each theme pertained to a specific technique. Some articles discussed more than one technique and therefore were included in more than one group. Following the thematic analysis, the sourced material was then evaluated to answer the research questions.

Methodology

Four (4) databases, namely, Academic Search Premier, CINAHL, Health Source: Nursing/Academic Edition, and Medline, were searched for this literature review study. All were searched via the EbscoHost platform as it allowed searching multiple databases at the same time. The sourcing of articles for this literature review comprised two phases.

In the first phase, a Boolean search for articles was done using the following search terms: “image guided radiation therapy” OR “image guided radiotherapy” OR “developments in radiation therapy” in the ‘title’ fields. The filters were set to include full-text, peer-reviewed journal articles published between January 2012 and August 2016; the expanders were set to ‘apply equivalent subjects’.

The search initially yielded 111 papers

but decreased to 52 papers after excluding all exact duplicates. At this point, the second phase of literature sourcing process was initiated. Skimming and scanning reading techniques were used to evaluate papers for inclusion, based on relevance and depth. Thirty-three (33) papers were excluded as they focused on other topics and contained insufficient information on image guided radiation therapy. A further four (4) exact duplicates, three (3) abstracts, and one (1) letter to an editor were found; all were excluded. Their exclusion resulted in 11 English peer-reviewed full-text journal articles to review. A further four (4) hand-picked articles were considered to bring significant contribution to the study. The final number of journal papers reviewed was fifteen (n=15). Table 1 summarises and shows the described information sourcing process that was followed.

Table 1. Information sourcing process.

Results	Excluded	Added	Total
	PHASE 1		
111 papers (initial search)	59 (exact duplicates)		= 52
	PHASE 2		
52 papers (beginning of phase 2)	33 (irrelevant)		= 19
	4 (exact duplicates)		= 15
	3 (abstracts)		= 12
	1 (letter to editor)		= 11
		4 (hand-picked)	= 15

DISCUSSION

Radiation-based and non-radiation based systems are discussed below.

Radiation based IGRT systems

There are different types of technological imaging systems used in IGRT. They are divided into two main categories: radiation based systems, and non-radiation based systems. The radiation based IGRT systems refer to all systems that make use of ionising radiation, both in the kilovoltage (kV) and megavoltage (MV) ranges.[8] Conventionally, radiographic films were positioned beyond a patient to acquire an image using a linear accelerator (LINAC) MV range beam, this was followed by the development of the electronic portal imaging device (EPID).[4,9]

The EPID was succeeded by the flat panel imager (FPI), and later the cone beam computed tomography (CBCT) and the fan beam computed tomography (FBCT). [4,9] Commonly used IGRT technologies include the EPID, CBCT (kV and MV) and FBCT (kV and MV).[9,10] Nonetheless, the most recent advancements in radiation based image guided radiation therapy involve the use of x-ray 4D real time tracking systems.[8] However, more attention is given to the most commonly used systems.

» *The EPID and flat panel imager*

The EPID was developed in the 1980s as a direct successor of radiographic films and has since become the primary technology in IGRT.[8] This device is mounted on to the LINAC, at a 180 degree angle from the gantry head using a retractable arm. Its technology uses the LINAC's beam to acquire digital images, which consequently allow for online verification of the treatment and automatic analysis. These devices are available in three different designs: video based design, scanning liquid-ion-chamber-based design, and the hydrogenated amorphous silicon design.[9]

EPIDs have several clinical advantages and include, but not limited to, their capacity to image during treatment and the direct use of the LINAC beam. However, the use of the LINAC treatment beam, which is in the MV range, results in relatively poor contrast yet higher dose when compared to kV imaging.[8,11] This challenge was addressed by mounting a kV x-ray source on the LINAC gantry, in such a manner that they share a common isocentre. This system, known as the FPI, uses a flat panel detector to process images. The integration of an x-ray source onto the LINAC lead to the possibility of acquiring tomographic slices of a patient by means of rotating the LINAC gantry with the kV x-ray source concurrently operational: this possibility subsequently birthed the inception of kV cone beam computed tomography IGRT.[4,9]

