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Literature Review

Towards an evidence-based portal imaging protocol for prostate cancer. A critical review of the literature

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Abstract

This article reviews portal imaging undertaken for prostate cancer with the intention of developing an imaging protocol for this category of patient. It explores the online and offline approaches of electronic portal imaging, when intervention for field placement errors (FPE) should take place and who actually makes this decision. The choice of reference image is discussed and the questions the use of re-simulation. This paper concludes that it is necessary to image for three fractions in the first week in order to highlight systematic errors, that an electronic portal imager is cost effective in time and money, and that radiographers should review images and make the decisions upon intervention strategies. Images will be reviewed via a quantitative template method rather than via a qualitative "eyeball" method.

Keywords

Portal imaging; prostate cancer; protocol

INTRODUCTION

The radiotherapy department in the North Wales Cancer Treatment Centre (NWCTC) opened in June 2000. Treatment practice developed via a team approach with radiographers, consultants and medical physics staff working in conjunction to provide treatment techniques and protocols. Staff came from differing centres in the UK; this ensured a diversity of technical knowledge for most treatment sites.

Portal imaging is undertaken for all radical patients but with one set of images being taken within the first three days of treatment. It was routine practice within the NWCTC to take double exposure portal images, the field component taken during normal treatment (electronic), or after the exposure (film) and the open field (plus 8 cm) taken after the exposure is terminated. Commonly 4 monitor units (μ) are given for this open field exposure. If a set up error is detected another image is obtained and either the treatment altered or the patient re-simulated. Whilst this process had been adopted as an imaging protocol was it satisfactory?

A critical analysis of the literature has been undertaken to develop an evidence-based portal imaging protocol for prostate cancer. Prostate cancer was chosen in part for the amount of information available for this site and also for the ease of obtaining good quality orthogonal images of

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pelvic anatomy. On average there are approximately 16 new prostate patients treated per month all of which will be included within this imaging protocol. This patient group is treated on a Varian Clinac 2100 (2100 C) with multi-leaf collimator (MLC) and a Varian mark 2 portal imager. This linear accelerator treats on average 36 patients in a 7-hour day.

This paper will explore how field placement error is detected (FPE) and the costs of imaging in terms of time and money. It will consider online and offline approaches to electronic portal imaging, correction thresholds, when intervention for field placement errors (FPE) should take place and who actually makes this decision. This article will discuss quantitative methods of image analysis versus more historical "eyeball" methods of image review. The paper will also evaluate the reference image and the role of re-simulation.

ERROR DETECTION

To facilitate a reproducible treatment technique it is necessary to detect treatment errors. Treatment field placement errors may lead to treatment failure or local recurrence. Reproducible treatment will also allow for reduction of treatment volumes and escalation of treatment dose.[1] A method of error detection is to undertake portal imaging of treatment portals or fields. These treatment images will show if the treatment was directed as envisaged and if there are discrepancies between what was planned and what actually took place. These discrepancies can be divided into random and systematic errors. A systematic error is a consistent error in the same direction. A random error is of an arbitrary nature, which can be in any direction around the origin Mitine et al.[2] states *they are by definition single events*. Random errors should be taken into account within the margin allowed between the clinical target volume (CTV) and the planning target volume (PTV).[3]

ICRU report 50[4] states:

For external beam therapy, margins will have to be added around the CTV to compensate for the effects of organ and patient movements and inaccuracies in beam and patient set up.

ICRU report 62[5] clarifies PTV further with the concept of Internal Margin (IM) and Set-up Margin (SM). The resulting PTV has allowance for organ motion taken into account with IM and patient positioning and alignment uncertainties taken into account with SM.

To define an adequate PTV it is advisable for a department to undertake studies to identify the level of accuracy for various techniques.[2,6,7] The standard deviation (SD) of these inaccuracies will allow correction thresholds to be decided upon for each technique. Systematic errors will be highlighted which can be removed leaving only random errors allowing the SM to be decided upon. Studies may then be undertaken to reduce random error, for example improved patient positioning. It must be stated however that to just add the IM and the SM together may lead to a too large PTV. Williams and Thwaites pp. 237[3] state:

Both internal movement and set up errors are random variations and should therefore be combined in quadrature.

This approach to define uncertainties will allow systematic error trends to be highlighted and reduced, thereby leaving only random error and organ motion, facilitating a reasoned debate upon the PTV within institutions.

Within radiotherapy departments it is common practice to use either an electronic portal imaging device (EPID) or film to verify treatment accuracy.

