

---

# INTENSITY MODULATED RADIATION THERAPY

---

PHILIP G. MADDOCK, MD, FRCR

The last twenty years have seen amazing improvements in the technical aspects of radiation oncology, resulting in devices such as the Gamma knife and more recently the Cyberknife, a small linear accelerator mounted on a robotic arm, that allow highly precise treatment of intracranial lesions and lesions of the spinal cord. By their very nature, however, indications for these devices are quite limited and most non-radiation oncologists will rarely come in contact with patients requiring such treatments.

For common cancers such as prostate cancer, breast cancer and head and neck cancers the major advances have taken place in three areas: 1) linear accelerator design, 2) oncologic imaging, and 3) computerized treatment planning systems. Combining all three of these advances has given us a technique to shape the dose distribution so as to increase the tumor dose while lowering the dose to adjacent radiosensitive tissues. This technique is called Intensity-Modulated Radiation Therapy or IMRT and is now the Standard of Care in radiation treatment for cancer of the prostate and cancers of the head and neck. With increased access to the Internet, many patients are well aware of IMRT. At least 20% of patients with prostate cancer presenting for their initial consultation at my office ask whether the facility has IMRT capability.<sup>1</sup> This paper describes the technical and clinical aspects of IMRT and how it benefits the patient with cancer.

## STANDARD RADIATION THERAPY

Up to 1990 most radiation oncology centers had as a starting point a standard set of treatment plans for tumors in each anatomical location. Simulator films were taken and patient measurements were made. The information was fed into a treatment-planning computer; the resulting dose distribution was reviewed. Minor modifications in the dose distribution could be achieved by custom-designed shielding blocks cast for each individual patient or by changing the angulation for each portal.

Early cancer of the larynx was treated using standard right and left lateral portals to a dose of 66 cGy in 33 fractions and cure rates approached

90% at five years. There were minimal sequelae for normal tissues because the radiation portals for early cancer of the larynx are quite small and no radiosensitive structures were included. In contrast, similar but much larger right and left lateral portals were used to treat cancers of the base of tongue. Cure of tumors in this area however was associated with significant long-term side effects due to damage to the salivary glands, which were unavoidably irradiated to high doses. IMRT allows one to achieve a tumoricidal dose to the primary tumor while sparing the parotid glands and preserving salivary function.

---

**“IS IMRT WORTH  
THE ADDED TROUBLE  
AND EXPENSE?  
THE ANSWER FOR  
CANCERS OF THE  
PROSTATE AND  
HEAD AND NECK IS A  
RESOUNDING YES.”**

---

## IMRT

The main improvement in linear accelerator design has been the development of the multi-leaf collimator. (Figure 1) With monolithic collimators, modification of the dose distribution was achieved by using hand cast shielding blocks. Each block had to be inserted by hand which meant that treatment had to be interrupted after each portal so as to remove the first block and then insert the block for the second portal and so on. For a six-field 3D conformal plan for cancer of the prostate each treatment would take approximately thirty minutes, only five or six minutes of which was actual radiation exposure.

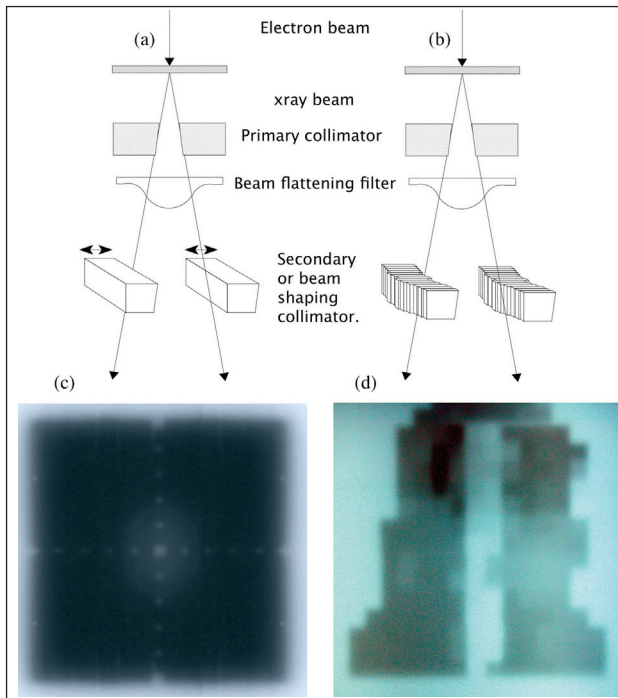
With a multi-leaf collimator the dose distribution in each field or portal can be continuously changed or modulated. A radical five-field IMRT plan for cancer of the prostate and approximately ten segments per field (an equivalent of approximately fifty separate fields) can be done in less than

fifteen minutes.

