Introduction

During a course of external beam radiotherapy the prostate gland moves both between radiotherapy fractions (interfractional motion) and during treatment (intrafractional motion). Some of this motion is related to changes in rectal and bladder filling, and movements are more marked in the antero-posterior direction as a result of rectal filling variability, compared to laterally and supero-inferiorly. Image guided radiotherapy (IGRT) is defined as: “Any imaging at the pre-treatment and treatment delivery stage that leads to an action that can improve or verify the accuracy of radiotherapy.” The importance of IGRT is to reduce the chance of geographical miss and treatment failure, and to improve rates of bladder and bowel toxicity.

For years bony anatomy was used as a surrogate for prostate position but now there are various IGRT modes in order to visualise the prostate gland itself. These include the insertion of fiducial markers into the prostate, an additional procedure for patients with attendant risks of infection, bleeding and marker migration. Prostate volume changes due to hormones or radiotherapy may alter the position of markers. Cone beam computed tomography (CBCT) scans are also used, which are dependent on gaining a satisfactory soft tissue image and subject to interobserver variability. Both the use of fiducial markers and CBCT scans require daily radiation exposure. Systems using magnetic resonance imaging (MRI), which does not require radiation exposure, are in development.

Clarity (Elekta AB, Stockholm, Sweden) transperineal ultrasound (TPUS) was introduced at the Bristol Cancer Institute (BCI) in February 2014 for interfractional IGRT using three-dimensional soft tissue matching (figure 1). Since January 2015 we have treated 240 patients with radiotherapy to the prostate and seminal vesicles using TPUS IGRT. This equates to more than 8,500 x-ray volume imaging (XVI) doses not being delivered as a result. We are the first centre in the UK to use this system clinically for prostate cancer IGRT.

Transabdominal versus transperineal approach

Both transabdominal (TA) and TPUS modes of IGRT are available. TPUS provides superior visualisation of the prostate, symphysis pubis and penile bulb due to the short distance between the perineum and prostate gland. Less bladder filling is required, making the experience more comfortable for patients. As the TA probe is removed prior to treatment the imaged anatomy may differ from that treated. The TPUS probe is left in situ during treatment, so any changes in anatomy are consistent for imaging and treatment, and it can be used for monitoring of intrafractional motion. Consistency of bladder filling can also be checked before each fraction.

Process

Ultrasound acquisition (US)

Standard departmental patient preparation is used which includes a microenema and three cups of water with 30-minute bladder fill. Patients have a planning CT scan and acquisition of the US image in the supine position, with knee supports and the TPUS probe in position (figures 2 and 3). The probe is pressed firmly against the perineum and is adjusted slightly to ensure visualisation of the required anatomy. The US image is used to match the daily pre-treatment image. Gel is used as a coupling medium to allow transmission of ultrasound to and from the patient to the transducer. An infrared camera on the ceiling tracks the ultrasound probe via infrared reflectors attached to the probe.

The reference positioning volume

Within the prostate, areas of calcification or ‘naturally occurring markers’ can be helpful during IGRT with US and indeed our experience is that the majority of prostate ultrasound scans identify these. US and CT images are registered by physics staff who also create an IGRT volume or reference positioning volume (RPV) within the clinical target volume. The RPV can be marked using US alone, but is usually done in combination with CT images.

Pre-treatment

Ultrasound images are acquired before each treatment and compared to the reference ultrasound images from planning to calculate and correct for any interfractional prostatic motion. Pre-treatment verification of the prostate using TPUS is achieved within routine appointment times (as used for XVI verification).

Interobserver variability in performing the Clarity match can affect the accuracy and reproducibility of the technique. Two senior radiographers, experienced in ultrasound and...
IGRT, who received applications training in Clarity matching, were identified as the departmental gold standard. Prior to shifting patients pre-treatment US images were acquired and matches were performed for training and audit purposes. These matches were repeated offline by the radiographers, and a selection was matched externally by a Clarity specialist based at Elekta. Results from the two radiographers were compared to each other to check for consistency. The aim is for 95% of repeated matches to agree within 3mm of those pre-treatment and it is acknowledged that matching in a clinical environment is more challenging than performing the matches offline. Since using the system clinically two competent radiographers are required for every match.

