

Intensity Modulated Radiation Therapy (MRT) : Its Scope in Radiation Oncology

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Abstract: Radiation therapy treatment has matured into an integral component in the management of cancer patients. The planning and delivery systems have evolved from superficial X-ray therapy to megavoltage therapy and highly precise deposition of radiation within the tumour and its margins has been made possible with the recent advent of intensity modulation of the radiation beams.

Key words : *Target volume, intensity modulation, Optimization*

Introduction

Radiation oncology is undergoing a technological revolution compared to that brought about with the introduction of medical megavoltage linear accelerators in the latter half of the twentieth century. Advances in medical imaging and computer hardware and software technologies have led to the development of image based three dimensional radiation therapy treatment planning systems and computer-controlled medical accelerators having advanced delivery and treatment verification features. These technologies have helped implement external beam radiation therapy techniques, in which the high-dose region is conformed much more closely to the cancer patient's target volume than previously possible, thereby, reducing the volume of normal tissue receiving a high dose. *In the late eighties*, articles began to appear in the literature suggesting methods to achieve a high degree of conformity of radiation dose to tumour volume from external beam sources¹. The major feature of this process was to divide the normal radiation port into a group of very small "beamlets" with weights that could be altered depending on the desirability of delivering radiation to the tumours through each beamlet. Such a system offers the advantage of reducing dose to normal tissues, boosting doses within the tumour volume concomitantly with standard doses to the remainder of the targets, and, if properly computerized, could perhaps be more effective than 3-dimensional conformal radiotherapy (3-D CRT). This computerization is the use of "inverse planning" to determine the best solutions to the many variables available (e.g. the position of the radiation ports, the weight of each beamlet etc.) and the use of computerized delivery systems which eliminate the need of fabrication and placement of beam modifiers for each treatment port.

The first clinical use occurred in 1994, within five years since the postulation of such a system². The term Intensity Modulated Radiation Therapy (IMRT) was applied to distinguish it from 3 dimensional conformal radio therapy (CRT), although it is an extension of the very same process. Since that time it has been impossible for the literature to keep pace with the rapidly expanding use of intensity modulated treatment.

Imaging in Intensity Modulated Conformal Radiation Therapy

The enabling technology for intensity modulated radiation therapy is geometrically correct computerized tomography (CT) image data sets of individual cancer patients, developed originally for the purpose of diagnosis. These data sets are accurate geometric

models of the individual patients if the image acquisition position is identical to the treatment position. CT data sets also encode information on electron density of the patient sufficient to compute accurate dose distributions. Magnetic resonance imaging (MRI), Positron Emission Tomography (PET), Single Photon emission computerized tomography (SPECT) and ultrasound studies may be fused to the treatment position study in order to obtain information on the target volume, as well as information on organs at risk. The soft tissue imaging provided by Magnetic resonance imaging augments CT reconstructions that approximate the electron density of the patients. In certain cases, the MRI images can resolve tumour volumes or normal tissues structures that are not visualized as clearly in the CT reconstructions. In order to use this information *fusion* imaging and DICOM-RT standards are used for image transfer and data exchange between various equipments. Integration of imaging and therapy has led to useful syntheses that have enabled the development of intensity modulated radiotherapy.

Patient specific target and normal tissue

Anatomy is identified with the acquired imaging data sets, with or without the use of contrast agents that can be used to select a Gross Tumour Volume (GTV) in three dimensions. The bounds of these volumes are geometrically accurate to within the resolution limits of the reconstructed data sets. Normally, the resolution will be about 1 mm in the transverse planes and will be set by the scan spacing (or spiral pitch) to about 2 mm to 10 mm in the superior/inferior direction. These data sets are processed for treatment planning using virtual simulation computer applications. The applications commonly provide for the determination of an origin and an orientation of a Cartesian coordinate system. Procedures have been developed to locate this coordinate system on the patient, using laser sidelight as the reference marks or alignment devices (fiducial markers) associated with the immobilization device and markings on the patient surface are employed.

The objective localization of the gross tumour volume (GTV) has been an area of active research. Determination of the bounds of gross tumour volume in three dimensions to within uncertainty of less than 5mm is rarely achieved because inter and intra-observer variations are considerable. However, this uncertainty, as well as occult tumour spread can be accounted for by expanding the gross tumour volume in three dimensions to define a Clinical Target Volume (CTV). To account for uncertainty in patient positioning and organ motion, a further expansion to a Planning Target Volume (PTV) is recommended. The selection of gross

tumour to planning volume expansion parameters provide the radiation oncologist with the opportunity to factor into the treatment plan the medical and technical issues specific to each patient.

