The Revolution in Radiation Therapy
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The Emergence of IMRT

Radiotherapy is one of the most effective modalities for the majority of cancers and, with surgery, remains the most cost-effective way of curing many cancers [1].

Researchers and clinicians are constantly striving to find new, more effective ways of treating cancer. As a hopeful world looks for the miracle that will cure cancer once and for all, a major revolution in cancer treatment has been quietly taking place in radiation oncology—a revolution that many consider has involved greater, more significant change within the past five years than the field had seen in the prior 30 years. With new research building upon these recent developments, there are many more changes to come. As a result of this on-going revolution in radiation oncology, many cancer patients now have increased chances of survival with a better quality of life.

Today, the most widely practiced radiation oncology treatment is a technique called three-dimensional conformal radiation therapy (3-D CRT). It is used to irradiate a tumor defined in a three-dimensional imaging study (typically a thin section CT) with an array of x-ray beams individually shaped to conform to a two dimensional projection of the target. If the tumor has a simple convex shape, i.e. if it has a surface with no dimples or concavities, and is geographically remote from sensitive structures, then the design of radiation therapy treatment can be solved with 3-D CRT.

In general, 3-D CRT is delivered with a series of fixed-shape fields. In this mode of treatment, the treatment therapist goes in and out of the room to change the machine angle and field size, and to insert new blocks and other field modifiers. Each treatment is then delivered in a
standard static fashion. To create conformal dose distributions, typically between four to eight static fields are treated. Each field is shaped using blocks or a multileaf collimator that has been manually designed to conform to the shape of the target volume as viewed from a particular beam position. Optimization of 3-D CRT plans is accomplished iteratively, by manually varying the weights, wedging, numbers and directions of beams until a satisfactorily uniform dose to the target is achieved without exceeding the dose tolerance of neighboring sensitive tissues.

The impact of 3-D CRT has been to make possible the safe escalation of dose to tumors in a variety of areas in the body that has led to an improvement in the probability of local tumor control. However, there are situations for which 3-D CRT cannot produce a satisfactory treatment plan due to target complexity and limitations of the technology. In some situations, for example, the machine angles required to avoid or minimize dose to normal tissues are either difficult or impossible to implement clinically. In addition, few if any beam directions can be found which completely avoid sensitive normal tissues surrounding the tumor. Finally, for situations where a concave tumor wraps around a sensitive structure, such as the spinal cord, no acceptable 3-D CRT plan can be found.

In recent years, a convergence of new technologies has made it possible to deliver radiation dose almost exclusively to a target volume while avoiding surrounding healthy tissue. IMRT, or intensity modulated radiation therapy, is one of the most advanced kinds of radiation therapy available today. It has enabled oncologists not only to shape the radiation beam, but also to modulate it, giving higher doses to some parts of the tumor and lower doses wherever sensitive structures are nearby.

Although the term IMRT is being increasingly disseminated, it is often used to mean different things. For this discussion, we will define IMRT as "therapy that uses custom dose intensity patterns within the treatment field for each patient." There are a number of different methods of producing these intensity-modulated distributions, some of which are relatively simple, but others that are quite complex.

With IMRT, each treatment field—the area irradiated when the beam is coming from one particular direction—is broken up into smaller areas called segments, or sub-fields, and each segment can receive a discrete or unique amount of dose. Therefore, when the beam passes through a critical structure, like the spinal cord or rectum, on its way to the target, the dose to that area can be reduced. When the beam is applied from a different direction and the critical structure is no longer in the beam’s path, the dose can be commensurately increased. An IMRT plan can incorporate any number of fields, with between 5 to 400 segments per field.

The basic level of IMRT delivery has been termed "segmental" or “move and shoot” IMRT, meaning the patient is treated through the use of multiple individual segments within each fixed field. It is similar to 3-D CRT except that computer control capabilities are used to deliver the segments automatically, thereby eliminating the need for the therapist to enter the treatment room to set each segment individually. Segmental IMRT may be thought of as a transitional technology.

The most sophisticated level of computer-controlled IMRT is termed "dynamic" or “sliding window” IMRT. This is a rapid delivery method that uses the leaves of the MLC to smoothly and continuously re-shape the beam aperture over the treatment area during irradiation. The moving beam delivers the prescribed radiation doses to the various parts of the tumor volume, while the surrounding healthy tissue is shielded. In the dynamic mode, an IMRT treatment
session generally can be completed within the standard 15-minute treatment session, allowing clinics to continue to handle normal patient loads. This speed is critical for minimizing tumor motion during treatment and also important for elderly and pediatric patients who can have trouble with being immobilized for lengthy treatments. [2]

The emergence of IMRT was made possible by three major developments over the last 15 years: the digital linear accelerator (linac) for generating high-energy treatment X-rays in a very accurate way; the computer-controlled multileaf collimator (MLC) for shaping the radiation beam; and sophisticated “inverse” treatment planning software programs.