**Systematic shifts**

When systematic shifts on an individual patient exceed 10mm further evaluation is performed to assess the accuracy of the matches. This involves checking image quality and registration, and an offline audit of a selection of matches. Systematic shifts exceeding 10mm do occur, often due to the prostate being systematically posterior of its position at planning. This is believed to be caused by the patient being tense during their initial TPUS scan, and then relaxing for subsequent scans. Efforts are being made to encourage patients to relax at their planning scan to avoid this.

In the majority of these cases, registration and audit results are acceptable and treatment continued, applying the systematic shifts from the Clarity system. If problems are identified the patient may be replanned, either with a new reference image or with an alternative imaging modality if the patient is deemed unsuitable for Clarity imaging.

**Patient acceptability**

Morbidity and patient acceptability of any additional procedure needs to be assessed in addition to clinical benefit, in this case the potential for improving the accuracy of daily radiotherapy delivery. This has previously been assessed for fiducial markers. Out of 26 patients who completed a questionnaire only 4% reported that the ultrasound procedure was either intrusive or uncomfortable and 88% would agree to having a further TPUS.

**Discussion**

Many studies comparing US IGRT systems to CT-based and fiducial marker IGRT have been with different US systems and focussed on the TA approach, rather than TPUS. Indeed some of these studies have also acquired CT and ultrasound images at different time points, introducing potential error from the initial treatment planning stage onwards. In comparison, using the Clarity system the ultrasound images are taken at the time of the acquisition of the planning CT scan and it is an intramodality system, ie ultrasound is matched to ultrasound, not another modality.

A more recent study found good concordance between CBCT/CT and TPUS/TPUS localisation of both prostates and prostatic beds, with the largest discrepancies in the AP direction for prostates, there being larger shifts posteriorly for TPUS. Probe pressure was also researched in this study and displacement in the superior direction only (up to >5mm) was observed in some patients with larger probe pressures, however these greater probe pressures were never used during treatment. Interobserver variability was found to be similar for CBCT and TPUS.

Our experience has been that with appropriate radiographer training we have been able to gain an optimal Clarity image at CT planning scan in over 98% of all patients. This also includes obese patients who will make up a larger proportion of the patient group in the future. This concords with the experience of the French group which found that 100% of TPUS images versus 80% of TA US images were of a suitable quality.

Another recent retrospective study has shown that TPUS compares favourably with fiducial seed matching using CBCT, measuring prostate position simultaneously using these two methods. The difference was not significant laterally or longitudinally and small, but not clinically significant, vertically.

Euclidean distance variance has also been looked at as well as standard translational comparisons between TPUS and CT, and has been found to be significantly different between the two modalities. The small sample sizes in these studies and the lack of a true gold standard comparator for TPUS means further research is required.

**The future**

**Intrafractional monitoring**

Clarity can be utilised for intra-fractional monitoring of the prostate gland which will be particularly relevant when patients are treated with the hypofractionated regimes of 60 Gray in 20 fractions as in the CHHiP study or stereotactic ablative body radiotherapy.

Our experience to date of intrafractional 4D monitoring of the prostate gland (looking at 526 fractions from 20 prostate cancer patients) is that prostate motion exceeds a displacement threshold of 3mm in 52% of fractions; 7mm in 8% of fractions and 10mm in 2%. Posterior motion was found to be greatest and a small proportion of patients exhibit greater prostate motion (Figure 4).

Further research into intrafractional monitoring using this system is needed, especially if planning target volume margins are to be reduced and the dosimetric consequences of prostate displacements should be considered.

**References**

2. National Cancer Action team paper: August 2012
15. Richardson A. Personal communication. Bristol Cancer Institute.
Figure 1
Some of the team at Bristol Cancer Institute with the Clarity TPUS cart and probe.

Figure 2
Patient position with Clarity probe in situ (courtesy of Elekta).

Figure 3
Clarity probe (courtesy of Elekta).

Figure 4
Intrafractional monitoring of the prostate using Clarity (courtesy of Jack Aylward, physicist, Bristol Cancer Institute).