NEW DEVELOPMENTS IN IMAGE GUIDANCE FOR RADIOTHERAPY

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Abstract
Image Guided Radiation Therapy refers to the concept of visualising the target or an important critical structure during radiotherapy to ensure accurate and reproducible radiation delivery throughout the course of treatment. There are many different methods for Image Guided Radiation Therapy, ranging from ultrasound to electronic portal imaging and volumetric CT scanning. In many circumstances, Image Guided Radiation Therapy can be enhanced by the use of implanted fiducial markers that are clearly visible and can make decision-making quicker and more robust. The most common application for image guidance at present is the accurate positioning of the target prior to treatment delivery. However, the availability of high quality imaging at the time of treatment delivery also facilitates management of intrafraction motion and adaptive radiotherapy. The latter encompasses a variety of methods to modify the treatment plan for individual patients in response to the images acquired during treatment. While there is still discussion as to what imaging approach is best for which purpose, there is no doubt that modern highly conformal or intensity modulated radiotherapy would not be feasible without some form of image guidance. The present article provides an overview of available techniques with the aim of illustrating their use in relevant clinical scenarios.

Radiotherapy is in most cases a local or loco-regional treatment, directing radiation to the tumour target while minimising the dose to surrounding normal structures. This requires the identification of the target and a means of delivering a high dose of radiation reliably to this target. Identification and characterisation of the target have improved significantly over recent years with state-of-the-art imaging technologies such as PET and MRI providing improved anatomical and functional definition of the target. This is discussed in detail in the article by Fay and Thomas in this issue of Cancer Forum.

Once the target is identified, successful radiotherapy is based on two key tasks – the generation of a highly conformal radiation dose distribution and the ability to place this dose distribution in the correct position within the patient over the whole course of treatment, which typically lasts for 30 or more daily fractions. This is illustrated in figure 1. There have been dramatic improvements in our ability to deliver a highly conformal dose distribution, particularly through the use of Intensity Modulated Radiation Therapy (IMRT). The article by Foote in this issue highlights these developments.

The final task is to ensure that the dose is actually delivered to the target in an accurate and reproducible fashion for every day of the treatment. This is in general associated with the term Image Guided Radiation Therapy (IGRT).

This article aims to review tools that have become available for IGRT and explore how they support the overall aim of radiotherapy. In doing this, the article first provides a working definition for IGRT and introduces methods that are available for image guidance. This is followed by trying to classify clinical applications and a discussion of adaptive radiotherapy, the logical extension of IGRT.

Definition of IGRT
There is no uniformly accepted definition as to where conventional verification imaging ends and where IGRT starts. However, there is general agreement that the key features of IGRT are:

- Availability of high quality imaging equipment in the treatment room.
- Ability to visualise the target (not just external markers or bony anatomy) with the patient in treatment position.
- A protocol to act on the findings. This could be done on-line, ie. prior to turning the radiation beam on, or off-line between fractions if more complicated decision making is required.

This article is based on the following working definition: IGRT is radiotherapy based on data pertaining to the relationship between beam and patient geometry acquired at the point of treatment delivery, with the intent to ensure geometric accuracy of radiation delivery appropriate to the clinical scenario. This definition is a result of discussions at a consensus workshop on IGRT in Melbourne in 2008. This implies that IGRT does not necessarily require an image to be taken. A system which can locate the target in three dimensions in relation to the radiation beams would suffice. Electromagnetic beacons implanted in the prostate and detected with an external antenna system (Calypso company, Seattle US) are an example.

Imaging methods
A large variety of imaging methods are now available. They range from optical methods, where one or more video cameras observe the patient, to ultrasound, x-rays and even magnetic resonance imaging (MRI), in particular
Achieving the aim of radiotherapy requires the identification of the target as well as the ability to deliver a highly conformal dose of radiation to the target. IMRT is the tool to produce the conformal dose distribution and IGRT guides it reliably and reproducibly in the correct position within the patient. The picture showing the target identifications shows a PET/CT image of a lung cancer while the one illustrating IMRT is the dose distribution for a meningioma treated with seven fields. The fluence distributions in each field are also shown. The picture for IGRT shows an ultrasound image for localisation of the prostate. Figure adapted from reference 39.

Identification of the target

Delivery of radiation

Local control

Conformal dose distribution

Accurate delivery

would be of considerable interest as it not only provides the best soft tissue contrast, but also promises functional information. As it uses a method completely independent of the treatment delivery, MRI can also, at least in principle, be used in real time to monitor motion and changes due to treatment. As such, it is not surprising that several groups are currently working on prototype units despite the formidable challenges of combining strong magnetic fields with the electromagnetic components of a linac. For the time being, ultrasound is a soft tissue imaging method available in the clinic; the picture illustrating IGRT in figure 1 is an ultrasound image for localisation of the prostate. However, by far the most commonly used IGRT tools are x-ray based. These methods can utilise the megavoltage treatment beam, for example in electronic portal imaging, or a dedicated diagnostic x-ray tube and detector.