Digital, computer controlled linear accelerators have been in routine clinical use for nearly two decades. As such, their fundamental technology is well proven and clinically reliable. [3-6]

In terms of delivering an IMRT treatment, it is important to point out a few subtle but important points. First, it is important that the linac and MLC work in concert with each other, such that all segments associated with a particular treatment field can be delivered at once. This makes the treatment times as short as possible, which increases patient throughput in the clinic and minimizes patient motion during treatment. Early studies suggest that shorter treatment times may actually increase the biological effectiveness of the treatment. [6]

Second, the control system must be able to simultaneous control both the mechanical motion of the linac and MLC, as well as the delivery of the high energy x-rays. Linacs with control systems that allow only for the control of the mechanical motion can only deliver segmental IMRT. These systems typically require longer treatment times, or they are limited to delivering lower resolution intensity patterns. [8]

Finally, it is important that the control system allows for the delivery of IMRT treatments in two different ways: 1) with the MLC moving to modulate dose delivery while the linac remains in a fixed position, and 2) with the MLC moving to modulate dose delivery while the linac is simultaneously rotating around the patient. The former configuration, which can be used to deliver either segmental or dynamic IMRT, has been discussed in some detail already. The latter configuration, referred to as “dynamic arc” radiotherapy, has been practiced for many years in Japan and is now seeing clinical interest in other parts of the world, particularly for stereotactic radiosurgery. [9-10]

The development of the MLC in the 1990s was an important milestone on the way to IMRT. This automated beam shaping and made 3-D CRT less cumbersome. The most advanced MLCs available today can deliver IMRT using either segmental or dynamic techniques, yielding high-resolution intensity patterns with segments as small as 2.5 x 5 millimeters. It is interesting to note that as IMRT clinical experience has matured, it is becoming increasingly common to modulate larger and larger fields, so a high resolution MLC that can also cover a full 40x40 cm field is important. [11-17]
The last piece of key enabling technology was the introduction of “inverse” treatment planning. With this approach, complex calculation algorithms are used to compare thousands of treatment plan options to determine the optimal plan for delivering a specified dose to the target volume, while constraining the exposure of nearby healthy structures to specified limits.
based on known tolerances. Instead of clinicians manually defining beam weights, wedges, blocks, etc., and then computing and displaying dose distributions to assess whether the treatment plan will lead to an acceptable outcome (the process that was employed for 3-D CRT), they do the opposite. They state their clinical objectives in terms of dose prescriptions, including the tolerances of normal healthy tissue, and let the inverse treatment-planning program work backwards to calculate the optimal delivery approach that will best accomplish those goals.

![IMRT Radiation Therapy Treatment Plan](image)

Figure 3: An IMRT radiation therapy treatment plan for prostate cancer, viewed in three dimensions. Precisely shaped radiation beams are delivered from different angles and converge on the tumor, shown here in red.

## The IMRT Process – How it is Practiced Today

Since its emergence in the mid-1990s, IMRT itself has undergone considerable refinement. The feasibility of implementing IMRT efficiently and effectively has come to depend on the integration of various constituent tools and processes. The basic IMRT process can be broken down into six steps: 1) patient immobilization; 2) imaging for treatment planning; 3) treatment planning; 4) post-plan verification; 5) treatment delivery; and 6) treatment verification. All of these processes must seamlessly work together. To meet this critical requirement, Varian Medical Systems has introduced a wholly integrated high-resolution IMRT solution called SmartBeam™ IMRT.
Figure 4: The Birth of Venus, showing how high-resolution SmartBeam IMRT can literally “paint” dose. The high-resolution image on the far right, containing up to 500 subfields, can be delivered in less than 1 minute.

Figure 5: Varian’s SmartBeam IMRT integrates the equipment, software, and processes for each treatment step, from imaging and treatment planning to treatment delivery and verification.

**Patient Immobilization**

An essential first step of the IMRT planning process is to ensure that the patient is in a treatment position consistent with the potential geometric beam arrangements that can be applied to the tumor site being treated. This requires some discussion between the physician and other personnel involved in the planning process. After the treatment position has been established, the patient must be immobilized in a reproducible manner so that the geometric parameters defined during the patient image acquisition can be accurately transferred from the imaging device to the treatment planning system, and ultimately reproduced on the treatment machine. [18-23]
**Building a Virtual Patient**

Volumetric CT and/or MRI scans are performed with the patient in the treatment position using the immobilization devices previously constructed. The full volumetric 3-D image set must be "contoured," that is, each small voxel (volume element, the three-dimensional equivalent of a pixel) must be labeled by tissue type and combined with abutting similar voxels into identifiable structures. Delineation of tumor and normal tissue contours is performed by treatment planning staff and the radiation oncologist. Some structures have distinct boundaries and, in theory, a computer can be programmed to assign the labels by rote, according to each voxel's brightness. Indeed, certain structures, such as the skin, lung and bone, are often obvious and can have their labels locked in immediately by the computer. Tissue boundaries, however, may be difficult to distinguish on the basis of simple readings and require the "hands-on" effort of the radiation oncologist.