EPID OR FILM

Electronic portal imaging is the production of an image electronically. The image is produced via one of two methods, a video camera system or a matrix of electrodes filled with an organic liquid.[3] The latter is the type of EPID in use at the NWCTC. For film verification it is common practice to use a film cassette system. The system in use at NWCTC is the Kodak ECL film cassette system, this has been specifically designed for treatment verification with mega voltage energies. The following table (Table 1) contrasts the use of EPID versus film.

An evidence-based portal imaging protocol for prostate cancer would use either an EPID or film

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Table 1. Contrast of the use of EPID versus film[3,8]

	EPID	FILM
Size constraints	Only as large as electrodes/camera	35 × 43
Speed of image production	fast	slow
Dark room/light room	no	yes
Ease of use	Require training then simple	simple
Image manipulation	yes	no
Treatment representation	During treatment real time	Pre or post treatment
Image viewing	Can directly compare to digital simulator image/DRR	Need to work out magnification etc
Offline intervention	yes	yes
Online intervention	yes	no
Time constraints	Fast to use	Slow to use
Dose	Can take image during treatment	Image taken pre or post treatment
Image quality	Good-poor	Good-poor
Calibration	yes	no
Cost	High?	Low?
Storage	electronically	Requires considerable space

system for images due to the ease of obtaining orthogonal images of pelvic anatomy. However electronic portal images (EPI) can be enhanced digitally and viewed against simulator digital images or digitally reconstructed radiographs (DRR) without the need for de-magnification or hardcopy. A film system will require images to all be taken at the same magnification or to be de-magnified and does not allow images to be viewed digitally without the use of a scanner. An EPID allows images to be taken quickly with ease; the image is taken during treatment causing little time to be lost out of the treatment day. Whereas using film requires an extra visit into the treatment room by the radiographers in order to position the film cassette once the treatment exposure is complete.

In terms of cost, EPID is high due to initial capital outlay but the Kodak ECL film system is not cheap with continuous purchase of film, plus labour to develop the film and dark room facilities. An EPID (in 2002) can cost in the region of £90,000 dependent on system and manufacturer, this is compared to £390 for a film cassette, £3000 for a film holder and approximately £390 for a box of 100 films dependent on quantity purchased and supplier. It would appear that a film system is cheap however it depends upon the number of films that are required within an imaging protocol. Herman et al.[9] state:

It has been shown that for large centers, or even smaller centers that image frequently, EPIDs can be more cost effective than film. It is therefore expected that with more frequent use an EPID should be more economical than film.

Film and EPID allow treatment images to be viewed after treatment takes place, termed offline correction. The EPID however will allow pre-treatment images to be produced easily and swiftly, and any FPE corrected prior to giving treatment; this is termed online correction.

The portal imaging protocol for prostate cancer at NWCTC will use an EPID due to its cost effectiveness in time and money, there is no need to de-magnify images, and images can be viewed directly against the digital simulator image.

OFFLINE CORRECTION

Offline correction is intervention after treatment has taken place. It is however important to establish if the error is systematic or random. This poses the question, how many images should be taken to allow quantification of a systematic error before intervention takes place? Historically some institutions adjusted the treatment field after only one image.[10,11] However Denham[12] states:

The results from our pilot study and from statistical treatment demonstrate clearly that when random day-to-day variations are greater than a few millimetres, it is impossible to know whether a discrepancy between

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intended field center and actual field center as demonstrated on any single portal film (whether the first or the nth) is due to the presence of a systematic error or is merely the result of random variation in day-to-day set up.

On the other hand to undertake daily imaging will highlight trends and allow systematic errors to be removed. Daily imaging however may be time consuming due to the number of images that will need to be evaluated before the next treatment fraction. However there needs to be correction of an error as soon as possible to minimise any FPE.[13] Various authors have looked at this area, the following table (Table 2) summarises their findings.

In consideration of Table 2 it is not an easy choice to decide upon how many images will show a systematic error. To follow a mathematical route to decide upon number of images would be the most scientific approach but might require a computer package.

If the RT01 trial[17] is perused, portal imaging is undertaken daily for the first week of treatment if an EPID is available but if film is used a minimum of 2 images are required in the first week. This suggests that an EPID will enable ease of imaging, however viewing images, in the author's experience, can be time consuming approximately 10 minutes per image and consequently minimal imaging will require less time spent viewing images. It is also slightly ambiguous within the RT01 trial as to how many images are needed to indicate a systematic error. The MRC[17] state:

Treatment accuracy to within 2–3 mm is to be obtained whenever possible and positioning errors ≥5 mm are unacceptable. Corrections of patient positioning and appropriate resimulation will be employed if errors greater than this magnitude are apparent before the next radiotherapy fraction is delivered.

