Introduction

Three dimensional (3D) imaging is key to the successful planning and delivery of pelvic radiotherapy treatment and is integrated into every step of the radiotherapy treatment pathway. Diagnostic and therapeutic imaging technology has evolved in the last decade, increasing the complexity of imaging choices available for target localisation, and introducing soft tissue visualisation into the treatment room. These technologies are particularly relevant to pelvic targets where the ability to identify the soft tissue target in 3D and the surrounding organs at risk (OAR) with clarity have driven the development of advanced planning techniques and adaptive strategies, leading to reduced margins and clinical benefit of reduced toxicity and personalisation of radiotherapy delivery.

This article will review the importance of imaging in pelvic radiotherapy at key points in the radiotherapy planning pathway namely target delineation, verification and adaptation.

1. Imaging for target delineation in pelvic radiotherapy

While CT-based target delineation remains the standard of care for radiotherapy treatment planning, in the pelvis this is limited by low soft tissue contrast. This can result in significant inter-observer variability in target delineation and significant differences in the target volume receiving the prescription dose. Advances in imaging techniques with magnetic resonance imaging (MRI) and positron emission tomography (PET) provide improved soft tissue contrast and biological information, which can improve the accuracy of target and OAR delineation (figure 1). Delineation on anatomical T2-weighted MRI results in smaller target volumes and reduces inter-observer variability. Multiparametric MRI with diffusion weighting imaging (DWI), dynamic contrast-enhancement (DCE) and spectroscopy can provide additional information on tumour biology. This is used in disease stratification and response assessment, but can also be used to identify areas for dose escalation. In prostate cancer this is being used in clinical trials to identify the dominant intra-prostatic lesion and investigate the benefit of dose painting to improve local control. PETCT also provides functional information. It is well established in cervix cancer where it is superior to MRI in evaluating lymph node involvement. This influences the superior extent of the nodal clinical target volume (CTV) and identifies gross nodal disease for simultaneous integrated boost.

However, as treatment planning software remains CT-based, any additional imaging used for target delineation must be registered to the reference planning CT, which introduces error and uncertainty. Additional images have usually been acquired at different time points, in different patient positions and immobilisation and without appropriate organ filling compared to the reference CT. Any error in registration will lead to a systematic error throughout treatment, which would negate any benefit from improved target localisation. MRI is the best imaging tool for obtaining diagnostic information in the pelvis, thus an MRI-only radiotherapy simulation would seem optimal. However, the intrinsic geometric distortion and lack of electron density information inherent to MRI needs to be addressed.

Approaches to generate synthetic CT images from MRI datasets that provide electron density information can be segmentation or atlas based. Segmentation techniques divide patient anatomy into different tissue classes, assigning electron density to each class. The atlas approach uses multiple paired CTMRI data and deformably registers the MRI atlas to the patient’s MRI to segment structures. This is followed by application of the electron density atlas to generate the synthetic CT. Planning studies in prostate cancer have shown that radiotherapy planning and dose calculation on MRI using these strategies are comparable to dosimetry on CT.

Rationale for image-guided radiotherapy in pelvic radiotherapy

Intensity modulated radiotherapy (IMRT) is routinely delivered for pelvic targets, improving conformity and reducing dose to normal tissue, but the accuracy of treatment delivery is complicated by geometric uncertainty. The sources of this uncertainty are multifactorial:

- Inter and intrafraction motion of targets caused by substantial changes in bladder and rectal volume (figure 2).
- The CTV may involve multiple structures, which move independently of each other, and extended pelvic fields are highly susceptible to rotational set-up error.
- Tumour regression during treatment (eg cervix tumour regression of 50% and rectal volumes reductions of 35% are frequently observed.

The ability to visualise soft tissue targets at the time of radiotherapy is therefore key to minimising these uncertainties.

2. Current image guidance strategies and their limitations

Image-guided radiotherapy (IGRT) enables the verification of target volume location before and during treatment delivery and has been summarised previously. The goal is to image the target and OAR in the treatment room, at the time of delivery, to ensure accuracy. Cone beam CT (CBCT), integrated with the linear accelerator, has been widely introduced in pelvic radiotherapy, providing 3D information and permitting safe reductions in set-up margins.

Alternative IGRT solutions for pelvic RT include 3D ultrasound and marker tracking. Transperineal ultrasound is being implemented clinically in prostate cancer for continuous intra-fraction motion assessment and transabdominal ultrasound is being investigated in cervical cancer for intra-fraction motion assessment. Ultrasound is cheap and widely available and provides good soft tissue contrast with no additional radiation exposure. Disadvantages are the significant inter-user and inter-scan variability in image quality and interpretation.

Real-time tumour tracking can be performed with systems integrating x-ray detectors (Cyberknife and VERO) or electromagnetic transponder localising systems (Calypso). These provide intrafraction motion assessment and the Calypso system is non-ionising. Both require implanted markers, which are invasive to patients and there is a risk of seed migration.