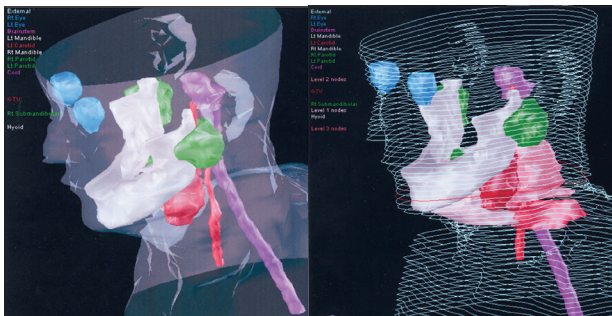
The second advance to make IMRT feasible has been the improved CT, MRI, and PET scans. A major improvement in the delineation of normal anatomical structures and in particular areas of nodal drainage has come from studies relating functional anatomy to diagnostic imaging studies.<sup>2,3</sup> The patient is seen initially in the radiation oncology department and scout films are taken on a simulator. Reference marks are tattooed and the patient is sent for a CT scan or MRI in the treatment position and with small alloy bb's on the reference marks. The imaging information is digitally returned to radiation oncology in a format that is readable by the treatment-planning computer. The surface contours are identified and, using the computer cursor or cross-hair, the relevant normal anatomical structures are delineated. A patient, status post-surgery for a carcinoma of the left submandibular gland, is shown in Figure 2. Computer software allows one to depict the structures as a solid, transparent or wire frame figure. The tumor and other target volumes are also outlined.

The planning computer produces a list of all the structures and targets that have been entered from the CT data. The clinician or dosimetrist then enters into the treatment-planning document a set of dose parameters for each of these structures or targets. These parameters specify a minimum and a maximum dose for the tumor volume and different dose parameters might then be prescribed for each of the different organs or tissues that are to receive limited dose. Each of these dose parameters, or constraints, is then assigned a relative cost function, or weight. For radiosensitive normal structures a maximum radiation dose would be specified. For critical structures such as the spinal cord the maximum dose would be an absolute with a higher weight while for less critical structures it might be reasonable to specify that 95% or 85% of the volume of the structure should not exceed the tolerance dose (Table 1).

Given these parameters and contours, the treatment-planning computer will perform repeated iterations to generate a treatment plan that best



**Figure 1**  
 Linear Accelerator with (a) standard collimator on the left and, (b) a multi-leaf collimator (MLC) on the right. In (a), the beam is defined by a set of monolithic tungsten/lead collimators that give a square or oblong field of irradiation, as shown in the film on the left, (c). The beam can then be shaped by custom, molded lead shields unique to each field. In (b), the collimators are made of separate leaves, and each leaf is positioned by a servo motor. The servo motors are in turn controlled by a computer that is networked to the treatment planning system in the medical physics department. This allows the beam intensity to be modulated continuously during treatment, as shown in the cumulative dosimetry film on the right (d).



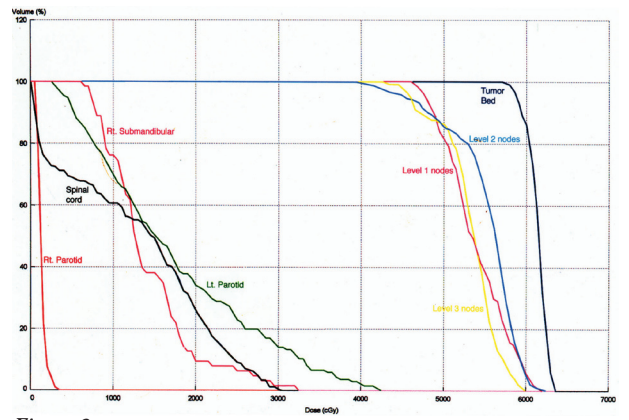
**Figure 2a**  
 The target volume has been added (red). The relevant normal structures are delineated. The spinal cord is purple, the parotids are green, and the mandible is white, etc.

