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Original Article

Provision of IMRT in the UK. Part 1: A review of planning, delivery and related technologies

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Abstract

The concept of intensity-modulated radiotherapy is now familiar to everyone working in radiotherapy in the UK. To date however, the majority of UK radiotherapy departments have yet to offer this technique clinically. Implementation of IMRT represents a significant change in practice from the delivery of conventional or conformal treatment, requiring careful planning and a full understanding of the issues and new technology involved.

This paper provides a review of the stages involved in the IMRT process; from localisation and immobilisation through inverse treatment planning and quality control to delivery and verification, highlighting those aspects that represent a significant change in practice or approach.

Current and future developments that are expected to enhance or provide alternatives to IMRT, such as developments in radiobiological modelling, functional imaging, tomotherapy and proton therapy are discussed.

Keywords

Intensity-modulated radiotherapy; radiotherapy-related processes and technologies

INTRODUCTION

There is little doubt that if correctly implemented, intensity-modulated radiotherapy (IMRT) offers a major step forward for external beam radiotherapy. The ability to produce dose distributions that conform to irregular 3D targets has the potential to greatly reduce normal tissue complication probability (NTCP) through greater sparing of normal tissues or to increase tumour control probability (TCP), through dose escalation.

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Like any other new technique or technology to be implemented, many lessons have to be learned and issues addressed during the initial transition from theory to clinical practice. In parallel with the growing experience of clinical staff and the wider implementation of IMRT, the associated equipment for planning and delivery will be refined and improved by equipment manufacturers. This will be expected to result in a rapid development of technology that staff will need to keep abreast of.

Advances in radiobiological modelling offer the use of biologically-based, rather than dose-based optimisation for IMRT planning. This development is discussed, as are alternative methods of IMRT delivery and a consideration of the potential benefits of proton therapy.

A quantitative review of the current and planned capacity for IMRT in the UK, including lessons learned by those centres having already implemented this technique clinically will be presented in a second paper.[1]

LOCALISATION AND IMMOBILISATION

The reduction of systematic error (in target localisation and patient position) and random uncertainty (reproducibility) is increasingly important with the progressively more complex treatments now offered from conformal and IMRT treatments.

A significant reduction in the amount of normal tissue irradiated can be achieved through the greater dose conformity to irregular 3D target volumes provided by IMRT, without any reduction in the margins between clinical and planning target volumes (CTV and PTV respectively). To illustrate this consider a simple case of conformal radiotherapy, shown in Figure 1, applied to a spherical CTV of 3 cm diameter. Applying a uniform 0.5 cm margin leads to an irradiated volume of over twice the GTV volume, even when fully conforming to the GTV shape. Compare this with an unconformed cubic PTV that irradiates over four times the GTV volume. In a similar manner we would expect significant reductions in total irradiated volume through conformity to irregular, particularly concave, target shapes through IMRT.

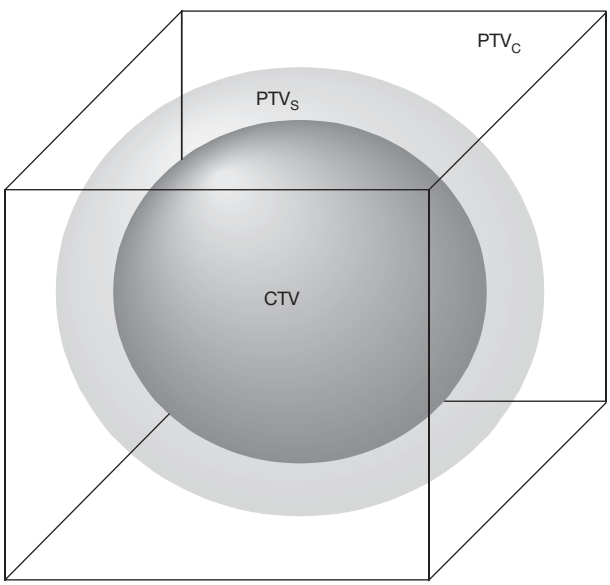

Figure 1. Illustration of the importance of margin size and dose conformity on the volume of normal tissue irradiated. A central CTV of 3 cm diameter is surrounded by a 4 cm diameter spherical PTV (uniform 0.5 cm margin, PTV$_S$) and unconformed cubic PTV of side 4 cm (PTV$_C$). The corresponding volumes are 14.1 (CTV), 33.5 (PTV$_S$) and 64 (PTV$_C$) cm^3.