Three-dimensional treatment planning systems have the ability to display and simulate all the functions of a conventional radiotherapy treatment unit. The "virtual patient" is displayed on the computer monitor with contoured normal tissues and tumor volumes utilizing various renderings (wire frame or solid surface), colors and degrees of transparency. The three-dimensional tumor volume and normal tissue renderings allows the oncologist to appreciate the position of the tumor relative to normal tissue much more effectively than would be possible using solely two-dimensional radiographs.

**Picking Fields and X-ray Energies**

The choice of beam directions can be made based on a pre-determined policy (i.e., a standard 5-field prostate plan), or individually optimized by using a Beam's-Eye-View. The advent of high resolution IMRT has made the selection of beam directions less important, since the intensity within the individual fields can be varied to deliver more dose to the target or less dose to nearby sensitive structures. It has been demonstrated that the dose conformality does not increase if more than 7 to 9 fixed fields are used. [24-26]

Beam energy is usually selected at the same time as beam direction. It has been shown that IMRT is no different than normal radiation therapy, i.e. the need to get dose to a deep-seated target requires high energy x-rays. Lower energy x-ray beams can be used to treat deep-seated
tumors, but the side effects can be more pronounced, as superficial sensitive structures receive higher doses. [27]

**Modern Computer Workstations as Medical Assistant**

The manual optimization of a conventional 3-D CRT plan is more accurately described as plan improvement as opposed to automated computer optimization. It allows for modification of beam direction, aperture shapes, beam weights or beam modifiers (e.g., wedges, compensating filters) to improve the treatment plan. However, all these parameters must be manually adjusted, which can be very involved and time-consuming. In contrast, with IMRT, plan optimization is achieved utilizing the power of the modern computer workstation.

Before plan optimization can begin, the physician describes all the clinical parameters necessary for the planning system to optimize the treatment, e.g., desired dose to the tumor volume, and the maximum allowable doses to each of the adjacent normal tissues and structures. In many cases, the same parameters used to evaluate the results of conventional 3-D CRT plans are used as inputs to the IMRT planning process, which is one of the reasons that such computer-assisted treatment planning is often referred to as "inverse treatment planning." Depending on target shape, computing power and the specific inverse planning algorithm, the computerized optimization process can be quite quick—as short as a few minutes for a plan that would have taken an experienced medical dosimetrist hours or even days. With inverse treatment planning, the physician is able to sculpt a radiation dose around the target in a way that would not be practical, or even possible in some cases, with conventional manual planning methods. The first inverse treatment planning systems typically operated in a “batch-mode”, with several different plans, each with different optimization parameters, being submitted to the inverse planning system at one time. The system would optimize each plan, in succession, typically overnight. More recently, inverse treatment planning systems have been introduced that operate so rapidly that the oncologist can change the optimization parameters on-the-fly and immediately see the results on the dose distribution. This not only saves considerable time, but also has proven to be a very useful training aid, allowing the oncologist to more quickly learn how the new inverse planning tools work. [28-33]

**Essential Evaluation Tools**

After the treatment has been optimized, the treatment planning software calculates and displays the 3-D dose distributions. This 3-D display of the dose distribution is a critical part of the plan evaluation methodology. Planning tools must be able to spotlight the areas of particular clinical interest. 2-D displays are helpful for evaluating dose distributions on axial, sagittal, or coronal reconstructions of the CT scan. To further assist the radiation oncologist, dose-volume histograms (DVHs) are calculated and displayed for each contoured structure and target volume. DVHs are extremely helpful in determining that target volumes will be adequately covered, and evaluating the dose that will be delivered to surrounding critical structures. Dose statistics, including the percent volume receiving the prescription dose (or tolerance dose for normal tissue), as well as the minimum, maximum and mean doses going to each contoured volume, are also typically provided to the oncologist.

Digitally reconstructed radiographs (DRRs), 2-D reconstructed X-ray images produced from the 3-D CT data set, are typically produced for each field, and compared with radiographs taken with the patient in the treatment position as part of a quality assurance process.
Aligning the Virtual Patient with the Real Patient

A verification procedure must be used to confirm the validity and accuracy of an IMRT treatment plan. This verification procedure may be performed as a simulation on the treatment machine (linac) prior to the first treatment, or more efficiently, using an X-ray machine, such as the Acuity™ simulator from Varian Medical Systems, which mimics the treatment machine. For the verification simulation procedure, the patient is placed on the treatment table in the treatment position, using the immobilization device employed in the initial plan localization. Orthogonal radiographs are taken and then compared to the orthogonal DRRs to confirm isocenter position. Next, the treatment fields are filmed and compared to the DRRs from the treatment plan to verify treatment field shape and position. [34-35].

Figure 7: The Acuity™ simulation and verification system.

