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Original Article

An evaluation of ultrasound localisation for verification of external beam radiotherapy to the prostate

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Abstract

The recent advent of highly conformal three-dimensional radiotherapy techniques and Intensity Modulated Radiotherapy now allows higher radiation doses to be delivered. It is well-documented that the prostate is susceptible to both interfraction and intrafraction movements due to various physiological processes. Therefore there has been a recent general consensus that good immobilisation and electronic portal imaging is no longer sufficient to ensure accurate treatment verification. This idea has led to the concept of image-guided radiotherapy, which includes modalities such as cone-beam computed tomography and ultrasound to localise the prostate prior to treatment.

There has been considerable research undertaken to determine the effectiveness of each of the image guided modalities and these studies have identified the benefit and limitations of each modality. Ultrasound is a non-invasive technique using a suprapubic ultrasound probe, which seems to be quite promising in terms of cost and time. However until large scales studies are performed which demonstrate the value of using ultrasound localisation, as an alternative to electronic portal imaging, it is likely that current practice will remain unchanged.

Keywords

Image guided radiotherapy; ultrasound localisation; electronic portal imaging

INTRODUCTION

The advent of three-dimensional (3D) conformal techniques and Intensity Modulated Radiotherapy (IMRT) to the prostate has meant that it is now possible to deliver radiation doses to small complex target volumes. However, such techniques are of little use if they cannot be accurately positioned inside the patient.

There has been a recent general consensus that rigid immobilisation devices or electronic portal imaging (EPI) are no longer sufficient to ensure accurate target positioning. This is especially true for the prostate because bony landmarks are visualised and organ movement due to physiological processes such as rectal or bladder filling is not taken into consideration. Langen et al.[1] provides a descriptive summary on various prostate motion studies, which conclude that the prostate can shift position by an average of 0.2–0.4 cm.[1] It is well-documented that the prostate can move relative to the pelvic bone.[1] There are two types of prostate movement that can occur and these are known as interfraction and intrafraction movement. Intrafraction movement refers to any movement that occurs during any single treatment fraction once the patient has been correctly aligned. Huang et al.[2] reported that intrafraction motion predominantly occurs in the anterior and superior directions but was clinically insignificant.

Interfraction movement refers to any movement, which may occur between treatment fractions. Interfraction movement has been studied

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more extensively and has been found to be more significant than intrafraction movement with more than 20% of treatments requiring shifts greater than 0.5 cm.[1]

As well as the translations and rotations of the prostate due to physiological processes it is also prone to shape variation, which is less well-documented. However, Deurloo et al.[3] found that deformation of the prostate and seminal vesicles in comparison to organ motion is so small that it is reasonable to assume that they are rigid.

During the planning process margins are added to the clinical target volume and gross tumour volume to allow for these movements as defined in the International Commission on Radiological Units reports 50 and 60.[4] However, these margins need to be a compromise between adequately covering the prostate and sparing neighbouring sensitive structures such as the rectum.

This is further complicated when dose escalation occurs. There have been a number of studies that have shown that dose escalation leads to better cure rates for prostate patients.[5–7] The findings of Symon et al.[5] suggest that a higher dose can only be delivered safely if the dose per fraction to normal tissues is not significantly increased. So the extra margins needed to account for prostate motion in turn limits the level of dose escalation due to the presence of surrounding organs at risk such as the rectum.[5]

The issues detailed above have contributed to the concept of image guided radiotherapy whereby the prostate can be localised immediately before each treatment and realigned into the planning target volume before treatment. Image guidance is routinely used in brachtherapy of the prostate. Organ motion has little impact on such treatments as radioactive seeds are implanted and these move along with the prostate, therefore, allowing a higher dose to be delivered than conventional external beam radiotherapy.[8] So if image guided techniques could reduce the effects of organ motion and set-up uncertainties then similar biological doses could be administered.

There have been various approaches taken to minimise this prostate motion such as rectal probes, rectal balloons, radioopaque markers, implanted gold seeds and urethral catheters.[8–10] However some of these require invasive procedures and lead to increased patient discomfort, therefore, image guided techniques seem to be a more promising approach.