An evidence-based portal imaging protocol for prostate cancer at NWCTC based on the above data would use between 3 and 10 images to adequately predict systematic error. It is apparent that error should however be corrected as soon as possible and if more images are obtained then more time will need to be spent viewing them. The best protocol therefore may be one that uses the least amount of imaging to predict systematic error. Consequently the protocol at NWCTC will undertake 3 images in the first week of treatment this is seen as an achievable number of images that will not inhibit the uptake of this protocol due to workload issues as found by De Boer[11] in the application of the shrinking action level (SAL) protocol reported by Bel.[14] Once this protocol is in place it will be necessary to check upon its feasibility via audit and to evaluate if 3 images will allow systematic error to be predicted.

ONLINE CORRECTION

Online correction of FPE will allow intervention prior to treatment allowing errors, random or systematic to be adjusted before treatment is given. There is no need to establish which type of error is present prior to correcting it. This approach would be ideal but there is a downside, there will be increased treatment times for the patient due to time taken viewing the image, thereby limiting patient throughput. Pisani et al.[18] found the process added 10 minutes and Van de Steene et al.[19] found an increase in time of 40 percent.

Table 2. *The number of images needed to highlight systematic error*

Author	Number of images needed to show systematic error
De Boer[11]	One third of the images required by Bel et al. (1993) on average 3 images
Denham et al.[12]	Requires up to 8 images to determine if error systematic or random. The bigger the random error the more images that are required.
Amer et al.[13]	Dependent upon size of PTV margin 5–7 mm required 3 images. PTV margin ≥8 mm requires no imaging.
Bel et al.[14]	Correction undertaken after first fraction if action level reached however De Boer et al. (2001) found this protocol may require 10 images to indicate systematic error
Mubata et al.[15]	Between 3 and 8 images are evaluated before a decision is made upon systematic error. The number of images is dependent upon the day the images are reviewed rather than any mathematical principle.
Yan et al.[16]	4–9 images

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Pre-treatment exposure every fraction via the double exposure method of portal image production will also cause increased dose to the patient. Commonly 3 to 4 μ are given to the open field this equates to an additional 120 μ over a 20 fraction course of treatment for lateral and AP images to an area outside the treatment field. It may be difficult to correct for this exposure, as it is a larger size than the treatment field however the treatment field portion of the exposure can be corrected for easily. It may be advisable therefore, if daily online pre-treatment imaging was undertaken, to do a single exposure of the treatment field only, allowing dose to be easily corrected for. However this may impede the use of the image due to lack of anatomy to match the image against with prostate patients having a small field.[20]

To use online verification will allow correction on a daily basis but is it really necessary for all prostate patients? To undertake online correction will decrease patient throughput, only 20 patients treated in a day if 10 minutes was added to each patients' treatment time. The implications of this increased treatment time at NWCTC would mean increased waiting lists; prostate patients are not the only patients that need treatment on the 2100 C. However online correction may have a place in a portal imaging protocol that uses offline images for all patients with a threshold value that when passed necessitates online correction. To find this value a reproducibility study should be undertaken within a department this will enable the standard deviation (SD) of any error to be found. It would not be unacceptable to use two standard deviations (2 SD) as the threshold value because 95 percent of the population observations in this case portal images will fall within two standard deviations of the mean. Without this data from an accuracy study it is reasonable to use SD quoted in the literature. Hurkmans et al.[21] state:

In general, a standard deviation of 2.5 mm and 3 mm or less for the random and systematic error can be considered "state of the art" for prostate and pelvic treatment techniques, respectively.

Thus an intervention value of 2 SD is 6 mm so consequently any FPE that is 6 mm or over should have an online image taken on the next treatment fraction. This will avoid large geographical field placement error and allow intervention to take place prior to treatment if a similar discrepancy is seen. If a similar error is not seen it may have been a random error on the first fraction however it may be of value to undertake online imaging prior to the third fraction to confirm all is well.

CORRECTION THRESHOLD

It is apparent that whichever method of imaging on or offline that an intervention threshold is chosen within a protocol to enable consistency. Is it reasonable to make movements of 1 mm for FPE and indeed can we be this accurate in our measurements? The following table (Table 3) highlights the amount of FPE before intervention takes place in various articles.