Double Checking the Dosimetry

IMRT dose verification involves performing quality assurance testing of two major components, the delivery system and the patient plan. Regular quality assurance (QA) testing of the linear accelerator and its major sub-component, the multi-leaf collimator (MLC), is already conducted on a routine basis, as described by a treatment center’s policies and various legal requirements. QA for delivery of IMRT treatments can be thought of as extension of the existing machine QA program. QA of the linac and MLC are beyond the scope of this paper; fortunately, there are already several excellent sources that cover this topic in detail. [36-43]

With IMRT, unlike 3-D conformal radiation therapy, QA checks on patient-specific intensity patterns must be performed. In some clinics, this is done on a field-by-field basis; in other clinics the entire plan is checked at once. In either case, the QA process involves delivering radiation to a phantom according to the patient’s treatment plan, either one field at a time, or using the entire plan at once. The resulting dose is calculated in a process that can be quite time
consuming. Consequently, these measurements are usually made during nights or weekends, when clinic personnel are not treating patients. This can present administrative issues.

Recently, Varian Medical Systems introduced a capability called “portal dosimetry” to alleviate many of these issues and save considerable time. It allows clinicians to convert the electronic image from the PortalVision electronic portal imaging device into a dose distribution and then compare the acquired portal dose to the predicted portal dose from the inverse treatment planning system. Quantitative comparisons can be performed for machine quality assurance (to verify MU, or dose delivery calculations in terms of monitor units), or for pre-treatment verification of IMRT fluence distributions. It has been reported that manual measurements that formerly took up to 2 or 3 hours can be completed in as little as 15 minutes. [44-47]

![Electronic Portal Dosimetry™ image](image)

**Executing the Plan**

Once the treatment plan has been optimized and verified, patient treatment can commence. Since radiation therapy is fundamentally a non-invasive procedure, many treatments can be completed on an outpatient basis, and patients can continue with many of their normal routines.

At the time of treatment, parameters that were optimized for a specific patient are recalled by the therapist from a central database and loaded automatically into the treatment machine. The patient is placed on the treatment table in the treatment position, using the same immobilization device. [48]

Orthogonal radiographs, using a kilovoltage x-ray or the megavoltage treatment beam are taken and then compared to the DRRs to confirm isocenter position. On-line electronic imaging systems like Varian’s PortalVision™ or On-Board Imager™, generate digital images that can be computer-matched to DRRs for precise patient position analysis. If the intended target is soft-tissue, a good example being the prostate, then cone-beam CT or marker seeds can be used to localize the target immediately prior to treatment. If a “gated” treatment is employed, using RPM™ gating, then a quick kilovoltage fluoroscopic session can be employed to confirm the gating thresholds.
During the actual delivery of the treatment, which usually lasts only 5 to 6 minutes, the patient lies on the treatment couch while the machine rotates around him or her to deliver the desired sequence of beams. To assure the treatment is delivered as planned, on-line electronic imaging can be done while the treatment is being delivered using PortalVision™.

Planning for IMRT - Secrets of Success

Until recently, capital or strategic planning in radiation therapy was easy. Once every 10 to 15 years, the department manager would procure a new linear accelerator. With all the changes that have taken place in radiation therapy, and especially with all the new technology involved, it is clear that capital budgeting for radiation therapy requires a totally different approach. New capabilities and refinements appear almost every year. Software-based systems such as information management and treatment planning are continually evolving, making replacement and upgrade decisions necessary on a frequent basis. Radiation therapy departments now need a strategic capability plan that looks at the following:

- Current technologies and capabilities
  - Choosing an integrated system or looking for “best-of-breed” components from different vendors and solving technology integration problems
  - Acquiring new equipment or upgrading existing equipment
- Capital Equipment Acquisition Strategies
  - Purchase vs. lease or pay-per-use
- Defining the market opportunity for offering IMRT services
  - Estimating clinical case mix and market size, with demographic data of the market region
  - Analyzing referral patterns
- Developing a revenue model and business plan
  - Pricing methodologies
  - Reimbursement mechanisms; APC, RBRVS, global, etc.
  - Operational budget models
  - Managed care contracting strategies

Careful consideration of these factors can allow a radiation oncology department or facility to assemble a cogent plan supported by medical and economic implications. Departmental administrators must examine the immediate and long-range environment in terms of the advancements occurring in the field, pressure coming from consumers for access to new capabilities, payment and reimbursement opportunities, and revenue models. They may
determine that, while they possess reliable equipment, without upgrades they will not be capable of offering the new techniques that promise better outcomes. At the same time, the ability to offer IMRT can become a competitive advantage for other centers nearby. Adding an IMRT capability may become key to retaining and possibly increasing a patient referral base. In the near future, IMRT may become the standard of care for many types of cancer.