**Figure 2b**  
 The level 1, 2, and 3 nodal groups have been added (deeper shades of pink).

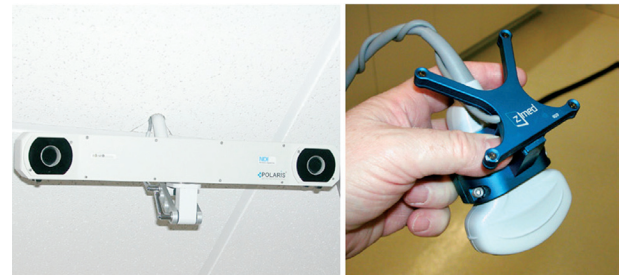
satisfies the entered constraints. This process takes from one to three hours of computation time. The optimized plan will specify the number and shape of MLC modulations of each portal, known as segments, and the discrete amount of radiation to be delivered through each segment to achieve the optimum dose distribution. The system will then generate a series of vir-

tual X-rays to be compared with further stimulation films that are taken using the portal angles generated by the planning computer. The 3D dose distribution is reviewed on the computer system and also on the dose volume histogram to see that all of the dose target and constraint parameters have been met. (Figure 3).

The final step in the implementation of an IMRT treatment course is to ensure accurate daily treatment setups throughout the full five to eight week course of treatment. Currently there are two systems for ensuring day-to-day accuracy of treatment. The first, which is usually limited to use in



**Figure 3**  
 Dose Volume Histogram. In this particular IMRT plan, the right parotid sees virtually no radiation while only 40% by volume of the left parotid sees more than 2000 cGy. The spinal cord dose is similarly limited. 90% of the tumor bed volume receives more than 6000 cGy.



**Figure 4**  
 Image guidance using 3D ultrasound. The ceiling mounted stereoscopic digital cameras locate the ultrasound images by tracking the embedded reflectors in the handheld transducer.

prostate cancer treatments, is to implant fiducial markers in the prostate and to take a portal X-ray every day.<sup>4,5</sup> The main advantage to this system is its simplicity as the gold seeds are usually quite easily seen on the portal viewer. Relative disadvantages are that the gold seeds can occasionally migrate. Also, implanting the seed is an invasive procedure, done in patients who are already worn out by all the prior procedures.

An alternative method of daily localization is to use interactive, real-time ultrasound. In this system a pair of a stereoscopic digital cameras, mounted in the ceiling of the treatment room, is calibrated each morning so that the ultrasound transducer is integrated with the linear accelerator. The trans abdominal transducer is used to locate the prostate bladder and rectum relative to the isocenter of the accelerator and the 3D ultrasound images are fused with the patient's CT images. (Figure 4). Changes in the three axes of table movement are given so as to bring the prostate to the correct posi-

ORGAN AT RISK	Goal Full Volume Min. Dose (cGy)	Full Volume Min. Dose (cGy)	Goal Max. Dose (cGy)	Volume in Violation @ Goal Max. Dose (%)	Goal Overdose Volume (%)	Dose @ Goal Overdose Volume (cGy)	Goal Limit Dose (cGy)	Volume in Violation @ Goal Limit Dose (%)	Limit Dose (cGy)
Rt. Parotid	250	71.52	2000	0	10	181.29	2500	0	322.02
Lt. Parotid	250	281.58	2000	0	60	1255.23	2500	22.96	4245.08
Cord	250	31.91	3000	0	5	2750.32	4000	0	3023.12
Lt. Mandible	100	190.82	5000	11.86	5	5697.78	6000	1.74	6086.42
Rt. Submand.	250	608.54	2000	0	10	1984.53	2500	6.35	3243.71
Rt. Mandible	500	84.92	5000	2.4	5	5457.12	6000	1.08	6162.22
Brainstem	N/A	117.48	N/A	N/A	N/A	N/A	N/A	N/A	646.18
External	N/A	0	N/A	N/A	N/A	N/A	N/A	N/A	6365.68
Rt. Eye	N/A	50.88	N/A	N/A	N/A	N/A	N/A	N/A	127.62
Hyoid	N/A	2381.65	N/A	N/A	N/A	N/A	N/A	N/A	6177.51
Lt. Eye	N/A	54.36	N/A	N/A	N/A	N/A	N/A	N/A	115.57
Lt. Carotid	N/A	246.25	N/A	N/A	N/A	N/A	N/A	N/A	5849.08