» *Cone beam computed tomography based IGRT*

There are two types of cone beam computed tomography (CBCT): kV CBCT and MV CBCT. The former employs a kV x-ray source mounted on the LINAC to acquire tomographic images. This type of CBCT has a number of benefits when applied to IGRT. Firstly, it rapidly provides volumetric datasets with the capacity to assess both rotational and translational errors. Secondly, unlike the EPID, kV CBCT provides 3D information of a patient's anatomy allowing a radiation therapist to use both bone and soft tissue to compare patient position.[8,11,12] Furthermore, the introduction of remote-controlled treatment couches that automatically carry out shifts following image assessment by a user, to account for any deviations, has enhanced the clinical implementation and increasing widespread of kV CBCT based IGRT.[11] Figure 1 depicts LINAC mounted CBCT systems, (A) is the Varian OBI with a tube voltage of 30-140 kV, (B) is the Elekta XVI able of producing 70-150 kV x-ray photons, (C) is the Siemens MVision capacitated with 6 MV photons and (D) is the Mitsubishi VERO system.[9]

The primary advantage of MV CBCT on IGRT is its employment where there are dense metal objects such as hip prostheses. In such cases, MV CBCT eradicates the artefacts on kV CBCT images, due to the absence of kV x-ray photon attenuation.[8] However, this modality comes with a relatively low contrast and high dose when compared to kV CBCT. CBCT based IGRT provides increased accuracy and precision, which allows for greater

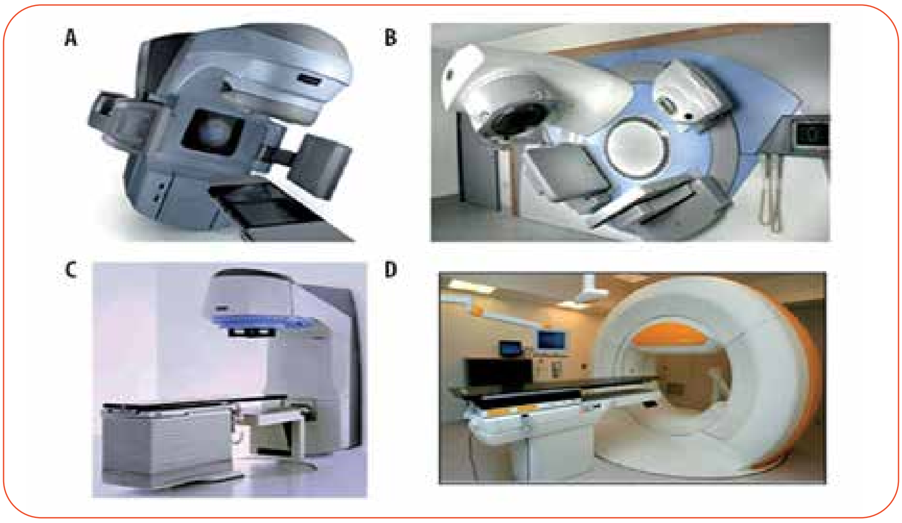

Figure 1. Cone beam systems mounted on medical linacs.
(A) Varian OBI Imaging system (courtesy and Copyright ©2007, Varian Medical systems, Inc.); (B) Elekta XVI system (courtesy and Copyright© 2008, Elekta AB (publ)); (C) Siemens MVision (courtesy and Copyright© Siemens AG, 2002–2008) and (D) Mitsubishi VERO system (courtesy and Copyright MHI Ltd., Tokyo, Japan) as published by Srinivasan, K., Mohammadi, M.S. & Shepherd, J.C. in Polish Journal of Radiology 2014. DOI:10.12659/PJR.890745.

potential of margin reduction, decreased tumour toxicity and finally yielding increased tumour control probability.[2,7,13-15]