Upgrading a Facility

Varian Medical Systems works with medical facilities to develop optimal upgrade paths and long-term plans for implementing them. The company helps radiation oncology department managers take stock of their current technology, determine what additional hardware and software elements are needed for offering IMRT, and develop a timeline and plan for accomplishing the goal within budgetary constraints. Issues that are considered include: what kind of linear accelerator(s) are already in place; what types of cancer will be treated; how many patients are typically seen in a day; and what is the shortest distance between the status quo and the facility that is being envisioned? For example, in terms of hardware, hospitals that already own a Varian C-series Clinac® can be upgraded with any of three MLC models capable of executing all forms of IMRT using Varian’s software. For every step of the treatment process, Varian offers the VARiS Vision™ information management system, which is anchored by VARiS Clinic, incorporating patient registration, patient chart, mini-schedule, patient check-in and system administration. As a facility grows, so can VARiS, a complete electronic health record that uses a scalable architecture to accommodate more patients, and more treatment techniques and machines.

A migration to IMRT usually follows a typical sequence, with a customized path that proceeds, via phased development, to build on a facility’s current capabilities. Phase one generally involves installation of the basic technology, including the dynamic multileaf collimator, the inverse treatment planning system and the integrated information management system to get an IMRT program up and running. Phase two further enhances the clinical process and improves efficiency by adding additional integrated patient data and image management tools for tracking all information about a patient in a single file. Automated QA tools could also be added in Phase 2. Phase three introduces additional technique refinements such as See and Treat® Cancer Care modalities, which deploy CT and PET scanning for accurately localizing the tumors to be treated.

Respiratory gating can be added at any point after the dynamic MLC is operational, to manage respiratory motion during imaging and treatment. The goal for a representative facility might, over time, be to establish a digital, paperless environment, upgrade to 3-D conformal and high-resolution IMRT treatment planning, incorporate functional imaging, upgrade patient positioning capabilities, and integrate all clinical data management. The entire process is flexible, and Varian Medical Systems works with each hospital or clinic to customize a plan based on its unique situation and goals.

Implementing IMRT – Executing The Plan

Hospitals and clinics adding an IMRT program often find that a specific sequence of actions can smooth the way. An essential set of steps would be:

- Choose a champion or project leader
- Create an IMRT implementation team
- Initiate a planning phase that includes acquisition of necessary equipment
- Choose a disease site
- Establish IMRT procedures and responsibilities
- Test the IMRT process
- Treat the first IMRT patient
- Evaluate the process, improve procedures, implement change as needed
- Move on to treat another disease site

Creating the Team

The IMRT team might include the radiation oncologist, medical physicist, departmental administrator, dosimetrist, a radiation therapist and a nurse. It works best if there is an IMRT champion or team leader to drive the project and to marshal resources as necessary.

The Planning Phase

During the planning phase, the team concentrates on acquiring and commissioning the necessary equipment. Many facilities hire an experienced consultant at this point, for a time-limited assignment. Often times, the designated medical physicist is relieved from normal department duties during the implementation, so he or she can focus on learning how to use the new treatment planning system, and on developing necessary QA tools. At this point, the team would select the initial disease type to be treated. The team might experiment with the appropriate immobilization devices to ensure accurate patient positioning. Most radiation oncology departments start with a focus on one type of disease—often prostate cancer—and add protocols for other sites as they gain experience. Initial disease sites for consideration also include the head and neck, pancreas, gynecological organs, and brain tumors.

Establishing and Testing IMRT Procedures

During this phase, the staff roles are worked out. The radiation oncologist prescribes IMRT for a patient, manages that patient’s treatment, and evaluates the outcome. In most settings, the medical physicist and dosimetrist work together to commission the treatment planning equipment, outline QA procedures, and plan the treatments. Radiation therapists simulate the patient, fabricate custom immobilization devices, treat the patient, and capture images of the treatment fields at treatment. As the team gains experience with inverse treatment planning and dose volume histograms, they can create a “beam library” that will facilitate the treatment planning process. When the team is ready, the IMRT process is tested using a “test phantom” and a treatment protocol that includes treatment verification.
Since its appearance in 1995, Varian Medical Systems’ integrated solution for IMRT, called SmartBeam™ IMRT, has evolved as the company continued to work with clinicians to incorporate process efficiencies. Patient demand helped to drive the market for this technique as access to data on the Internet provided patients and their families with up-to-date information about their treatment options.

Some have noted that the widespread adoption of this powerful treatment approach has been rapid; others say it hasn’t happened fast enough. Keeping his eye on the issue is Arno Mundt, M.D., radiation oncologist at the University of Chicago and medical director for radiation oncology at the University of Illinois Hospital.