**Table 1**  
Analysis of how well the treatment plan achieves the dose constraints.

TARGET	Goal Minimum Dose (cGy)	Minimum Dose (cGy)	Volume in Violation @ Goal Min Dose (%)	Goal Prescription Dose (%)	Volume in Violation @ Rx Dose (%)	Goal Underdose Volume (%)	Dose @ Goal Underdose Volume (cGy)	Goal Limit Dose (cGy)	Volume in Violation @ Goal Limit Dose (%)	Limit Dose (cGy)
GTV	5500	5732.17	0	6000	11.74	2	5845.06	6400	0	6365.68
Level 1 Nodes	4250	4604.76	0	4500	0	2	4697.85	6400	0	6173.03
Level 3 Nodes	4250	4281.74	0	4500	0.13	2	4496.92	6400	0	5955.19
Level 2 Nodes	4250	3913.15	2.31	4500	2.36	2	4238.01	6400	0	6202.99
Margin: GTV	4750	4900.74	0	5000	0	5	5367.57	6400	0	6365.68

**Table 2**  
Dose targets for tumor and nodal areas.

tion for treatment. This system is non-invasive and is more versatile as it can be used in sites that are inaccessible to implantation of a fiducial marker. Patients like the ultrasound system and the fusing of the three images on the ultrasound screen to be quite reassuring. A disadvantage is the steep learning curve for staff.

Is IMRT worth the added trouble and expense? The answer for cancers of the prostate and head and neck is a resounding yes. IMRT has improved local control rates while at the same time decreasing radiation induced side effects on normal tissues.<sup>f,g,h,i</sup> IMRT is also useful in certain types of breast cancer, particularly those involving the left breast in patients who have received Adriamycin, which is potentially cardiotoxic. Retrospective studies show that radiation to the myocardium can have consequences ten to fifteen years after treatment. IMRT plans reduce the myocardial dose dramatically. Studies in the use of IMRT at other anatomic sites continue.

## REFERENCES

- Mell L, Mehrotra A, et al. Intensity-Modulated radiation therapy use - The US, 2004. *Cancer* 2005; 104: 1296-303.
- Levendag P, Gregoire V, et al. Intraoperative validation of CT-based lymph nodal levels, Sublevels IIA and IIB. *Int J Radiat Oncol Biol Phys* 2005; 62: 690-9.
- McLaughlin P, Troyer S, et al. Functional anatomy of the prostate. *Int J Radiat Oncol Biol Phys* 2005; 63: 479-91.
- Kupelian P, Willoughby T, et al. Intraprostatic fiducials for localization of the prostate gland. *Int J Radiat Oncol Biol Phys* 2005; 62: 1291-6.
- Litzenberg D, Balter J, et al. Retrospective analysis of prostate cancer patients with implanted gold markers using offline and adaptive therapy protocols. *Int J Radiat Oncol Biol Phys* 2005; 63: 123-33.
- Michalski J, Winter K, et al. Toxicity after three-dimensional radiotherapy for prostate cancer on RTOG 9406 dose level V. *Int J Radiat Oncol Biol Phys* 2005; 62: 706-13.
- Jacob R, Hanlon A, et al. Role of prostate dose escalation in patients with greater than 15% risk of pelvic lymph node involvement. *Int J Radiat Oncol Biol Phys* 2005; 61: 695-701.
- Bussels B, Maes A, et al. Dose-response relationships within the parotid gland after radiotherapy for head and neck cancer. *Radiation Oncol* 2004; 73: 297-306.
- Zapatero A, Valcicel F, et al. Risk-adapted androgen deprivation and escalated three-dimensional conformal radiotherapy for prostate cancer. *J Clin Oncol* 2005; 23: 6561-8.

*Dr. Maddock, a radiation oncologist at 450 Tollgate Road in Warwick, is a Clinical Associate Professor of Medicine, Brown Medical School.*

*Reprinted from Medicine and Health Rhode Island, February 2006.*