Dose calculation algorithms in IMRT : Dose calculation algorithms can be broadly classified into correction-based and model-based approaches. Correction-based approaches correct the dose distribution in a homogenous water phantom for the presence of beam modifiers, contour corrections, and tissue heterogeneities encountered in treatment planning of real patients. The homogenous dose is obtained from broad field measurements obtained in a water phantom or reconstituted from a representative sample of such measurement. The *convolution/superposition method*³ is a model-based dose calculation method. Model-based methods directly compute the dose in a phantom or patient. the calculation takes into account the beam energy, geometry, beam modifiers, patient contour and electron density distribution. The Monte-Carlo method is another model-based method. Both convolution method and the Monte Carlo method compute dose per unit fluence (or energy fluence) which allows the beam monitor units (dose delivery units) to be expressed in a phantom in an independent manner as energy fluence per monitor unit.

In *intensity modulated radiation therapy* the beam is non-uniform in intensity (Fig. 1) The beam intensity pattern from one beam direction can be thought of as a two-dimensional map of energy fluence dependent on a patient. This map can be discretized into beam elements or "bixels". A bixel corresponds to a finite region of a compensator, a portion of the travel of a leaf of a conventional multileaf collimator or a leaf of a temporally-modulated (binary) collimator.

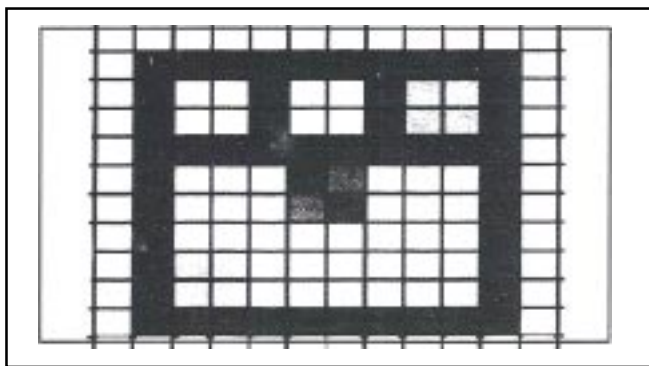


Fig.1: A test non uniform intensity pattern using a radiographic film.

The non-convolution dose model for high energy photon beams is the analytical method and is based on central-axis absorbed dose in a unit density material, including that under lateral and longitudinal electronic disequilibrium. The model is based on observations made by Nizin et al⁴ during the last ten years regarding the behaviour of the primary and scatter dose in photon beams. It is characteristic of the model that the knowledge of energy-fluence spectra is not required and majority of the necessary parameters can be derived from conventional beam data.

Computer Optimization and inverse planning

Computer optimization of radiation therapy treatment uses computer algorithms to find the best treatment plan for an individual patient or for a group of patients. A number of radiation optimization

techniques have been employed. Radiation therapy optimization is not new. Radiation oncologists, physicists and dosimetrists have employed trial-and-error optimization of radiation therapy dose distributions even when dose computations were not computerized. Computer-based radiation therapy optimization is often called the '*inverse method*' of dose calculation to distinguish it from the '*forward method*'. In the forward method the beam portals (beam orientation, shape and modifier) are first designed and then dose computation is performed. Forward optimization can be performed by then either changing the portal or adding another beam to make up for some dose that was missed in the target volume. The results of forward planning can produce radiation therapy plans with non-uniform beam intensities.

Treatment plan optimization, now referred to as "inverse planning", approaches the problem of designing a treatment from a more natural clinical perspective. The planning problems and constraints are defined in terms of clinical objectives and then the computer determines the best configuration of beams or beam intensities. If the results are not satisfactory, then there is no doubt that the required clinical objectives cannot be met within the range of available treatment configuration. Adding more treatment options, such as more beams, more energies, more modulation, etc., might produce a successful result. Otherwise, compromises must be made in the clinical goals, namely, tumor dose requirement must be relaxed or normal tissue doses increased. However, the planning focus is shifted away from the details of treatment delivery and onto the clinical consideration.