» *Fan beam computed tomography IGRT*

Employing a LINAC treatment beam instead of a mounted x-ray source to acquire tomographic images enables what is referred to as MV fan beam computed tomography (MV FBCT) imaging.[10] An example is the TomoTherapy Hi ART II system, which produces radiation beam energies of 3.5 MV and 6 MV for imaging and treatment respectively. This system is equipped with a xenon detector at the opposite site of the LINAC gantry to collect the exit data for the production of MV FBCT images. MV FBCT based IGRT is easy to use; it is used for patient alignment, anatomic changes monitoring and dose computations.[8]

kV FBCT is quite different from MV FBCT in design. It is characterised by a gantry-moving CT scanner and is referred to as the in-room CT-LINAC system. However, dissimilar to conventional CT scanner, a CT-LINAC moves across a patient on rails instead of moving the couch through the scanner.[6] This design allows for the system to obtain CT images without compromising patient immobilisation in the treatment position. Moreover, recent designs of the kV FBCT include a gantry opening of more than 80 cm to accommodate big immobilisation devices, and a multi-slice image detector allowing for faster CT images acquisition.[8,11]

The main benefit of this system is that it produces images of a similar diagnostic quality as the scans used for treatment planning, consequently improving accuracy and reducing observer based variations.[8] It does present some disadvantages. It requires a larger treatment room than a standard LINAC. Moreover, the imaging unit does not share the same gantry as the treatment unit and this results in some uncertainties in patient movement and couch readouts.[8,12] Furthermore, it takes relatively longer to use. It is the most time consuming radiation based IGRT system, taking up to 15 minutes per fraction in pelvic IGRT.[7,11]

» *X-ray 4D real time tracking*

There are several methods used to achieve X-ray 4D real time tracking: the 2D kV stereoscopic imaging (cyberknife), real time tumour-tracking (RTRT) system, Vero system, and the combination alignment systems (optical imaging and 2D kV orthogonal imaging). These systems employ different technological mechanisms and physical principles to provide 4D real-time tracking with the use of ionising radiation. As a result, they allow for superior intra-fraction patient monitoring with high accuracy and precision. Nonetheless, their use is not as widespread as that of the above discussed systems, owing to the fact that they are relatively expensive and require special certification for use.[8,11]

Summary

There are three commonly used radiation based IGRT systems: the EPID, the CBCT, and the FBCT. The EPID is the earliest among the three and is available in three different designs. Nonetheless, the low contrast images and higher radiation doses owing to its employment of the actual treatment beam (MV range) eventually led to the innovation of the CBCT based IGRT. CBCT provides 3D patient data that allow the use of both bone and soft tissue anatomy for position comparison. This system is divided into kV CBCT and MV CBCT. The kV CBCT uses a kV x-ray source mounted on the linear accelerator; the MV CBCT uses the actual treatment beam.

Similar to CBCT, FBCT is also divided into MV FBCT and kV FBCT. The MV FBCT uses the treatment beam to acquire tomographic slices; the kV FBCT uses an in-room CT scanner that moves across a stationery patient to obtain images. The most advanced systems in this division are the X-ray 4D real time tracking systems, but are not commonly used in clinical practice due being expensive and the need for certified personnel.

Non-radiation based IGRT systems

The above discussed systems make use of ionising radiation to achieve image guidance which results in additional radiation dose to a patient. Consequently, with the aid of new technological advancements in imaging modalities, there are other systems employed in IGRT that do not necessitate the use of ionising radiation. These systems are referred to as non-radiation based IGRT systems. The currently used systems include camera based, electronic tracking, magnetic resonance imaging (MRI) based IGRT and ultrasonography (US) based IGRT systems.[9]

» *Camera based IGRT system*

This system is also referred to as the infrared or optical tracking system. It allows for automatic couch adjustments to match the treatment couch isocentre with the treatment planning isocentre. This is achieved by identifying the reference points for patient setup in relation to the planning coordinate system.[11] Furthermore, it enables a radiation therapist to continually monitor the actual patient surface motion during treatment delivery with benefits such as speed and with no use of ionising radiation.[8] Moreover, camera based IGRT may also be used for intra-fraction monitoring and has been clinically applied to the treatment of breast and prostate cancers and respiratory gating techniques.[11]