The current available IGRT strategies are limited by the inability of rigid registration to account for the complex geo-
metric changes that can occur in the target and OARs, poor soft tissue contrast, additional imaging dose and the need for implantation of markers for tumour tracking.

3. Adaptive planning strategies in pelvic radiotherapy

To react to the changes seen in target and OAR position now visible with online image guidance a number of different adaptive planning strategies are proposed in an attempt to further improve the accuracy of treatment delivery. A 'plan of the day' approach involves modelling a range of motion, usually based on variable bladder filling, and generating a number of plans from which the most appropriate can be selected daily based on CBCT imaging. This has been implemented in bladder and cervix cancer radiotherapy.12-14

An alternative strategy is the composite plan approach, which defines a composite CTV based on the observed CTV position on CBCT scans acquired during the first week of treatment. This is subsequently expanded to create a composite planning target volume (PTV). In bladder cancer this strategy can reduce the irradiated volume by 40% while maintaining target coverage.14

In prostate cancer there is a move towards more hypofractionated treatment. This is possible because of better understanding of the tumour biology together with improvements in tumour localisation. Real-time tumour tracking of implanted markers with either x-ray based or transponder localisation systems allows adaptation of treatment delivery based on information about target position and safe reduction of margins.

Integrating imaging into future IGRT and image-guided adaptive radiotherapy

As previously stated, MRI is the current gold standard for imaging the pelvic soft tissues and therefore the obvious modality to adapt to the radiotherapy planning pathway. Presently, a number of systems for MRI-guided radiation delivery are available, which can acquire MRI immediately before and simultaneously with the radiation treatment beam. The Elekta Unity system combines a 1.5T MRI with a 6MV linear accelerator. The MRIdian system by ViewRay incorporates a 0.35T MR with a three-headed 60Cobalt system.

Current research strategies using this technology are also examining online re-planning (ie creating a new treatment plan based on the imaging each day) and safe reductions in margins, which planning studies have shown increase tumour coverage and reduce dose to OARs in prostate, bladder and cervix radiotherapy.15-17 These strategies require fast and reliable auto-segmentation techniques together with treatment planning systems that can accommodate fast re-planning with the patient on the treatment couch and real-time dose reconstruction.

Other future image-guided adaptive radiotherapy strategies include adaptation based on biological changes in tumour and normal tissue during treatment to identify patients that are good and bad responders. DWI MRI during rectal cancer radiotherapy can predict more aggressive hypoxic components within prostate and cervix tumours for dose painting and use of DCE and DWI during chemoradiation for cervix cancer may permit adaptation of dose and volume depending on response.

Conclusion

Imaging is central to accurate radiotherapy delivery in the pelvis. MRI provides the optimal soft tissue discrimination and is being increasingly incorporated into the planning and delivery pathways. Current future direction focuses on the implementation of an MRI-only workflow and the use of functional imaging of biological targets for dose optimisation.

References

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<thead>
<tr>
<th>Technique</th>
<th>Advantages</th>
<th>Limitations</th>
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<tbody>
<tr>
<td>Ultrasound</td>
<td>Non-ionising and non-invasive</td>
<td>Relative low quality&lt;br&gt;Geometric distortion&lt;br&gt;Possible target displacement&lt;br&gt;Inter-user and inter-scan variability</td>
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<td>Inexpensive</td>
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<td>Reasonable soft tissue contrast</td>
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<td>2D or 3D available</td>
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<tr>
<td>CBCT and tomotherapy</td>
<td>High geometric accuracy&lt;br&gt;Widely available&lt;br&gt;Inexpensive</td>
<td>Ionising&lt;br&gt;Poor soft tissue contrast&lt;br&gt;Susceptible to motion artefact</td>
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<tr>
<td>MRI</td>
<td>Excellent soft tissue contrast&lt;br&gt;Non-ionising</td>
<td>Not widely available&lt;br&gt;Expensive&lt;br&gt;Geometric distortion&lt;br&gt;Specialist knowledge required</td>
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<td></td>
<td>Potential for real-time assessment</td>
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<tr>
<td>Marker-based tracking</td>
<td>Potential for real time tracking&lt;br&gt;2D or 3D</td>
<td>Invasive&lt;br&gt;Surrogate for target&lt;br&gt;Obstruction in image viewing angles</td>
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**TABLE 1**
Pelvic IGRT strategies advantages and limitations.

**Figure 1**
Improved soft tissue contrast of MRI compared to CT in a male patient with rectal cancer.

**Figure 2**
Interfraction motion in cervix cancer as seen on CBCT acquired at weeks 1-5, compared to the reference planning CT (pCT), CTV in pink and bladder in blue.

**Figure 3**
IGRT strategies in prostate cancer. (A) CBCT. (B) CBCT fused with transperineal US. (C) Transperineal USS. (D) Planar XR with markers for real-time tracking on Cyberknife.