The most difficult task in optimization is mathematically defining the treatment goals. Increasing tumour dose, increasing tumour dose uniformity, and decreasing normal tissue doses are all incompatible goals yet, these conflicting goals for the target and normal tissues must be combined into a single figure of merit for each possible plan. This figure of merit is variously referred to as an *objective function*, *cost function*, or *score function*. It is used to compare alternative solutions and select the best one. A wide variety of objective functions have been developed and studied. Some use probability models for biological response, but most evaluate plans on the basis of dose alone. In general, dose-based objective functions are designed to favor uniform dose to the target and to apply penalties to plans that exceed tolerance doses of normal tissues. The relative merits of uniform tumour dose versus excessive normal tissue doses are controlled by the planner according to the judgement of the radiation oncologist. The mathematical methods and computer algorithms for optimization must be matched to the desired objective function.

To arrive at an optimal plan the radiation oncologist defines dose constraints to the normal tissues based upon the volume of tissue irradiated, critical tolerance of the specific normal tissues available from literature, his/her experience and the desired outcomes in a given case. Another example is prescribing the minimum dose to the target volume, but if the limit is too low the target coverage may be poor and if it is too high the normal tissue may get unnecessary dose. (Fig. 2) An alternative to use of constraints is to use *penalty functions* which are also called "soft constraints". Penalty functions are most often additional terms placed into the objective function. The penalty functions act to discourage, but not prevent, crossing the boundary out of a feasible solution had a constraint been used instead. Dose-volume-constraints are often

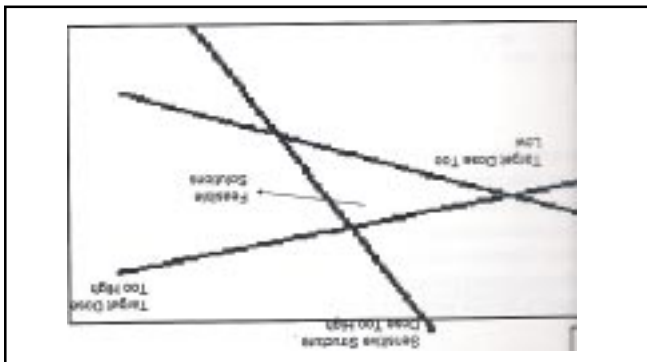


Fig.2: Dose constraints a feasible solutions.

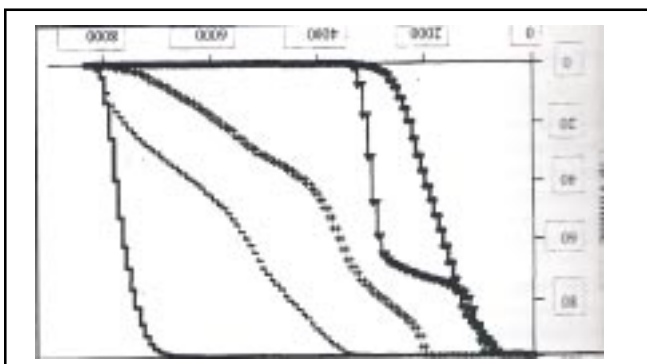


Fig.3: Shows the dose volume histograms for a seven field intensity modulated radiotherapy nasopharynx plan.

penalty functions⁵. Dose volume histograms are the pictorial representation of the dose delivered to percentage volume of the target and organs at risk (Fig.3).

Delivery systems for IMRT

There are various delivery systems available for delivery of intensity modulated radiation therapy and each has its own advantages. It is the comfort level and financial budgets of the treating team with each technology that has made departments equip themselves with different systems. Three important considerations to be given to the delivery process are (i) How accurately does the delivery system create the dose distribution created in the planner? (ii) How easily can we verify the safe operation of the delivery system? (iii) How long will it take to deliver the plan?

The commonly used delivery systems are :

A. Detachable tertiary collimating systems attached to the accessory tray holder of a linear accelerator e.g. physical intensity modulators and Peacock System® from NOMOS.

B. Inbuilt Multileaf Collimating systems (MLC): The multileaf collimator is primarily an efficiency device and makes the implementation of complex treatments involving many fields practical. The leaves are made of 5 to 6 cm thick tungsten and are typically 1 cm wide. More recently leaves of width as small as 1mm have been introduced.

i. **Dynamic mode** : The multileaf collimator (MLC) is primarily an efficiency device and makes the implementation of complex treatments involving many fields practical. The leaves are made of 5 to 6 cm thick tungsten and are typically 1 cm wide. More

recently, multileaf collimator with leaves of width as small as 1mm have been introduced. In the dynamic mode, leaves can be used to modulate intensities to produce two-dimensional non-uniform profiles of arbitrary shape. In a typical dynamic method, the gap formed by each pair of opposing leaves is swept across the target volume under computer control while the radiation is being delivered. The gap opening and its speed are continuously adjusted during motion, and the dose rate of the accelerator may be altered to achieve the desired result. Since the dose rate of the treatment machine might fluctuate slightly, the motion is indexed to monitor units (MUs) rather than time. The basic idea is that as the gap sweeps across a point, the radiation received by the point is proportional to the number of MUs delivered during the time the tip of the leading leaf goes past the point and exposes it until the tip of the trailing leaf moves in to block it again. Knowledge of the maximum leaf speed is taken advantage of to maximize the gap between the opposing pair of leaves and, therefore, to minimize the treatment time and the sequencing of leaf motions also can be optimized.