ULTRASOUND PROSTATE LOCALISATION

The Nomos Corporation[11] has developed an ultrasound based target localisation system, which is commercially available under the trade name B-Mode acquisition and targeting (BAT). The system consists of a user-friendly suprapubic ultrasound probe and a computer based targeting system inside the room.[11]

The BAT system is a B-mode scanner also known as brightness modulated and is capable of producing real time 2D images of structures. This is accomplished by the rapid scanning of the ultrasound beam through the tissue. Each of the returning echoes is displayed as grey scale dots and varying shades of grey represents the amplitude. The position of these dots is therefore determined by the time of arrival of the echoes and the orientation of the beam thus a grey scale image is built-up as a slice through the tissue. Each bright spot represents an interface within the body. However, the probe of the BAT system differs from conventional ultrasound probes because it can recognise its position in 3D spaces and so it can be manoeuvred in all directions but remain orientated to the isocentre through a docking system.[11] The ultrasound beam is scanned in the orthogonal dimension and the operator captures both a transverse and saggital image. The system then displays the transverse and saggital computed tomography (CT) contours that have been outlined on the CT planning scan and the operator who can manoeuvre the contours using a touch screen menu.

Once the contours have been accurately aligned, the software first calculates and then displays the 3D couch shifts required to produce an accurate field alignment.

More recently, Zmed medical solutions have also developed a 3D ultrasound localisation and

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optical tracking patient positioning system commercially known as Sonarray. It is very similar to the BAT system. However it does differ from the original BAT system in that it integrates optical tracking devices with 3D ultrasound reconstruction technology hence produces real-time 3D images.[12]

The Sonarray system is an optically guided system where ceiling mounted infrared cameras register with fiducial markers such as gold seeds implanted into the prostate to ensure accurate patient positioning. The operator then acquires a 3D ultrasound image of the prostate. A touch screen similar to that used in the BAT system is used to manually align the CT contours on the planning scan to the ultrasound image and the Sonarray software can then calculate the couch shifts needed for accurate localisation.

There have been few studies to investigate the usefulness of this system since the BAT system seems to be the more popular choice. Although Chinnaiyan et al.[13] found it to be valuable in comparison to electronic portal films to correct for set-up error and organ motion in the treatment of prostate cancer.

A possible reason for the lack of recognition of this system is that it requires the utilisation of some form of fiducial marker and the procedure is an invasive one, which would contradict one of the major advantages of ultrasound localisation, namely that it is a non-invasive procedure. There is also a cautious attitude towards the use of implanted seeds in the prostate due to the possibility of seed migration even though Poggi et al.[14] demonstrated that seed migration is negligible over a course of radiotherapy.

Image registration

The way in which the daily ultrasound images of the prostate are compared to the CT images used for planning is an important factor to ensure that the prostate is localised accurately.

There are a number of techniques, which have been designed to register the treatment plan with the ultrasound verification images. Various studies have been undertaken to evaluate manual, automatic and semi-automatic registration techniques.[15–17] However, these automatic registration techniques contain algorithms that have been designed mainly for CT image guided modalities. Although Smitsmans et al.[16] speculate that they could be applied to ultrasound localisation.

There is currently no available automatic registration technique that can be applied to ultrasound. However, the manual technique utilised, despite being more time consuming and subject to interuser variability, allows the operator to override the system if necessary. In addition, a computer generated algorithm can be unreliable at times and can be misled by the presence of variable amounts of faecal gas in the rectum.

Pouliot et al.[15] and Lattanzi et al.[18] both used a manual technique where the GTV contours from the treatment planning scans such as the prostate and seminal vesicles are overlaid onto the daily ultrasound image and then manually shifted to match the anatomical position of the prostate on the planning scan. As mentioned, a potential disadvantage to this technique is interobserver variability when outlining the target volumes onto the CT planning images and when manually aligning these contours onto the actual ultrasound image, although this uncertainty is likely to be reduced with increased experience of the system and the alignment process.