Image fusion of CT, MR and PET modalities, provides more accurate data for establishing the position and extent of the CTV and therefore PTV. Indexed treatment couches allow immobilisation devices to be fixed during treatment, minimising the risk of variation.[2] Skills in their use and the development of acceptable protocols for imaging are roles radiographers have developed with the changing emphasis in the treatment process. These parallel developments in localisation and immobilisation techniques offer the potential of further reduction in normal tissue irradiation through the reduction in margins between CTV and PTV.

TREATMENT PLANNING

Inverse treatment planning requires not just the identification of target volumes and organs of risk (in 3D), but also the identification of dose limits (both maxima and minima) and relative importance weightings for each region in order to obtain the desired dose distribution. It is important to appreciate that the term "optimised" does not mean that the best possible plan has been produced, as this is fully dependent on the particular dose and weight parameters used. A truly optimised plan would also take account of the radiobiology involved.[3–8] An example of dose and weight constraints used to guide the inverse planning optimisation process for IMRT to the prostate is given in Table 1. These volumes and

Table 1. *Examples of parameters required for inverse treatment planning of the prostate. GTV and PTV refer to gross tumour volume and planning target volume respectively*[32,33]

Region	Max dose (Gy)	Weight (%)	Min dose (Gy)	Weight (%)
GTV	74	10	68	50
PTV	66	100	64	100
Body	50	50		
Rectum	40	30		
Bladder	50	10		
Femur	30	1		
Bowel	50	10		

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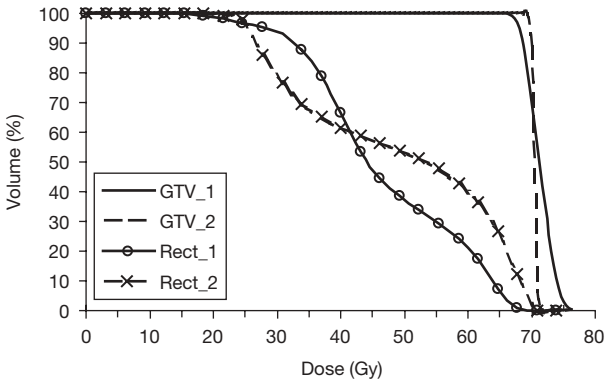

Figure 2. Comparison of prostate IMRT plans using dose-volume histograms (DVHs). GTV_1 and GTV_2 represent the DVHs for the gross tumour volume in two alternative beam arrangements. Rect_1 and Rect_2 are the corresponding rectal DVHs.

constraints alone, however, are unlikely to be sufficient to produce satisfactory dose distributions. Additional volumes, with corresponding dose and weight constraints may need to be specified to guide the optimisation process.

The choice of best plan from alternative multiple-segment beam arrangements may make use of dose-volume histograms, an example of which is shown in Figure 2 for two possible IMRT plans for a prostate tumour. As the figure indicates, it is not immediately obvious which of the two plans would be superior. The choice requires an understanding of the relative biological effects resulting from these two different dose distributions to the rectum, in particular. In this case, this involves knowing whether a large low-dose volume is less likely to lead to complications than a small, high dose volume. The use of single-valued radiobiological quantities such as tumour control probability (TCP)[9,10] and normal tissue complication probability (NTCP)[11,12] can greatly ease this distinction between alternative plans, however the parameters used in these models remain to be firmly established.[13]

QUALITY CONTROL AND VERIFICATION

Verification of predicted dose distributions represents a significant challenge for staff with responsibility for dosimetry. For conventional treatments, in vitro point measurements could be made in fairly uniform dose regions, where the finite size of detectors used and the effects of small uncertainties in measurement position would not lead to significant differences in measured dose. For IMRT fields however, one or both of these assumptions may fail when considering the cumulative dose from many field segments. A full arsenal of point and array detectors, film, TLD, mosfet and polymer gels have been used to help in this dose verification process.[14–16] Great care and consequently time is needed, particularly in the commissioning phase of IMRT implementation.

Verification of anatomical position through traditional imaging of each beam portal becomes problematic for multiple static segments of small size and varying intensity, encompassing little or no distinctive anatomy. Dynamic IMRT delivery methods pose similar problems. The taking of orthogonal images to define the isocentre appears currently to be the favoured method. Despite being of little use for anatomical verification, cumulative electronic portal images (EPI) of each beam segment can be used to verify multi-leaf collimator (MLC) leaf positions and intensity distributions.[17]

Further developments are now available to monitor on-line positioning and movements during treatment such as the use of fiducial markers[2] and ultrasound for prostate positioning.[18] These developments will become an integral part of the treatment process but will initially, at least, impact upon the time taken for each treatment.