ii. **Step and Shoot** : In this delivery mode, the multileaf collimator is positioned into a predetermined configuration, a fraction of dose delivered, the dose turned off, the leaves moved to another position and verified, and another fraction of dose delivered. Enough "segments" are delivered until the desired intensity map is achieved. The gantry then moves under computer control to another position and the process repeated. The order of segments can be optimized to reduce delivery time.

(iii) **Tomotherapy and intensity modulation** has been introduced at Wisconsin University Madison and its clinical utility needs to be determined.

Verification of Incident Fluence and Patient positioning

The repetitive treatment delivery facilitated by the complex movements of leaves, placement of physical intensity modulators etc are verified on the therapy unit by either Radiochromic film exposure or by Electronic Portal Imaging Devices (EPID). At the first session of any radiotherapy treatment, it must be verified that the patient has been positioned such that the isocenter of the treatment has been placed at the correct anatomical location. Then the positioning of the patient must be correct on the day to day basis⁶. The isocenter locations can be verified by comparing portal films with Digitally Reconstructed Radiographs (DRRs) from the CT imaging data. The other parameter that can be matched is the superposition of the field boundaries of multileaf collimators on the DRRs using computerized virtual simulation programme. Acquisition of cranial photographs using optical images from a stereo camera system is a very useful method for patients undergoing brain irradiation.

Gated Breath Hold Devices and IMRT

Despite the external immobilization and laser localization on fiducial markers on surface of the patients it is not possible to bring to a stop all the internal organ motion. Intra treatment cardiac, respiratory and bowel motion can compromise the daily reproducibility of the complex intensity modulated beams. The patient can participate in Active Breath Hold Procedures or the

software can be tailored to deliver radiation dose during either inspiration or expiration as programmed. The CT imaging for planning also need to be taken with the help of similar programmes. Active research is ongoing to study and target radiation synchronized to internal organ motion in resting state.

Clinical considerations

Anatomical sites where IMRT has been extensively used are cancers of the head and neck^{7,8}, and cancer of the prostate⁸, cervical cancer⁹, breast cancer¹⁰, paediatric tumours¹¹, colorectal and intrathoracic malignancies are the areas being explored where the surrounding tissues have been a dose limiting factors. Intra-abdominal malignant conditions especially carcinoma pancreas and retroperitoneal tumours can benefit with this modality as the low tolerances of small bowel, kidneys, liver and spinal cord do not permit conventional radiation to deliver adequate tumoricidal doses.

Radiation therapy is essentially a physical solution to what is a biological problem; it will never be the entire answer to the problem of cancer therapy. Yet it remains an important component of the answers. A local treatment is best assessed for efficacy by probabilities of local control. Intensity modulated radiotherapy is an important tool in treatment delivery as it can provide us the corollary for dose-escalation to tumour, keeping the normal tissue morbidity levels at the lower end.

Cost considerations

The above discussion does lead to a few outstanding observations that intensity modulated radiotherapy is an expensive proposition in terms of (a) space, hardware and software that is required (b) the time involved in preparation of plans and execution of treatment (c) the manpower available to carry out such planning and treatment (d) the expenditures that go along with all these resources. The finite gain in terms of higher cure rates versus lowered morbidity however is the goal to be achieved and the economic considerations will appear miniscule if healthcare gains are kept in mind.

Conclusions

Intensity modulated radiation treatment (IMRT) has evolved from the three dimensional conformal radiation system over the last one decade. It has the promise of a new born technology that if used judiciously and with caution can lead to delivery of tumoricidal doses to control loco-regional malignant tumours with low distant

(haematogenous) metastatic potential e.g. head and neck cancers, early prostate cancer, anal canal, uterine cervical cancer; malignant astrocytomas and medulloblastomas. The latter especially amongst the paediatric age group patients to prevent neurocognitive and growth retardation sequelae. The studies in the next decade will hopefully show the mature results of the introduction of this technology and the improvements in tumour control/reduction in normal tissue morbidity.

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