Modulated Radiotherapy—Current Status and New Developments

a report by

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Current Status

Intensity modulated radiotherapy (IMRT) has been widely adopted as a new tool in RT for the delivery of high doses of radiation to the tumor while providing maximal sparing of surrounding critical structures.

Long-term clinical results are still limited; however, initial results appear promising. At Memorial Sloan-Kettering Cancer Center, IMRT has allowed the physicians to escalate the dose to the prostate while reducing the toxicities to the rectum and bladder, resulting in improved local control and reduced complications compared with conventional three-dimensional (3-D) conformal therapy. A randomized trial comparing 3-D conformal therapy and IMRT for prostate cancer also confirms the advantage of IMRT. Chao et al. showed that the IMRT technique has greater capability in sparing salivary functions in patients receiving RT for head and neck cancers. Eisbruch et al. analyzed the relationships of dose, volume, and fractionation schemes with salivary gland functions for patients treated with 3-D conformal therapy and IMRT for head and neck cancers, and also showed advantages of IMRT in salivary gland sparing. With increased use of IMRT, more encouraging results will emerge.

For each patient, the anatomy dictates a unique set of preferred beam orientations and the preferred locations within the radiation field in each beam orientation. IMRT offers an additional freedom compared with 3-D conformal therapy because the radiation intensities within a radiation field can be varied according to these location preferences. It is this theoretical advantage that led to the initial developments of the IMRT technology. Both rotational and gantry-fixed IMRT techniques have been implemented clinically using dynamic multileaf collimation (DMLC). In gantry-fixed IMRT, multiple coplanar and non-coplanar beams at different orientations, each with spatially modulated beam intensities, are used. Rotational IMRT employs temporally modulated fan beams. The use of overlapping arcs to deliver modulated beam intensities around the patient were also proposed but have not been widely adopted for clinical use.

Problems Associated with Current IMRT Planning

The IMRT planning process begins by defining the beam arrangements, such as the number of beams and their orientations. The desired doses to the targets and critical structures, as well as the penalties for not meeting these requirements, are also specified. These parameters are used to construct a mathematical function, commonly called the cost function. The final value of the function—calculated using the overall dose distribution as input—is used to compare competing plans. The weights of all the beamlets, which form the intensity patterns in each beam, are said to be optimized when the cost is minimized. To reach the optimal solution quickly, different optimization algorithms are used to guide the adjustments of the weights of the beamlets.

Optimizing the intensity distribution is the first step of the planning process. In order for the desired intensities to be delivered, they have to be translated into machine-specific settings. After the optimization is complete, a leaf-sequencing algorithm is used to translate the final intensity distribution for each beam direction into a sequence of deliverable beam shapes called segments.

This two-step process (intensity optimization and leaf sequencing) employed in the current treatment planning process for MLC-based IMRT creates numerous problems. The leaf-sequencing is constrained by the delivery hardware, and so a large number of complex field shapes are often needed. This can lead to a loss in efficiency and an increase in collimator artifacts. Consequently, the highly conformal dose distributions of the ‘optimal’ plan, as shown on the computer, cannot be realized in the patient.

New Developments

Direct Aperture Optimization

Instead of using the two-step process, a system has been developed that directly optimizes aperture shapes for step and shoot IMRT delivery. The aperture shapes and weights are simultaneously optimized using a simulated
annealing algorithm. Physical constraints of the MLC, such as leaf movement limits, inability to interdigitate and minimum gap between opposing leaves and opposing adjacent leaves, are considered in the optimization process; the need for leaf sequencing is eliminated. Without leaf sequencing, the number of apertures can be significantly reduced while maintaining the conformal capabilities of IMRT, considerably reducing the complexity of IMRT.

The method has been commercialized by Prowess, Inc. and used clinically at several institutions. Numerous tests have been run against other commercial treatment planning systems. The test results and initial clinical experience indicate that direct aperture optimization (DAO) can produce highly conformal treatment plans that rival other inverse planning systems, using only three to seven apertures per beam direction.

The key to the success of DAO lies in the fact that a limited number of apertures can create a large number of intensity levels and complex intensity pattern. Theoretically, the number of intensity levels, N, that can be created by n apertures of distinct weights is: N=2^n -1. Seven intensity levels (excluding the island 0 intensity) can be created with only three segments. With five segments, it is possible to create 31 intensity levels.

**Dynamic Conformal Arcs**

Many of the available micro-MLCs are capable of delivering dynamic conformal arcs in which the shape of the beam changes continuously during delivery of the arc to conform to the beam’s-eye-view of the target. Arcs can also be designed to dynamically block a critical structure. The weights of arcs can also be optimized. This delivery approach combines the dosimetric advantages of arcs with the beam-shaping capabilities of a micro-MLC. With a limited number of arcs, a conformal dose distribution can be created with a highly uniform tumor dose. For planning and delivery control, each arc is approximated as a series of fixed fields.

**Intensity-modulated Arc Therapy**

Intensity-modulated arc therapy (IMAT) is a rotational approach to IMRT in which the leaves of the MLC move continuously during arc beam delivery. Overlapping arcs are used to deliver optimized intensity patterns from each beam direction. The intensity patterns have been optimized, so IMAT provides a more rapid fall-off in dose at the tumor boundary than can be achieved with dynamic conformal arcs. Compared with fixed field IMRT, IMAT provides both dosimetric advantages and efficiency gains. IMAT serves as an alternative to serial tomotherapy (using an add-on binary MLC) and helical tomotherapy (a dedicated tomotherapy machine). However, IMAT has the advantage that it can be delivered on a conventional...
linear accelerator with an integrated MLC. An additional advantage of IMAT is the ability to deliver non-co-planar arcs.

Tomotherapy can be considered the current gold standard in IMRT delivery. Exquisite IMRT dose distributions can be created using tomotherapy because the large number of delivery angles provides almost infinite flexibility in how the dose is distributed within the patient. Initial plan comparisons between tomotherapy and IMAT have been performed at the University of Maryland. The preliminary results shown in Figure 3a and 3b are encouraging because they demonstrate that IMAT may be able to consistently match the quality of plans produced by a tomotherapy system while delivering efficient treatments on a conventional linear accelerator. Due to fact that there are fewer than 50 tomotherapy units installed in the US, IMAT could greatly expand the numbers of patients who would benefit from the highly conformal dose distributions achievable with arc-based IMRT delivery.

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**Future Directions**

RT is heavily leaned on by a number of key technologies, including imaging, planning, and treatment delivery. These technologies are pushing each other, aiming to improve the treatment precision and ultimately improving a cure. This phenomenon has resulted in a rapid expansion of new technologies for RT in the last decade. The precision in dose delivery with IMRT has accentuated the inadequacy in precise tumor targeting and resulted in the new research focuses on image-guided RT (IGRT). While improving tumor targeting with imaging guidance is the logical next frontier, recent research and developments on IMRT has demonstrated that there is still substantial room for improvement in both IMRT planning and delivery. The marriage of the new developments of IMRT and IGRT will push the field to adopt new treatment techniques including different fractionation schemes and total doses.

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