X-ray based IGRT approaches can be roughly divided into two main imaging approaches:

1. Acquisition of one, two or more planar x-ray images of the target volume (typically two orthogonal images which allow localisation of an object in three dimensions). Examples for this are electronic portal imaging as shown in figure 2, or diagnostic x-rays mounted on the gantry. The advantage of electronic portal imaging is that the treatment beam is used for imaging, which also allows verification of the field shape of the treatment beam. However, the image quality of a dedicated diagnostic x-ray system is superior and most manufacturers have implemented a version of this technology. A linac with both imaging modalities, electronic portal imaging using the treatment beam and on-board imaging using a dedicated diagnostic x-ray tube, is shown in figure 3.

Figure 2: Electronic portal image of a prostate cancer patient. Shown is the outline of the treatment field collimated by a multileaf collimator (MLC). The three fiducial gold markers implanted in the prostate gland can be clearly visualised in the treatment field.
For IGRT with projection imaging, target visualisation is often enhanced through the implantation of fiducial markers into the target.\textsuperscript{17,18} These markers can be small gold seeds (1mm diameter) that can be easily visualised using x-ray imaging. Figure 2 shows an electronic portal image of a patient treated with radiotherapy for prostate cancer. The implantation of markers overcomes the problem that the prostate (or other soft tissue targets) cannot be identified using projection x-ray imaging. Fiducial markers in the target volume can be easily visualised and allow for easy and fast decision making.

**II. Volumetric three dimensional imaging of the target area.**\textsuperscript{3,19} This is most commonly performed using x-ray CT technology such as cone beam CT (CBCT),\textsuperscript{20} or an in-room CT scanner where the linac and a CT scanner are housed in the same bunker.\textsuperscript{21} Volumetric imaging provides significantly more information about the target region and the surrounding normal structures. This is illustrated in figure 4, which shows a planning CT and a CBCT of a patient treated with extracranial stereotactic radiotherapy for early stage lung cancer. On the axial and coronal images shown, the three dimensional location and shape of the target are clearly visible. As CBCT images are acquired over an extended period of time as the linac gantry rotates around the patient, the CBCT also allows some assessment of motion.\textsuperscript{22} Also, information on critical structures such as the parotid in head and neck cancer,\textsuperscript{23} or the rectum in prostate cancer,\textsuperscript{24,25} can only be obtained using volumetric imaging. Volumetric imaging therefore allows for more complex decision-making, which is accompanied by an increased need for adequate operator training.

**Figure 3:** Modern linear accelerator for radiotherapy. The treatment beam points down and an image can be generated using an electronic portal imaging device. A diagnostic x-ray tube and detector are mounted rotated by 90 degrees on the gantry.

**Figure 4:** Illustration of image guidance using volumetric imaging. Shown is an axial image of a planning CT (left side) and the corresponding CBCT images acquired at the time of treatment for a patient treated with extracranial stereotactic radiotherapy for early stage lung cancer. The contours for the Internal Target Volume (ITV) used for image matching are shown.
Table 1: Advantages and disadvantages for selected methods for image guidance.
Rating: - not good, 0 may be considered, + acceptable, ++ good, +++ excellent. Please note that this is for illustration purposes only: not all technologies are listed and the table does not constitute an endorsement of any of the techniques.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Electronic portal imaging</th>
<th>kV imaging</th>
<th>CBCT</th>
<th>MVCT</th>
<th>Ultra sound</th>
<th>MRI</th>
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<tr>
<td>Dimensions</td>
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<td>2</td>
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<td>3</td>
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<tr>
<td>Allows assessment of beam portal</td>
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<td>no</td>
<td>no</td>
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<tr>
<td>Available while beam is on (‘real time’)</td>
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<td>possibly</td>
<td>unlikely</td>
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<td>possibly</td>
<td>yes</td>
</tr>
<tr>
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<td>+</td>
<td>++</td>
<td>+</td>
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<tr>
<td>Spatial accuracy</td>
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<td>+</td>
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<td>0</td>
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<td>Need for fiducials</td>
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<td>Unwanted dose</td>
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<td>yes</td>
<td>no</td>
<td>no</td>
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<tr>
<td>Time per treatment session (min)</td>
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<td>1</td>
<td>5</td>
<td>5</td>
<td>3</td>
<td>?</td>
</tr>
<tr>
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<td>head and neck, fiducials</td>
<td>most</td>
<td>most</td>
<td>prostate, breast</td>
<td>pelvis, lung, abdomen</td>
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<tr>
<td>Cost</td>
<td>small</td>
<td>medium</td>
<td>high</td>
<td>high</td>
<td>small</td>
<td>very high</td>
</tr>
</tbody>
</table>

Table 1 gives a summary of features for a variety of imaging modalities.