» *Electromagnetic tracking IGRT system*

Electromagnetic transponders, known as beacons, are implanted within a tumour and the motion thereof is real-time tracked making use of detector array coordination. This system is known as the electromagnetic tracking based IGRT system.[11] Major components of this system include a tracking station that is situated in the control room/area and components in the treatment room, which include a hub, 3 ceiling-mounted infrared optical cameras, a receiver array, an AC electromagnetic console, and, finally wireless transponders that are going to be implanted into the tumour.[8] The procedure of embedding the transponders into a tumour must be minimally invasive and note must be taken that they may cause artefacts on MRI scans.[11]

» *MRI based IGRT system*

MRI guided IGRT uses magnetic resonance imaging technology to enable real-time monitoring of anatomy and motion of soft tissue during treatment delivery, respectively. This is achieved by employing continual imaging for soft tissue; it allows for intra-fractional adjustments with an accuracy of about 1-2 cm.[11] This system provides superior soft tissue visualisation without necessitating the use of ionising radiation.[8] It has a disadvantage of image distortion due to non-uniformity in the magnetic field. Furthermore, it is subjected to all the limitations found in diagnostic MRI; its cost is very high.[8,11]

» *Ultrasound based IGRT system*

Ultrasound based IGRT (US-IGRT) system has been used clinically since the late 1990s; it was primarily used for prostate cancers. Recent research advocates its use in breast, abdominal and lung cancers.[8] US-IGRT generates 3D images with an accuracy of 3-5 mm to allow for intra-fractional adjustments.[11] This system provides the possibility of real time 4D intra-fraction monitoring with no use of ionising radiation. It may be regarded as a routine technique where the risk of secondary malignancy is a concern.[8]

Summary

Four non-radiation based IGRT systems were discussed. They are categorised as non-radiation-based because they provide image guidance without necessitating the use of ionising radiation. The camera based system allows for intra-fractional assessment with a unique capacity to monitor the actual patient surface motion during treatment. The electromagnetic tracking system makes use of electromagnetic transponders implanted within a tumour to real-time track the motion thereof. The MRI guided system provides enhanced soft tissue visualisation. The US-IGRT currently provides 3D and a potential 4D intra-fractional patient monitoring.

LIMITATIONS

Hand-picked journal articles that were not from the search were added to the total of papers. This may impact on the reproducibility of the study. Papers published between 2012 and 2016 were used in this study. However, due to the rapidly advancing nature of the radiation therapy field there may be other publications of advanced image guided radiation therapy techniques that were not addressed in this paper

CONCLUSION AND RECOMMENDATIONS

Radiation therapy is characterised by rapid advancement in both equipment and techniques. Image guided radiation therapy (IGRT) is one of the key developments in radiation therapy. Under radiation based IGRT systems, the electronic portal imaging device (EPID), flat panel imager (FPI), cone beam computed tomography (CBCT) based IGRT, the fan beam computed tomography (FBCT) guided IGRT, and the more advanced x-ray 4D real time tracking systems, were highlighted. These techniques make use of ionising radiation to provide image guidance.

Technological advancements in IGRT imaging modalities have resulted in several non-radiation based IGRT systems: the camera based system; the electromagnetic tracking system; the MRI-guided IGRT; and ultrasonography based IGRT.

Image guided radiation therapy is a very broad but extremely important technique of radiation therapy. It provides high precision and accuracy necessary for dose escalation with a reduction in normal tissue toxicity and increased probability of tumour control. It allows for the development of other advanced radiation therapy techniques, which necessitate high precision and accuracy. Nonetheless, the inception, development, and success of IGRT is due the technological advancements in imaging modalities; there is no technique without equipment.

It is recommended that (a) peripheral dose to a patient from radiation based IGRT systems be incorporated into the treatment planning systems to account for this accumulative dose, and (b) the radiation dose to a patient be kept as low as reasonably achievable (ALARA) in all clinical applications.

CONFLICT OF INTEREST

None

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