What should our level of accuracy be? The MRC (17) RTO1 states:

Treatment accuracy to within 2–3 mm is to be obtained wherever possible and positioning errors ≥5 mm is unacceptable.

Table 3. *The amount of FPE before intervention takes place in various articles*

Author	Intervention	Online or offline
Valicenti et al.[10]	>5 mm	Offline
De Boer et al.[11]	≥1 mm	Offline
Mubata et al.[15]	Each viewed on its own merit >6 mm adjusted by next set up	Offline
Yan et al.[16]	≥2 mm	Offline
MRC[17] RT01 trial	≥5 mm unacceptable	
Pisani et al.[18]	>2 mm	Online
Van Lin et al.[22]	>2 mm	Offline
Alasti et al.[23]	>5 mm	Online
Balter et al.[24]	>5 mm	Online

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Hurkmans et al.[21] supports this 2–3 mm accuracy, certainly if we can measure discrepancies this accurately we should act upon them rather than waiting for >5 mm FPE before intervening. A point to note however is that to have an achievable action threshold it is necessary to know the SD of any error, it is pointless to try and correct for an error that is below the SD of a particular technique. This protocol will use 3 mm as an intervention value, it is realistic to correct for error of 3 mm and over however it is also necessary to undertake an accuracy study to ensure that the SD of error at NWCTC is not above this level.

TIME TRENDS

Whilst the above is about intervention to enable initial accuracy there is evidence to suggest that there may be a drift of accuracy over time.[21] If any inaccuracies are present in this fashion they should be able to be seen via weekly offline imaging rather than online imaging. Yan et al.[16] found that only 1 out of 20 patients in their study benefited from continuous imaging. These images were looked at offline but it does highlight limited need for daily imaging which is, in essence, online imaging. The portal imaging protocol for prostate patients at the NWCTC will undertake weekly imaging to ensure there is no drift in accuracy over the treatment course. If any FPE is seen, then more images will be undertaken to ensure all is well for an individual.

WHO MAKES THE DECISION UPON INTERVENTION?

It is imperative with online and offline correction to establish who decides upon any intervention, doctor or radiographer? It is well known that in a busy department that to expect a clinical oncologist to be available to view images online may be impractical.[20] These time constraints may also inhibit the viewing of images for offline portal imaging. Hardcopy images have been described by Hatherly et al.,[20] which may allow images to be viewed in an effective manner, however the time constraints that doctors face will still remain paramount. It may be more effective for radiographers to follow a training programme and then for radiographers to assess and decide upon any intervention required to agreed guidelines. Indeed with the advent of in-house postgraduate education, recognition of the radiographers ability and expertise can be shown, thereby providing reassurance to the doctor that radiographers are best placed to review images. Perera et al.[25] found that the doctors and radiographers fared equally in identifying FPE although they did find great subjectivity in the viewing of portal film. This subjectivity may be reduced if images are viewed digitally; digital simulator images are reality with modern simulators. This will facilitate ease of viewing without the need to calculate magnification factors. Simulator images will be able to be viewed side-by-side and indeed overlaid allowing quantitative assessment of the images. Indeed in a study undertaken by Pisani et al.[18] using a template alignment technique (areas of anatomy are highlighted on a reference image and aligned on the portal image), there was an average inter-observer variability of less than 2 mm. There is at the NWCTC the facility within The Vision environment (Varian) to view images digitally and use a template technique similar to Pisani et al.[18] A template technique should also allow more accurate information to be measured as it relies on a number of points rather than just measuring from a single point on an image. It should be stated however that anatomy can be distorted due to patient rotation and anatomical distortions due to alteration in flexion of the patient differing pelvic tilt for example.[6,18] If digital simulator images are not available the simulator radiograph can be scanned into the system via a suitable scanner and transferred via a network. Indeed most manufacturers of modern radiotherapy equipment are making equipment Dicom 3 RT compliant to facilitate ease of networking. This networking will allow images to be viewed digitally enabling ease of quantitative assessment rather than hard copy images viewed qualitatively by eye alone, which may cause subjectivity in viewing the image.

The portal imaging protocol at NWCTC will allow radiographers to assess the image to an agreed protocol, subject to training, any images that are a cause for concern will be discussed with the clinical oncologist and a paper hard copy will be stored with the treatment card allowing the doctor to see any images taken when the patient is reviewed. The images will all be assessed via a quantitative template method rather than by eye alone.