**IGRT applications**

IGRT applications can be distinguished using several different features:

1. Volumetric versus projection based imaging – as discussed in the previous section.
2. Radiation dose – In the light of increasing use of image guidance, the American Association of Physicists in Medicine has devoted a task group report to this issue. The use of imaging methods that use ionising radiation have to be restricted to minimise risk to the patient.
3. Imaging frequency – Imaging may be performed at specified time points during the course of treatment when particular decisions are required. Examples would be the use of decision-making models to reduce systematic errors, or adaptive radiotherapy based on significant changes in the anatomy. Daily imaging is the usual practice for targets that may move from day-to-day, such as the prostate. More frequent imaging is required for motion management where imaging is used to track the motion of a target in real time. Electromagnetic markers have been used for prostate cancer, while a variety of techniques are available for following breathing motion. Motion management affects targets that are likely to move during the delivery of radiation. This is typically illustrated by breathing motion and needs to be considered for the treatment of lung, breast, liver and other abdominal cancers.
4. Decision-making – This pertains to both the person making a decision and the immediacy of the decision-making. While complex decision-making is currently restricted to off-line image guidance, a lot of research is directed to making it feasible to allow decision-making at the time of delivery. Autosegmentation, registration and computer aided decision making tools are the subject of intense research.
5. Reliance of fiducial markers – This typically requires a few additional steps in the patient management process. For example, in IGRT of prostate cancer, implantation of fiducial markers would need to occur about one week before imaging for treatment planning to allow for reduction of swelling after the implant and reduce the chance of migration of the fiducial markers.
6. Resource requirements – This includes not only the cost of the system, but also training requirements and the time added to the patient treatment appointment by IGRT.

Estimates for some of the features discussed above are given in table 1 for common IGRT tools. It is the responsibility of the user to select the most appropriate technology for a particular clinical scenario. A good example for a systematic review of IGRT for rectal cancer was given recently by Gwynne et al.
Adaptive radiotherapy

Volumetric imaging in the treatment room is the prerequisite for a logical extension of IGRT – adaptive radiotherapy. At present, IGRT is mostly used for repositioning of the patient to align the target with the radiation beams. In adaptive radiotherapy, the treatment plan is modified to take into account changes in patient shape, target volume or the spatial relationship between target and surrounding structures. This requires either the preparation of multiple treatment plans from which to choose the ‘plan of the day’, or the creation of a new treatment plan based on the image information from a small number of treatment fractions.

Even one step further, biologically adaptive radiotherapy utilises functional imaging such as positron emission tomography to determine treatment response after part of the treatment and leads to modification of treatments in response to the biological changes observed. This could result for example, in a boost to metabolically active or hypoxic regions.

IGRT processes and infrastructure

In the context of IGRT there is an increased number of decision-making points in the patient’s treatment. The decision-making can be on-line while the patient is on the treatment couch, or off-line when the images are reviewed after a given treatment fraction. The resulting action will then affect future treatment fractions. It is intuitive that this will improve patient management. However, it also adds new costs and work processes to the treatment:

- cost of imaging equipment which is not always included in conventional linac purchases
- maintenance and quality assurance thereof
- training of staff
- development of protocols
- creation of new or modified reference images.

On the other hand, it also adds to the confidence that the correct treatment is delivered to the patient. In addition to this, the increasing responsibility for treatment staff and the need to acquire new skills in respect to image acquisition, interpretation and decision making, has the potential to improve job satisfaction.

Figure 5 illustrates the workflow in IGRT. In practice, there are additional implications of image guidance for a radiotherapy department, which extend beyond the individual patient. The large amount of data generated in IGRT can be used to analyse departmental processes, determine the performance of equipment (eg. immobilisation devices), and decide on departmental procedures such as margins in a rationale way. Margins are placed around a target in treatment planning and allow for organ motion and daily variations in patient set-up. Appropriate choice of margins has a significant effect on treatment quality and the increasing availability of IGRT has the potential to help optimise them for different treatment scenarios and the practice in individual radiotherapy centres. This process may require additional infrastructure such as a database. However, the benefits from the additional information available for decision-making and departmental planning would likely be significant.

Outlook

Image guidance has had profound implications for radiotherapy. Without IGRT, modern delivery techniques such as IMRT would not be possible. IGRT also has the potential to link observations made during the course of treatment back to the planning images that have defined the target in the first place. More decision-making points...
in the patient’s treatment course are the result. This not only has implications for staff and workflow, such as more training and quality assurance steps, but also increases confidence of all stakeholders that what was planned for management of the disease is actually happening for an individual patient. It is likely that IGRT in the future will provide more opportunities for adaptation of the treatment; why stick with the original treatment plan when one could adapt the plan to what has been seen during treatment? However, this will require communication and learning, and setting up an infrastructure that can facilitate this is essential for making optimal use of the new imaging tools available directly at the time of radiotherapy delivery. Image guidance has had profound implications for radiotherapy – and will continue to do so.

References