FUTURE DEVELOPMENTS AND ALTERNATIVES TO CONVENTIONAL IMRT

As indicated in the introduction, radiobiological modelling is expected to have an increasing role in radiotherapy treatment planning. This can be either as simply providing single-valued parameters indicating plan effectiveness (TCP, NTCP), or as an integral part of the inverse-planning algorithm, optimising on biological outcome rather than physical dose. Establishing robust and reliable models for equivalent uniform dose (EUD), TCP and NTCP is ongoing.[3,4,6,7,19,20] Accurate modelling also requires appreciation of the expected systematic and random uncertainties in delineation of the target and organs at risk at the planning stage and during delivery of IMRT.[21,22]

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Minimising these uncertainties is being addressed through various approaches, from the use of a number of immobilisation systems to improve positioning reproducibility,[23] aiding identification of organ movement on portal images through the use of seed implants,[24] improving the quality of imaging on the treatment unit through kV and MV cone-beam CT,[25,26] through to gating radiation delivery according to the breathing cycle.[27]

An alternative to delivering IMRT via conventional 2D beam segments is provided by helical or serial tomotherapy.[28] In this delivery mode a target is treated slice by slice by rotating the radiation source around the patient in much the same way as a CT scan is acquired. Intensity modulation is provided by simple multi-leaf collimators that can be in either an open or closed state. Tomotherapy can be delivered using a standard linac with an externally mounted collimator to provide a narrow slice (nominally 1–2 cm width).[29] Development of a purpose-built tomotherapy unit in which a vertically-mounted accelerating waveguide is housed within a CT-like gantry has been under development for some time.[25,28,29] A diagnostic tube is also mounted in the gantry, allowing both kV and MV quality CT imaging to be performed.

A more significant development in target definition itself may potentially be provided by functional imaging using positron emission tomography (PET) or magnetic resonance spectroscopy (MRS). The aim of this technique is to identify the relative metabolic activity or degree of abnormality within tumours and in a similar manner identify the more functionally important regions of normal tissue. This information could be utilised in IMRT inverse planning, to deliver non-uniform dose distributions in the form of concurrent boosts to active nodules within the tumour volume and also preferentially sparing functionally important regions of normal tissue.[30]

While (photon) IMRT is a significant step forward for conventional external beam radiotherapy in conforming dose to the tumour, charged particles offer the significant advantage of having well defined, finite ranges in tissue that are determined directly by their kinetic energy.[31] The availability of proton therapy has been increasing over recent years, with over 20 facilities currently operating and 9 new facilities in planning or construction stages world-wide. This provides the opportunity for both energy and intensity modulated beams, leading to greater concentration of radiation dose within the tumour and less peripheral dose to normal tissue. Figure 3 shows a comparison between single field photon (6 MV) and proton dose deposition, illustrating how the depth and width of a simple spread-out Bragg peak is custom made to the required target dimensions.

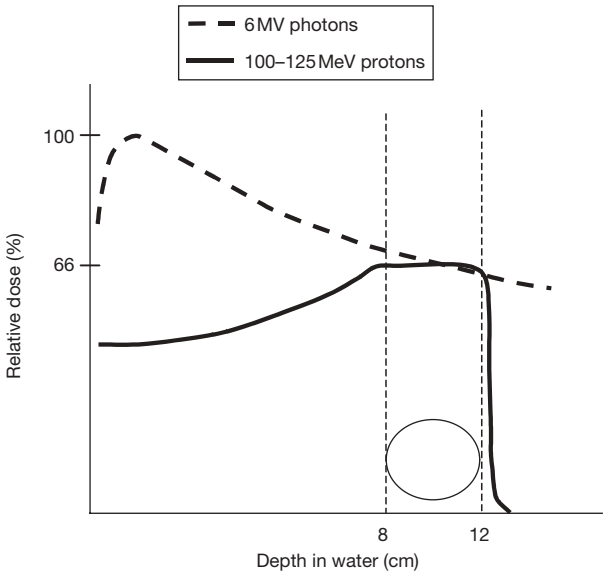

Figure 3. Comparison of dose deposition with depth in tissue for a single 6 MV photon beam and an energy-modulated proton beam. Target dimensions are indicated.

CONCLUSION

This paper reviews the major changes in treatment planning, delivery and verification that are faced by radiotherapy departments wishing to implement IMRT. This includes the use of inverse rather than forward treatment planning, itself requiring new skills in the identification of dose constraints for target and organs at risk and a familiarity with the representation of dose distributions by dose-volume histograms (DVHs). The difficulty in dose verification of many small field segments is discussed, as are the practical aspects of delivering this new treatment modality.

Developments that complement or offer an alternative to what is now conventional linac-based IMRT are also reviewed. These include ongoing

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work to increase the reliability of radiobiological models, advances in imaging equipment and techniques and the alternative approaches offered by tomotherapy and proton therapy.

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