Dr. Mundt studies IMRT in three ways. He conducts clinical studies, mostly on the use of IMRT to treat gynecological cancers. He conducts usage studies to learn how IMRT, still a recent advance, is being deployed across the U.S. And he has compiled a comprehensive textbook on IMRT, collecting 30 chapters from 183 contributors at 43 treatment centers in nine countries: Belgium, Canada, China, Germany, Great Britain, Spain, Switzerland, Japan, and the United States. [49]

The scope of Dr. Mundt’s new textbook illustrates just how far IMRT has come since its introduction in the mid-1990s. Chapters cover the use of IMRT to treat every kind of solid tumor cancer, including cancer of the head and neck, prostate, lung, breast, gastrointestinal organs, cervix, and uterus, as well as pediatric tumors, sarcoma, spinal metastases, and lymphoma.

“IMRT is coming into its own. It’s not just a matter of technology diffusion,” Dr. Mundt commented. “People are figuring out how to use it in more sophisticated ways, radiation oncology residents are all being trained, and there’s an explosion of literature showing the benefits of IMRT, and how it can be applied.”

Dr. Mundt and a group of colleagues conducted their first IMRT usage study in 2002, surveying 450 randomly selected radiation oncologists in the U.S. Published in the journal Cancer, the study showed that 32% of respondents were using IMRT at that point in time. Most had adopted it only during the prior 12-24 months, and were treating only head and neck tumors and prostate cancer.

In 2004, Dr. Mundt’s team did a follow-up study to see what was happening in the country at that time. They found that 73% of the respondents were using IMRT in their clinics. Of those who were not, 90% planned to adopt it within 1-3 years.

“There was a huge conversion of non-users into users,” Dr. Mundt observed. “We also surveyed the chief residents at 77 accredited training programs, and found that about 85% of the nation’s residents were being trained to use IMRT. That really sets the stage for the future.” [50-51]

Statistics about IMRT deployment at Varian-equipped hospitals echo Dr. Mundt’s observations. At the end of the fiscal year in 2003, the number of radiation oncology centers treating patients with Varian’s SmartBeam™ IMRT had more than doubled to 472. By September 2004, some 860 clinics had commenced treating patients with SmartBeam IMRT and that number was on track to approach 1,000 by the end of the year. About half of the
roughly 2,600 Varian-equipped sites around the world have acquired the technology needed for delivering IMRT. And nearly 95% of the new linear accelerators ordered in 2004 included the hardware and software required for delivering IMRT.

Looking Forward – The Future Is In Motion

The future of radiation therapy will be closely bound to the use of new imaging modalities and further improvements in tumor targeting. Currently, CT and MRI images are used to provide structural information about a patient’s internal anatomy in preparation for radiation therapy. However, more advanced imaging techniques offer the potential for the clinician to view the physiology of the tumor in order to improve IMRT treatment planning. For example, using modalities such as Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT) and Magnetic Resonance Spectroscopy (MRS), the oncologist can see where a tumor is most metabolically active. Since IMRT allows them to vary the radiation dose within the target volume, extra dose can be concentrated on these more active areas. Since late 2000, Varian Medical Systems has been working in partnership with GE Medical Systems to provide a single, comprehensive suite of integrated imaging, information management, and treatment solutions. This See and Treat® solution for cancer care enhances physicians’ ability to visualize potential targets more clearly and deliver more precise IMRT treatments. [52]

Figure 9: These diagnostic images of a lung cancer case were created using a Discovery LS scanner from GE Medical Systems, which combines PET and CT scanning in a single machine. On the left, a CT image shows anatomical detail, but the cancer is hard to see. In the central PET image, cancer shows up distinctly as a spot on the lung, but anatomical detail is hard to see. On the right, a fused PET/CT image can help doctors precisely localize the cancerous tumor.

Another challenge being addressed is the fact that tumors move around, both during and between treatments. They are subject to “intra-fraction” and “inter-fraction” motion as a
patient breathes, or as a result of day-to-day physiological changes. In addition, random set-up errors occur over a course of radiation treatment, which can take several weeks. Imaging and localizing tumors prior to and during treatment to monitor any changes in tumor position or size is part of a process Varian calls Dynamic Targeting™ IGRT (image-guided radiation therapy), a complementary process to IMRT that seeks to make radiation therapy more exact than ever before through real-time imaging procedures.

Figure 10: This sequence of MRI images shows the extent to which a reference point on the lung moves over a two-second period due to respiratory motion (intra-fraction motion).

Dynamic Targeting IGRT provides clinicians with a comprehensive workflow process that allows them to see clearly what they’re treating on a day-to-day basis. Varian has developed a number of Dynamic Targeting IGRT tools that work together to enhance precision and accuracy in the delivery of radiation therapy. These include the Exact® couch with Indexed Immobilization™, which enables clinicians to rapidly and consistently position patients for treatment; the RPM™ Respiratory Gating System, which is essentially a method to compensate “electronically” for tumor movement as a result of respiratory motion; the PortalVision™ electronic portal imaging system that allows the fast acquisition and instantaneous display of high quality megavoltage images critical for initial patient positioning or patient treatment verification; and the On-Board Imager™ device, which adds kilovoltage-imaging technology to the linear accelerator for daily imaging in the exact treatment position.