Court et al.[19] also suggested that a reference ultrasound image could be taken at the original simulation and anatomic contours drawn on this reference image rather than the imported CT planning image to reduce the uncertainty associated with interobserver variability.

Image quality

The typical BAT settings that tend to be used are: frequency 3.5 MHz, power 80%, gain 45%.[21] However, it is possible to make minor adjustments in order to improve image quality. From ultrasound localisation images the prostate, seminal vesicles, bladder and to a lesser extent the rectum are visualised which is illustrated in Figure 1.

It is actually the interfaces between these organs that are more clearly visualised. It is well-documented

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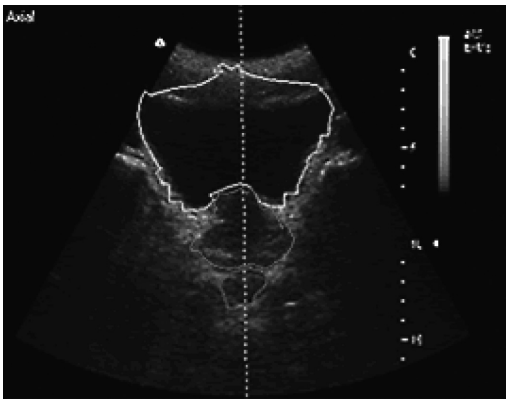

Figure 1. A BAT localisation image, which shows how the prostate, bladder and rectum appear dark and the interfaces between the organs appear light (North America Scientific; with kind permission of NOMOS Radiation Oncology, a division of North America Scientific).[12]

that one of the limitations of ultrasound localisation can be the quality of the image that is produced. This is due to a number of reasons:

- The poor propagation of sound in gases as the molecules in gases are widely separated and so any gas in the pelvis may limit its application.
- The physical characteristics of a patient, which may also affect the image quality. Serago et al.[10] reported on the patient specific anatomic features that may affect the ultrasound image quality. They concluded that patients who have a greater amount of prostate gland superior to the pubic symphysis, those who have a less amount of tissue anterior to the bladder and those with a small distance between the abdominal surface to the isocentre will ultrasound images with a better quality. They also found that bladder volume was not a significant predictor of image quality, which supports the findings of Langen et al.[9] Although patients who have poor bladder control are should be considered ineligible if they are unable to maintain their bladder status for the duration of the examination since a full bladder is a requirement of good image quality.[18]
- Patients who have received a prostectomy also appear to be a challenge. In some cases, it is possible to delineate the prostate bed and this can be used for alignment.[21] However if a total prostectomy has been performed and the prostate bed removed the patient would then have to be considered ineligible for ultrasound localisation. Although as an alternative some centres use the neck of the bladder as the primary reference structure for the alignment process.[13]

One example of a centre attempting to find a solution for poor image quality is that a pre-treatment ultrasound examination is done in order to determine the image quality obtainable for a patient.[9]

In reality, image quality cannot be considered as a major limiting factor as studies have shown that it is only unacceptable in less than 10% of examinations. Little et al.[20] found 90% of their study images of acceptable quality and Chandra et al.[22] found 93% of their images to be of acceptable quality.

ABILITY OF ULTRASOUND LOCALISATION SYSTEMS IN DETECTING INCORRECT FIELD PLACEMENTS

A number of studies have been carried out to evaluate the usefulness of the BAT system in detecting and correcting for incorrect field placements. Serago et al.[10] found that the ultrasound system is capable of detecting and correcting for significant patient alignment discrepancies. This study showed that the average shifts necessary to correct patient alignment from the skin markings were approximately 0.1 cm.[10] This is a very small figure and may undermine the necessity of the procedure in the first instance, as a margin of 0.1 cm added to the planning target volume would be considered reasonable. However, other literature would suggest otherwise. Morr et al.[23] reported larger average correction shifts of 0.3–0.5 cm being necessary. Lattanzzi et al.[18] recorded that mean shifts ranging from 0.3 cm to 1.2 cm were required to ensure patient alignment.

