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Editorial Comment

Intensity Modulated Radiation Therapy

Vedang Murthy *, Alan Horwich

Academic Unit of Radiotherapy and Oncology, The Royal Marsden NHS Foundation Trust and The Institute of Cancer Research, Downs Road, Sutton, Surrey SM2 5PT, UK

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For the non radiotherapist, the recent developments of conformal radiotherapy and Intensity Modulated Radiotherapy (IMRT) may represent merely an increase in mystification from a baseline already shrouded in the obscure dark arts of physics. However, the principles of these developments are simple and as the technologies become available, there are real opportunities to improve the local control of common cancers and to reduce some of the treatment related toxicities.

Previously, planned radiotherapy involved adding the effects of a small number of co-axial radiation beams. When viewed in a cross-section these produced a distribution of isodose lines akin to the altitude lines on a contour map. Calculations were based on a cross-section through the centre of the area intended for treatment. The isodose lines were extrapolated superiorly and inferiorly to cover the length of the tumour with margins added for factors such as microscopic tumour extension and patient and internal organ motion during and between fractions.

With improvements in imaging it became apparent that large volumes of adjacent normal tissues were receiving high dose radiation as a consequence of the simple field shapes. This normal tissue was at a greater risk of radiation toxicity in a volume-dependant way and limited the radiation dose safely deliverable to the target volume. Three Dimensional Conformal Radiotherapy (3D CRT) overcame this limitation with improvement in imaging and treatment planning programmes which allowed routine use of irregular beam shapes contoured to the shape of the tumour. A higher dose could potentially be delivered to the target volume than with the conventional rectangular or square fields as less normal tissue was treated and toxicity was reduced [1]. IMRT is an advanced conformal radiotherapy technique in which the intensity of radiation across each radiation beam may be varied. This enables more control over the dose distribution to the target area and in particular enables shaping of the high dose region to create a concavity to avoid a critical normal organ, as illustrated in Fig. 1. Also, IMRT can create intentional inhomogeneities within the target volume, such as areas of increased dose to parts of the tumour judged to be more resistant, a paradigm shift from conventional methods where dose homogeneity within the target has been the goal.

Planning of IMRT increasingly involves collaboration with a diagnostic radiologist for accurate delineation of the tumour volume and organs at risk, using multimodality cross-sectional imaging techniques, including MR and PET. The complexity of available beam directions, field shapes and intensity profiles has led to an inverse approach to radiotherapy planning in which, rather than trying out a preconceived field arrangement to see the subsequent dose distribution, dose constraints are placed on particular volumes of critical normal and tumour tissues describing the volume of each structure that is allowed to receive a particular dose. The planning computer then identifies the optimum plan. Treatment delivery is also complex, but can be performed by a number of automated techniques, many of them still evolving. A useful review of the technical and clinical issues involved in each approach and commonly used nomenclature has been published by the IMRT Collaborative Working Group [2].

Although IMRT has the potential to be used for any site, it has been investigated mostly in prostate, head and neck, breast and gynaecologic malignancies where

* Corresponding author. Tel.: +44-20-8661-3181; fax: +44-20-8643-8809.
E-mail address: vedang.murthy@rmh.nthames.nhs.uk (V. Murthy).

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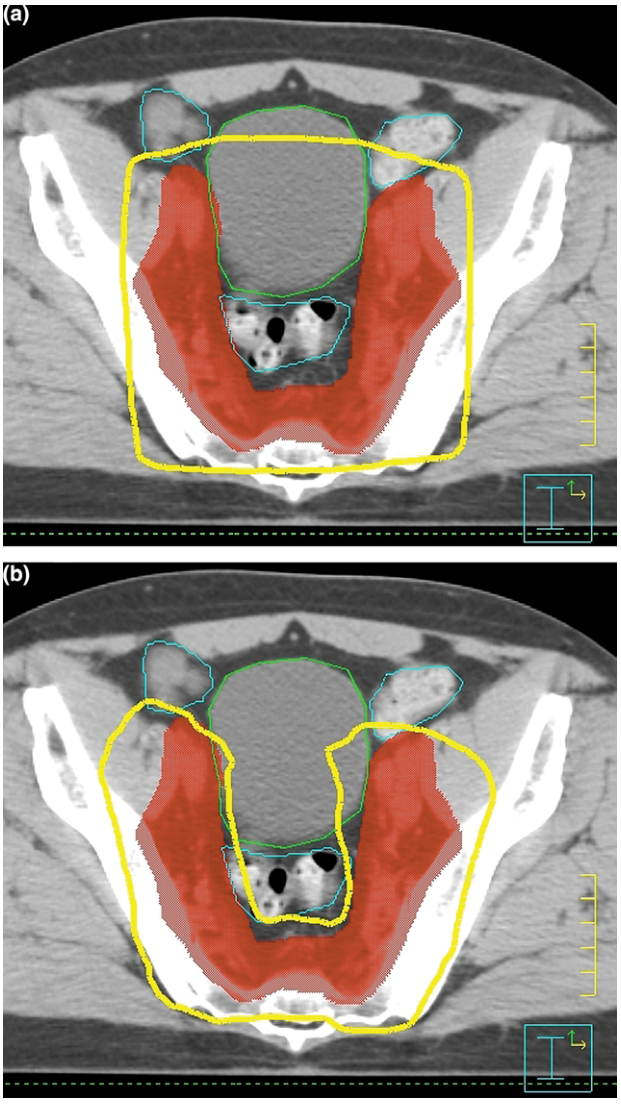