RPM Respiratory Gating™

One challenge for Dynamic Targeting IGRT is to monitor respiratory tumor motion in real time. Varian’s Real-time Position Management (RPM) respiratory gating system uses an infrared video system to track a lightweight marker block placed on the patient’s chest or abdomen. A tracking camera mounted on the wall sends infrared light toward the marker block and the signal generated by light reflected back is processed by the gating system to identify the patient’s rhythmic breathing pattern. This information is used to determine when the tumor is in a certain zone during the respiratory cycle so that the treatment planning images can be synchronized with the respiratory cycle. During treatment, the beam is then automatically “gated” on and off as the tumor moves in and out of the selected zone.

Dr. Anthony Berson, chairman of the Radiation Oncology Department at St. Vincent’s Comprehensive Cancer Center in New York, has pioneered respiratory-gated treatment protocols and treated more than 300 patients between 2001 and 2004. In commenting on Varian’s RPM™ respiratory gating system, he said: “Our initial goal is to increase the dose 10 to 20 percent. We expect that as we increase the dose, we should be controlling tumors at a higher rate. Traditionally, we probably used margins of anywhere from 3 to 5 centimeters around a tumor to ensure that we were getting adequate coverage. With respiratory gating the margin has been reduced to between 1 and 2 centimeters. That’s a huge improvement!”
In addition to lung cancer, Dr. Berson and his team have used respiratory gating in the treatment of upper abdominal cancers, including pancreatic, stomach and liver tumors, which also move as patients breathe. In those cases, he said, the large radiation fields required by traditional techniques combined with chemotherapy result in a high complication rate. “In that situation,” he says, “anything you can do to reduce the size of the field will reduce unwanted complications.” With Varian’s RPM respiratory gating, this is achieved easily and without disrupting or slowing a clinic’s workflow.

“We are a very busy community hospital, and our throughput is very high,” Dr. Berson said. “We see a lot of patients in a day. This is just a normal part of our day.” [53-64]

Dr. Francine Halberg of the Marin Cancer Institute in Greenbrae, California, has been using Varian’s RPM respiratory gating to treat left-sided breast cancer, where the ability to precisely target a cancerous site enables her to avoid irradiating heart tissue. At the time of this writing, she has already used the technology to treat more than two-dozen breast cancer patients after their tumors were removed by lumpectomy.

“It’s a wonderful technology,” said Dr. Halberg. “Respiratory gating protocols for lung cancer usually seek to deliver treatment at the point of the patient’s maximum exhalation. That’s a very stable point and very consistent relative to other parts of the breathing cycle. However, for treating breast cancer, we’re looking for the farthest inhalation, because that’s when the breast moves furthest from the heart. We now have a very, very low risk of recurrence after radiation therapy to the breast. As thousands of women get treated for breast cancer each year, respiratory gating has the ability to help a tremendous number of patients.”

**PortalVision™ Electronic Portal Imaging**

The Varian PortalVision electronic portal imaging system creates high-resolution, two-dimensional electronic images using the megavoltage treatment beam, and compares them to the digitally reconstructed radiographs (DRRs) from the treatment planning system or to digital images from the Acuity kilovoltage simulator. This comparison is done for two purposes: verification of the patient setup and verification of individual field placements. Electronic portal imaging systems are in routine clinical use at many institutions and are increasingly being used to measure setup errors. The use of amorphous silicon flat-panel imagers in lieu of film produces better portal images using less dose. The improvement in image quality has
enabled the practical use of implanted radiopaque markers for correcting a patient’s position just prior to treatment. [65-69]

Lane Rosen, M.D., is director of the Willis-Knighton Cancer Center in Shreveport, Louisiana. PortalVision enables his department to maintain a busy treatment schedule while providing very precise and complex treatments. Dr. Rosen said, “The older process of waiting for a film to develop would have limited our ability to use smaller fields and compromised the effectiveness of our immobilization devices. If people move, you need to use bigger fields, and if you’re using bigger fields, you can’t give higher doses. The online portal imaging fit perfectly into our model of reducing toxicity while giving higher doses. It also reduced the workload for our therapists, who were already taking on much more responsibility for complex setups.”

Figure 12: Varian’s PortalVision electronic portal imaging system uses amorphous-silicon flat panel digital imaging technology to check patients’ position and verify treatments.

**The On-Board Imager™ Device**

Varian Medical Systems has recently introduced the On-Board Imager™ device for the Clinac® and Trilogy™ medical linear accelerators. This imaging device is designed to improve the precision and effectiveness of cancer treatments by providing tools to target and track tumors more accurately. It allows clinicians to obtain high-resolution X-ray images to pinpoint tumor sites, to reference those images against planning images, to adjust patient positioning automatically when necessary, and to complete radiation delivery, all within the standard daily treatment appointment.