A comprehensive study performed by Little et al.[20] concluded that without BAT localisation, organ motion would have caused the clinical target volume to move outside the planning target volume in 23.3–41.8% of treatments within the study despite patient set-up verification with the use of electronic portal images. Also Fung et al.[21] recommended that additional planning target

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margins of 0.9 cm in the superior–inferior dimension, 1.02 cm in the anterior–posterior direction and 0.8 cm in the right–left direction would be needed if ultrasound localisation had not performed. These findings would suggest that ultrasound localisation is required if planning target volumes are to be reduced without compromising the dose delivered to normal tissue.

Quality assurance

From the available literature describing experiences with the BAT system few studies seem to have a well established quality assurance program for the technique as well as for the actual equipment. This is concerning considering good quality assurance is a prerequisite for guaranteeing good image quality and accurate alignments.

Serago et al.[10] was one of the few authors who addressed this issue. The Mayo Clinic, Jacksonville developed daily tests using an ultrasound phantom to verify the operation of the ultrasound unit and its ability to determine the isocentre of the linear accelerator. Monthly tests were also established to evaluate the reproducibility of the ultrasound arm position.[10] As the use of ultrasound localisation becomes more widespread it is likely that a more streamlined approach to quality assurance will be taken.

Interobserver variability

Another possible limitation of the use of this type of localisation system concerns problems with reproducibility if more than one operator is involved in both the acquisition and alignment process.

There have been a number of studies that have addressed the fact that the planning CT contour alignment process is a very subjective process that may be subject to interuser variability. Serago et al.[10] addressed this issue and found that duplicate ultrasound positioning by the same operator on the same day was reproducible within 0.3 cm at 95% confidence level and the reproducibility between two operators was within 0.3 cm at 80–90% confidence level. Certain studies such as that performed by Serago et al.[10] failed to assess whether their results were dependent on an individual operator or a set of operators.

This interobserver variability could perhaps be reduced if all operators received identical training, however there will always be a small amount of variability as there is with analysis of electronic portal images,[24] which are currently the most widespread method of verification used in radiotherapy departments today.

Ultrasound probe pressure

One of the major concerns arising from the use of an ultrasound localisation system is that the pressure exerted by the actual ultrasound probe could cause some further displacement of the prostate. However, it is difficult to quantify this displacement, as the amount of probe pressure applied will vary, from one patient to another and is also dependent on the operator.

Some studies have made an attempt to quantify this displacement. Serago et al.[10] found that the displacement of the prostate was less than 0.3 cm in any direction for all the patients included in the study with the exception of one individual. This was supported by the findings of Artigan et al.[25] who concluded that for each 1.0 cm of probe pressure the prostate was displaced an average of 0.31 cm. The only predictive factor found, as an actual indicator of the amount of prostate displacement is the actual amount of probe pressure applied. Therefore, it would seem that the amount of probe pressure applied should be as small as possible. However to achieve images of sufficient quality it is necessary to exert a probe displacement of between 1.0 and 2.0 cm.[25] This is a major limiting factor associated with the ultrasound localisation technique and it warrants the need for further studies to evaluate whether or not increased safer margins need to be included around the target volume if this technique is to be employed.

It also seems more large-scale studies are needed to further evaluate the effectiveness of the ultrasound localisation and its ability to detect and correct field placement errors. The studies, which have been performed thus far, have contained relatively small patient samples ranging from 10 to 50 patients with an average sample size of approximately 21 patients.[9,10,25–27] The Image Guided Radiation Therapy Committee predict that as equipment with image guided capabilities disseminates into

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the community more centres will participate in such trials.[28]

THE ADVANTAGES OF ULTRASOUND LOCALISATION

One of the major advantages of ultrasound localisation is that it is a non-invasive procedure, which produces minimal patient discomfort, hence patients are likely to be more amenable to this procedure.

In comparison to other image guided modalities it requires the least hardware and no additional software and therefore has the least cost implication. Both the commercially available BAT and Sonarray systems have been designed to be compatible with most digital image processing, transmission and storage applications, which aid the exportation of the planning CT images to the actual ultrasound unit. Most radiotherapy centres today already have some form of image transmission software in place to allow planning images to be imported to the treatment planning software and then onward to the portal imaging software to allow matching to take place.