Fig. 1. Cross-section through the pelvis showing the target volume (red). Normal structures such as bowel (blue) and bladder (green) are also outlined. The yellow line represents the high dose envelope (90%) encompassing the target volume using 3D conformal radiotherapy (Fig. 1a) and IMRT (Fig. 1b).

dose-limiting normal organs are close to the target. Theoretically, it has the largest potential to benefit patients where the target volume wraps around a critical normal structure [3] e.g. prostate cancer where the seminal vesicles may encircle the anterior rectal wall or pelvic lymph node metastasis surrounding the bowel.

IMRT may thus allow radiation dose escalation. For example, data is reported from the Memorial Sloan Kettering Cancer Centre (MSKCC) on dose escalation for localised prostate cancer up to 81 Gy with IMRT [4]. At this dose, they have reported a reduction in the incidence of significant rectal toxicity from 14% with 3D CRT to 2% with IMRT. Planning studies have shown that the IMRT technique achieved better target coverage while restricting the rectal and bladder dose [5]. These encouraging results have led to investigation of the dose being escalated further to 86.4 Gy. This is remarkable considering the fact that the standard dose in the UK is 66–70 Gy. IMRT is also being explored in locally advanced prostate cancer where recent evidence suggests that there may be a role for irradiating the pelvic lymph nodes [6]. Planning optimisation studies have shown that IMRT can reduce the volume of bowel irradiated to critical doses. When treating pelvic nodes to 50 Gy, the mean volume receiving a high dose (>45 Gy) was significantly reduced for rectum from 50% with 3D CRT to 6% by IMRT, for bladder from 52% to 7% and for small bowel from 28% to 8% [7].

IMRT also has great potential also in head and neck cancers. Loco regional failure is a major cause of treatment failure in these tumours and dose escalation may be of benefit. However, side effects such as xerostomia, myelopathy, and bone necrosis may be debilitating and have a direct bearing on the patients' quality of life. IMRT can achieve dose escalation while avoiding toxicity to the surrounding critical structures such as spinal cord and salivary glands [8].

Similarly, in breast cancer, radiotherapy with the aim of breast conservation seeks to maintain cosmesis with minimal risk of lung or cardiac damage. A recent meta-analysis suggested that the benefit from conventional radiation in terms of reducing breast cancer specific death was offset by increased risk of late cardiac death [9]. Mechanistic studies have shown abnormal myocardial perfusion after standard radiotherapy to the left breast [10]. Dosimetric studies of IMRT have reported significantly improved dose volume profiles for normal tissues like heart, coronary vessels, lungs and the opposite breast [11] and randomised trial data have confirmed improvements in dosimetry within the target volume [12].

Another potential application of IMRT is the ability to deliver differential dose to multiple targets within the treated volume. Hypoxic areas within the target are known to be resistant to radiation and therefore delivery of a higher dose to these areas may be beneficial. Development of imaging modalities such as endorectal MRI and MR spectroscopy (MRS) have made it possible to identify foci of carcinoma and areas of hypoxia within the prostate. Pickett et al. [13] used IMRT to boost an intraprostatic lesion, defined by MRI and MRS, to 90 Gy while the rest of the prostate was treated to the conventional dose of 70 Gy.

As with any technological advance, the uncertainties and potential disadvantages must be considered. IMRT tends to expose larger volumes of normal tissue to radiation, which may increase carcinogenic risk. There is also an increase in the total body dose. Patient movement and internal organ motion may be more significant with high precision treatment techniques due to the tight margins and can lead to increased need for accurate ver-

ification. It can also introduce uncertainties in the interpretation of the doses received by various organs. Complex planning, delivery and quality assurance programmes are resource intensive and have the potential for errors.

Integrating new technologies, such as respiratory gating, where the radiotherapy delivery is coordinated with the patients breathing motion, or functional imaging which provides information on the biological characteristics of the tumour and normal tissue, may further increase the effectiveness of advanced radiotherapy techniques like IMRT. But these technologies are expensive and their routine use can only be justified if objective improvement in outcome can be demonstrated in rigorous clinical trials [14,15].

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