Varian’s approach has been to integrate a kilovoltage (kV) X-ray source and large-area flat-panel image detector on a medical linear accelerator. The On-Board imager can generate radiographic, fluoroscopic, and volumetric cone-beam CT images. In effect this combines the imaging capabilities of a digital simulator and a CT scanner with the linear accelerator so that
the control system can orchestrate the interplay of imaging and delivery components in a single machine. Such an integrated approach offers the flexibility to employ a treatment-procedure-specific imaging strategy for real-time fluoroscopy, radiography, cone-beam CT, or a combination of all three. It also allows image-guided procedures to be performed within the tight time constraints found in the typical radiation therapy clinic.

Figure 13: Clinac with On Board Imager. The system incorporates of an X-ray tube and an amorphous-silicon flat-panel image detector on a pair of robotic arms. (Image courtesy of Emory University, Atlanta, Georgia, USA).

Varian’s On-Board Imager is mounted on the treatment machine gantry via two robotically controlled arms. Each arm operates along three axes of motion so that it can be positioned optimally for the best possible imaging of the target volume, or to capture the motion of other internal structures some distance away. The arms also allow the imager to be quickly retracted out of the way when not in use. The kV imaging system operates in a plane that is orthogonal to the megavoltage treatment beam and its associated amorphous silicon flat-panel imager. Thus the two imaging technologies can be used in concert, in a “bi-plane” imaging geometry, to rapidly locate the target exactly in three dimensions.

The On-Board Imager device yields digital images showing internal anatomic landmarks with a high degree of precision. Software tools are incorporated that allow rapid manual or automated image matching to reference images. By rotating the gantry 90 degrees, a pair of coherent kV images can be quickly acquired. Alternatively, the image pair can consist of a kV image and orthogonal MV image acquired in rapid succession without rotating the gantry. Imaging software then registers the image pair against a corresponding reference image pair. These can be radiographs acquired on a simulator, or they can be DRR images computed from the volumetric CT data set used in treatment planning. The image registration software takes advantage of common or coherent information in each image pair to search for the position and angular correction needed to minimize the difference in mutual information contained within the reference image set and the daily image set. This in-plane mutual information matching can be restricted to a user specified region of interest. The result from this 2D + 2D
anatomical matching is a computed offset with 5 degrees of freedom. The needed X, Y and Z axis translations, plus the in-plane rotations (pitch and yaw), are automatically computed, and the matched image sets are then overlaid with suitable tools for visual confirmation. Once the match is accepted, the corrected position offsets are automatically downloaded so that the treatment couch can be repositioned from outside the treatment vault, and the tumor shifted into the correct position with sub-millimeter accuracy.

In addition to anatomic matching, automated tools are also provided for matching the position of implanted radiopaque fiducial markers using similar kV image pairs. A volumetric CT data set can be acquired after implanting suitable gold fiducial markers, and then used for treatment planning. The Varian software can be used to quickly search the 3D CT data to locate the marker positions that correspond to the target volume. Each treatment day, a pair of kV images is acquired as described above. The system’s imaging software automatically locates the markers in each of those two images and registers those locations against the corresponding 3D coordinates of the same markers in the reference CT data set. From this, a full six-degree-of-freedom (6DOF) correction vector is computed. Again, after review and acceptance of the match, the couch position can be automatically corrected. In this manner, soft tissue structures, or target volumes such as the prostate, can be quickly targeted on a daily basis.

Operating in the fluoroscopic mode, the On-Board Imager device can track real-time anatomic motion and thus provide a clear indication of how a tumor moves during treatment due to respiration or other normal physiological processes. This modality can be used in concert with Varian’s RPM respiratory gating system to verify immediately before each treatment that the beam gating strategy will yield the desired margins and dose distributions. This may prove to be a useful tool as part of an extra-cranial radiosurgery or a radio-ablation program. Real-time tracking algorithms are under development that are anticipated to directly provide respiratory gating or tracking information from internal anatomic motion.

Possibly the most powerful imaging modality available with Varian’s On-Board Imager is cone-beam CT. In this mode an entire volumetric CT data set is acquired and reconstructed with a single gantry rotation. The system takes full advantage of Varian’s new PaxScan 4030CB amorphous silicon flat panel imager, made by the company’s X-ray Products business unit. This imager utilizes unique technology to provide exceptionally high dynamic range, great sensitivity, and rapid frame rates for fast image acquisition. Varian has also incorporated a unique 150 kV X-ray tube designed specifically for this application.

By using robotic technology and control software to position the On-Board Imager and patient couch, the Varian system offers the automation, speed and flexibility needed to make a Dynamic Targeting IGRT process clinically practical. The system is designed for full integration with Varian’s VARiS Vision™ image and information management system, as well as the company’s Eclipse™ treatment planning software products.

The new On-Board Imager is available as an option on all of Varian’s newly installed high-energy Clinac linear accelerators, and as an upgrade for most digital Clinac accelerators already in place at clinical sites. It is a standard feature on all Trilogy linear accelerators.
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