Other image guided techniques such as CT and Cone beam CT require the addition of both expensive hardware and software which features algorithms to reconstruct the CT data and allow registration of the images. The additional equipment required for CT and Cone beam CT has been acknowledged in many studies, which have reported on their operation.[15,18,29,30] Even though some would argue that CT could localise the prostate more accurately since CT can acquire images with larger volumes of prostate,[21] Lattanzi et al.[18] found ultrasound localisation to be functionally equivalent to CT localisation.

The reality in radiotherapy departments today is that decisions regarding the purchase of new equipment are based upon the financial implication, which would therefore make ultrasound localisation the more favourable choice.

Both of the commercially available ultrasound units are mobile units that allow the prostate image to be acquired at the treatment machine whilst the patient is in the actual treatment position. The mobility of the system also means it may be moved between treatment suites which means that potentially a large number of patients could be imaged.

The initial experience of the MD Anderson Cancer Centre reports that the entire ultrasound localisation process, from acquisition of the image to the alignment process required an extra 5 min.[19] This is favourable in comparison to other image guided techniques such as CT localisation, which requires 10 min or Cone Beam CT that can require 20 min extra.[19,31] In an era, where patient waiting lists are increasing, time constraints are becoming a priority and so in this respect ultrasound localisation seems a more promising option.

Localisation of the prostate is also advantageous in the respect that it does not involve any additional radiation dose to the patient. The IMER regulations 2000,[4] state that all exposures to ionising radiation should be justified prior to the exposure being made. The actual radiation dose administered from using either CT or cone beam is actually not very well-documented in the available literature.[17,29,31] This may be due to the fact that the dose is dependent on the required image quality. Davies et al.[32] reports that the dose received from a kilovoltage cone beam acquisition can range from 0.1 to 0.5 Gy. Van Herk et al.[33] supports these findings.

As practitioners, we should be conscious of the need to justify our exposures and these authors attempted to justify such doses by claiming they are comparable to that received from EPI. However, this reasoning cannot be applied to all centres performing EPI as some acquire their portal images using the actual prescribed dose and therefore avoiding extra dose to the patient.

One may also justify daily CT examinations with the philosophy that the prostate is being accurately localised prior to treatment and so the dose is going to be delivered accurately to the prostate volume. However is this justification as convincing when ultrasound localisation is available which results in no additional dose being delivered to the patient and has been proven by Lattanzi et al.[18] to be functionally equivalent.

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CONCLUSION

In UK radiotherapy departments IMRT is still in its infancy but with the gradual introduction of more sophisticated planning systems it is likely to become more widespread. This in addition to the fact that more organ motion studies are being well publicised is probably going to lead to a feeling that EPI is no longer an adequate means of ensuring accurate dose delivery for external beam radiotherapy for the prostate and so a trend towards image guided radiotherapy will evolve.

A number of image guided modalities including CT-linear accelerator combinations, cone beam CT and tomotherapy have been developed to accurately localise the prostate prior to treatment. They each have their advantages and disadvantages, which have been well-documented.[18,19,32,34] Ultrasound localisation seems one of the most promising as it is the most cost effective, less time consuming and involves no additional radiation dose. Therefore, in a time, where financial implications and time constraints are very important, ultrasound localisation is perhaps going to be a more attractive option.

In conclusion, in theoretical terms the principles of image guided radiotherapy are attractive because they increase the accuracy of dose delivery correcting for both interfraction and intrafraction movement of the prostate, hence allowing smaller planning target margins and dose escalation without compromising normal tissue toxicity which is the basic aim of radiotherapy treatment planning.

However, the way in which we currently verify our prostate treatment plans is likely to remain unchanged until more large scale studies become available. There is a need to demonstrate the long-term outcomes of using highly conformal techniques but in addition to show how verification of the prostate using ultrasound localisation is more valuable than EPI.

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