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Review article

Image guided radiotherapy: Current status of soft tissue imaging

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ABSTRACT

Image guided radiotherapy has evolved from two dimensional (2D) megavoltage imaging, which allowed verification with respect to bony anatomy, to three dimensional (3D) kilovoltage imaging which enables soft tissue structures to be used for verification. Alongside the technological developments, treatment delivery techniques have become more sophisticated and the potential to adapt treatment delivery to changes in tumour and/or organs at risk is increasing. This review explores the current status of soft tissue imaging techniques in conjunction with the potential clinical impact. The common tumour sites where the new treatment techniques are being investigated are identified and it is seen that to support the implementation of these techniques, investment in capital equipment and staff training is essential.

Introduction

Image guided radiotherapy (IGRT) is not a recent development, it has been mentioned in the literature as early as 1958 and was then achieved by mounting a portable X-Ray unit on a cobalt unit gantry.[1] Until electronic portal imaging (EPI) was developed in the 1980's, verification was performed using planar films.[2,3] Although EPI increased the efficiency of image acquisition and registration with the use of software tools to aid registration, the images remained 2 dimensional (2D planar). More recently, the development of in-room 3D imaging has had a major impact in on treatment verification.[4–6]

Scope of review

IGRT has been 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'.[7] However for the purposes of this review soft-tissue imaging will be the focus of interest and the current status together with the impact of clinical implementation will be discussed.

Literature searches

To establish the current status keywords 'Image guided radiotherapy AND organ motion' and 'Plan of the day AND radiotherapy' and 'adaptive radiotherapy (ART)' were entered into the online search engine Pub Med to retrieve articles which investigated soft-tissue image guided techniques. Duplicated articles were discarded and papers excluded if not relevant, for example, planning studies or dose escalation studies. In addition 'implementation and image guided radiotherapy' was used to identify important factors relevant to implementation. National experts were also consulted for knowledge of factors relevant in the UK.

Current status

The searches showed that the studies investigating 'IGRT and soft tissue motion' were focused on a limited number of sites; prostate cancer being the most frequent, followed by bladder, cervical, breast and paediatric cancers.

The 'plan of the day' and 'adaptive radiotherapy' (ART) searches revealed similar trends with the most common sites investigated were bladder cancer and prostate cancer followed by head and neck cancer and cervical cancer. The majority of the studies were performed in Australia, United Kingdom (UK), Netherlands, and United States of America (USA). The approaches to compensate for organ motion varied within each tumour site.

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Plan of the day

The plan of the day approach involves creating a library of plans with varying margins from either one or multiple planning CT scans. At the time of treatment, after image acquisition and bony anatomy registration, the plan which is the best fit i.e covers the tumour volume, can be chosen. This approach was investigated in bladder and cervical cancers.

Bladder

Initial studies investigating the plan of the day strategy demonstrated that although a choice of three plans benefited 75% of patients (15 out of 20), the remaining 25% would have required alternative approaches.[8] These five patients would have either required re-planning because of a systematic change in bladder volume or required repeat voiding because the bladder was outside the planning target volume (PTV). These changes were not predictable and it could be expected that using individual patterns of filling to create margins would improve the success rate of the adaptive plans. However this has been shown not to be the case in a later study which used individual patient predictive margins.[9] Whilst 51% of patients demonstrated the need for adaptive plans, 27% of treatments were not suitable for any adaptive plan.[9] Nonetheless, the closest adaptive plan did show improved coverage compared to the conventional plan. Plan of the day promises to be an effective approach for patients receiving radiotherapy for bladder cancer. However the variability of the mean bladder volume makes accounting for all eventualities difficult. Therefore it is essential that all professionals assessing the images have the appropriate skills to be able to use professional judgement to ensure confident and efficient daily image assessment.