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REFERENCE IMAGE

The reference image is the image that all others should be reviewed against, and could be regarded as the gold standard. It is however important to decide which image this should be, the digital reconstructed radiograph (DRR), the simulator image or the accepted portal image. Each may have their own inherent problems. The DRR quality is related to the thickness of CT slices, the thinner the slice the increased quality; certain planning systems however will not handle un-contoured slices.[26] The accuracy of the simulator image will depend on how robust the simulator verification procedure is, random and systematic error will not only manifest themselves on the treatment unit. The DRR is the only true representation of the patient's position from their planning scan.[26] The DRR is also made up of data from differing periods of time so consequently it is reliant upon the patient keeping still. The first accepted portal image may be within acceptable tolerance but not an exact replica of the simulator image however Rabinowitz et al.[6] found

The discrepancies between simulation and treatment are significantly greater than the treatment to treatment variations at most sites.

All things considered it may be best to compromise and verify patients on simulator against a DRR and to use this simulator image due to its increased quality, as it is not dependent on CT slice thickness. It is necessary however to consider that we may not always get consistency between the DRR and simulator image. It is necessary for each department to subsequently have a plan of action in this eventuality. Stanley[23] states:

When set-up errors have been encountered on simulator, the course of action has been to start the radiotherapy, take EPI's of all fields and reassess. If the same error is apparent then an isocentre movement is made.

This approach seems sensible; after all it may have been a random error at simulator stage. Certainly at the NWCTC the simulator procedure appears robust but it is not tested against DRR at present due to technical difficulties.

Once confidence is gained that the DRR is indeed the gold standard and that there is no systematic error between CT and the treatment unit this category of patients may be able to be verified against DRR alone without simulation.

RE-SIMULATION

If a large FPE is detected do patients require re-simulation? This question is posed because some may think that re-simulation is the only option with large FPE. In the authors experience re-simulation may not actually solve FPE the patient is re-simulated all appears well however the next portal image is the same, which is in keeping with Rabinowitz et al.[6] It is difficult to know why this happens for some patients and not others, it may be anxiety at having to be re-simulated, or unfamiliar faces. An EPI is taken during treatment and is representative of the patient's position any move should surely be based upon what is actually taking place. This would be a case for online imaging rather than re-simulation if the FPE were above certain threshold for example 6 mm in this protocol. If however the patients' contour has altered shown by FSD differences there is a case for re-simulating/planning because new outline may need to be taken. Indeed if substantial differences have occurred the patient may require a new CT planning scan.

CONCLUSION

The Portal imaging protocol for prostate cancer at NWCTC will need to take account of various issues. It is necessary to decide upon the method of imaging, film or EPID. An EPID system whilst initially expensive will allow fast and efficient imaging whereas film is slow and not able to be viewed online. This protocol will use an EPID due to its minimal impact on the working day and its cost effectiveness. The protocol will have an action threshold for intervention of 3 mm and an upper limit that facilitates immediate action via online imaging of 6 mm. This protocol will use an offline approach for viewing the EPI, unless the upper limit of 6 mm is reached. To highlight any systematic error three images will be taken before a decision is made on any intervention, and then weekly imaging will be undertaken. It is important to consider how much time is available for viewing images. Online imaging is time consuming but it is also time consuming if imaging is

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Table 4. Definition of an evidence-based portal imaging protocol for prostate cancer at the NWCTC

Mode	EPID
Number of images first week	3
Correction threshold of FPE	3 mm
Upper FPE limit before immediate action required	6 mm
Reference image	Simulator image
Weekly imaging	Yes
Offline imaging	Yes unless upper action limit reached
Online imaging	Only if upper action limit reached, then for next two fractions
Re-simulation	No

undertaken offline over several days, as images need to be reviewed. It is imperative that the reference image is one that is an accurate representation of the treatment field; at present, in the NWCTC, this is the simulator image. However it is important that departments decide upon which image will be used as the reference image DRR or simulator image, strategies will have to be put into place if conflict arises between DRR and simulator image. Decisions also need to be about who can review images. At NWCTC, radiographers will review images and make decisions upon any FPE. The images will be viewed digitally and reviewed via a quantitative template method rather than via a qualitative "eyeball" method.

Table 4 defines an evidence-based portal imaging protocol for prostate cancer at the NWCTC. Patients will not be re-simulated unless there is a change in their contour.

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