Gynaecological cancer

Patients receiving radical radiotherapy for cervical cancer are another potential group to benefit from IGRT. Motion and adaptive studies in these patients are more recent than those of bladder cancer patients and the knowledge gained in developing approaches for bladder cancer patients has been transferred. In order to develop appropriate IGRT and ultimately ART process it is essential to firstly characterise organ motion. An early study utilised magnetic resonance imaging (MRI) in a group of 20 patients with cervical cancer and results demonstrated that motion of the cervix could be as great as 2.2 cm in the superior-inferior (SI) direction and 1.5 cm in the anterior-posterior (AP) direction, whilst the uterus displayed motion up to 3.4 cm SI and 4.4 cm AP.[10] Large changes in rectal and bladder volume (relative change 380% and 450% in the bladder and rectum respectively) was a potential cause of motion and interestingly was despite the use of laxatives (12–12 h prior to scan) and bladder instructions (drink 500 ml of water 1 h in advance after voiding completely). Two more recent studies have shown similar results, although in a different group of gynaecological patients. Harris and colleagues assessed tomotherapy images acquired in 22 patients who were receiving post-operative radiotherapy and the centre of mass of markers placed in the vaginal wall moved a mean of 5.8 mm (0.6–20.2 mm).[11] They concluded that margins of PTV of 16 mm would be necessary to cover the vaginal wall in 95% of patients, although it was noted that the margin could be reduced in the RL direction. The motion reported was observed as random and could not be predicted by factors such as body mass index, age, menopausal status or maximum motion. Bondar compared individualized treatment strategies i.e either using a PTV that encompassed the entire motion determined by a full bladder and empty bladder CT scans or using a two plan library, a three plan library and a daily plan library, with standard population-based margins.[12] The margins using the adaptive planning were reduced by up to 3 cm and resulted in better rectum and bladder sparing. The online-adaptive RT, using a two-plan library resulted in the most organ-at-risk sparing for patients with large cervix - uterus motion.[12] This approach seems promising and the first clinical implementation studies have been presented using 4–6 plans.[13]

Implementation of plan of the day

The plan of the day approach involves creating multiple treatment plans which may or may not include multiple planning CT scans. To be effective the number of plans produced need to offer adequate variability without any plan being redundant. In a study that implemented plan of the day using a small medium and large PTV derived from two CT scans, the large scan was used only 6% of the time (8/139).[14] It may be possible to reduce the number of plans or alter the PTV margins to improve the distribution of plan choice. Using the average of images rather than one image was shown to improve the distribution of plan selection but at the cost of acquiring additional images, in this case CBCT images, and creating a new plan quickly. This approach would not be feasible for hypofractionated treatment.

Staff training is essential to allow confident and efficient assessment of plans. Training programmes can be adapted to the centres needs and include local programmes and/or in combination with higher education institutions, or indeed elearning methods. The latter has been shown to be effective where large geographical distances have made workshops impractical[15] but also may be useful where it is difficult to resource staff to attend workshops.

Prostate

Prostate cancer was one of the most common sites investigated using soft tissue imaging. However unlike cervical and bladder cancer sites where a 'plan of the day' strategy was the most common strategy investigated, the planning technique investigated for prostate cancer patients has been adaptive or composite planning. Characterising the motion, again an essential step in the process of developing an adaptive strategy, was performed using fiducial markers before the advent of soft tissue imaging at the time of treatment.[16–18] Independent prostate motion in the anterior-posterior direction was well defined but rotations are also a dominant feature in prostate motion and although was demonstrated with fiducial markers[16] it has been shown to be more accurate to determine rotations using 3D soft tissue imaging.[19] The prostate is also made a more complex target volume by the inclusion of the seminal vesicles which move significantly more than the prostate and so require independent margins.[20] The use of adaptive techniques have produced conflicting results and, whilst some studies show that the average of the first 4 treatment days images can improve dose delivery,[21] other studies show that up to 10 fractions are required before improvement can be seen.[22] Even so, the benefit of adaptive technique compared to on-line imaging is modest[23] possibly due to deformation and/or residual error and/or on-line correction.[24] With the increasing implementation and investigation of extreme hypofractionated radiotherapy for prostate cancer, on-line image guidance may be more appropriate.

Head and neck

The future of advanced radiotherapy techniques for head and neck cancer is moving towards adaptive radiotherapy by re-planning during treatment.[25] This can compensate for weight loss