

TOMOTHERAPY: A "REVOLUTION" IN RADIATION THERAPY

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Tomotherapy is a new modality of radiation treatment that combines the use of very sophisticated computer-controlled radiation beam collimation with an on-board computed tomography (CT) scanner to image the treatment site. It provides unprecedented accuracy in beam delivery allowing for an increase in tumour dose, thereby increasing the likelihood of cancer cure while at the same time reducing treatment complications in healthy tissues.

INTRODUCTION

Cancer and Radiation Therapy

Cancer is the most significant health care problem in the western world surpassing heart disease as the leading cause of potential years of life lost ^[1]. In Canada, about 134,000 people are diagnosed annually with cancer. This represents more than one in three people who will develop cancer during their lifetimes. Radiation will be used to treat approximately 66,000 new cancer patients per year of whom 33,000 will be treated with an attempt to cure the disease.

The radiation therapy process is complex and involves multiple steps as shown in Figure 1. The process begins with patient diagnosis and three-dimensional (3-D) imaging, through various steps that prepare the patient for treatment and, finally, to treatment verification and actual radiation dose delivery. Patients who are treated for cure receive high radiation doses of 60 to 70 Gy, given in 30 to 40 daily fractions at the rate of 5 fractions per week. There are several critical steps in this process. One of these is the use of sophisticated 3-D imaging using computerized tomography (CT), magnetic resonance imaging (MRI), single photon emission tomography (SPECT), or positron emission tomography (PET). These imaging modalities have evolved dramatically over the last decade and provide information about tumour location and tumour extent, with each modality providing unique information that is especially relevant for specific tumour types. An example of the combined use of MRI and CT is shown in Figure 2 and illustrates how the use of these imaging modalities aids in the definition of the tumour and its extent. Figure 2 also illustrates the location of the eyes and surrounding brain, both of which need to receive minimal radiation dose to avoid treatment complications.

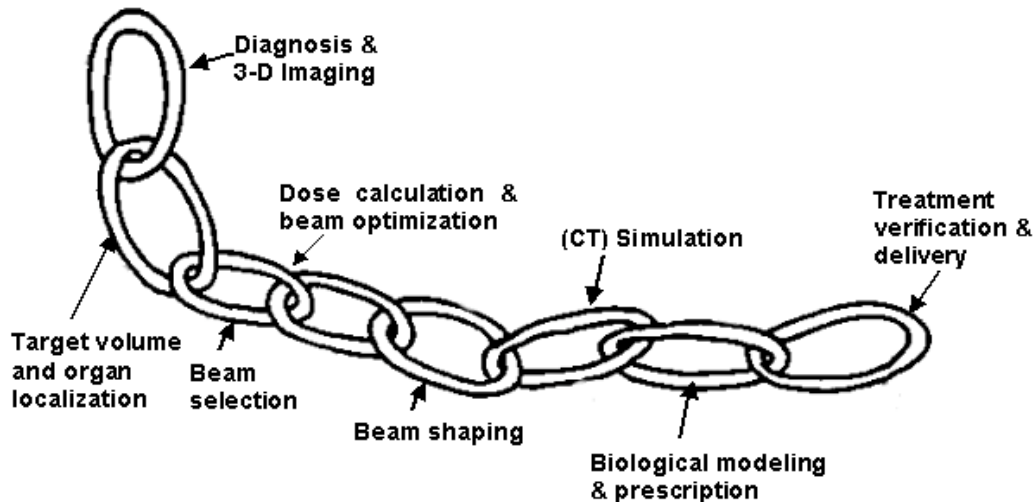


Figure 1. The various steps in the radiation treatment process are represented by links in a chain ^[2].

With such image data, sophisticated dose calculations can be performed using shaped radiation beams from various directions to yield optimized treatment plans.

In addition to imaging for therapy planning, there are a number of requirements in order to deliver a prescribed radiation dose to the patient with a sufficient control and accuracy. These relate to the technologies used to deliver the dose to the patient and the computerized calculational procedures that are required to optimize the treatment technique and to predict precisely the dose that will be given to the patient using complex radiation delivery technologies.

Modern Dose Delivery

One of the unique features of radiation therapy, compared to other forms of cancer treatment, is that the radiation can be delivered in an anatomically and geometrically specific fashion by using radiation field collimation and beam shaping. Today, linear accelerators (linacs), generating electron energies between 4 and 25 MeV, are generally used for producing x-ray beams for the treatment of tumours. Conventionally, these machines have collimators that produce rectangular fields between 4 x 4 cm² to 40 x 40 cm². The newer machines have collimators which are divided into multiple segments from two opposite sides. The "leaves" in these "multileaf collimators" are motor-driven and computer-controlled and can project shadows at the level of the patient that are 0.5 or 1 cm in width. Figure 3 shows such a multileaf collimator (MLC) and an example of a field shape that can be produced by such a unit.

In addition to simple field shaping, computer-controlled multileaf collimators provide the capability of defining multiple field shapes either for individual directions or for multiple fields aimed at the tumour from different directions. This, combined with "automated" optimization programs using "inverse" dose calculations, allows control of the beam *intensity* pattern at the patient such that a well-defined and uniform dose can be delivered to the target and normal tissue doses can be minimized. This process has become known

as segmented field, intensity modulated radiation therapy (IMRT) or when using moving leaves and a moving machine gantry, it is known as dynamic IMRT.

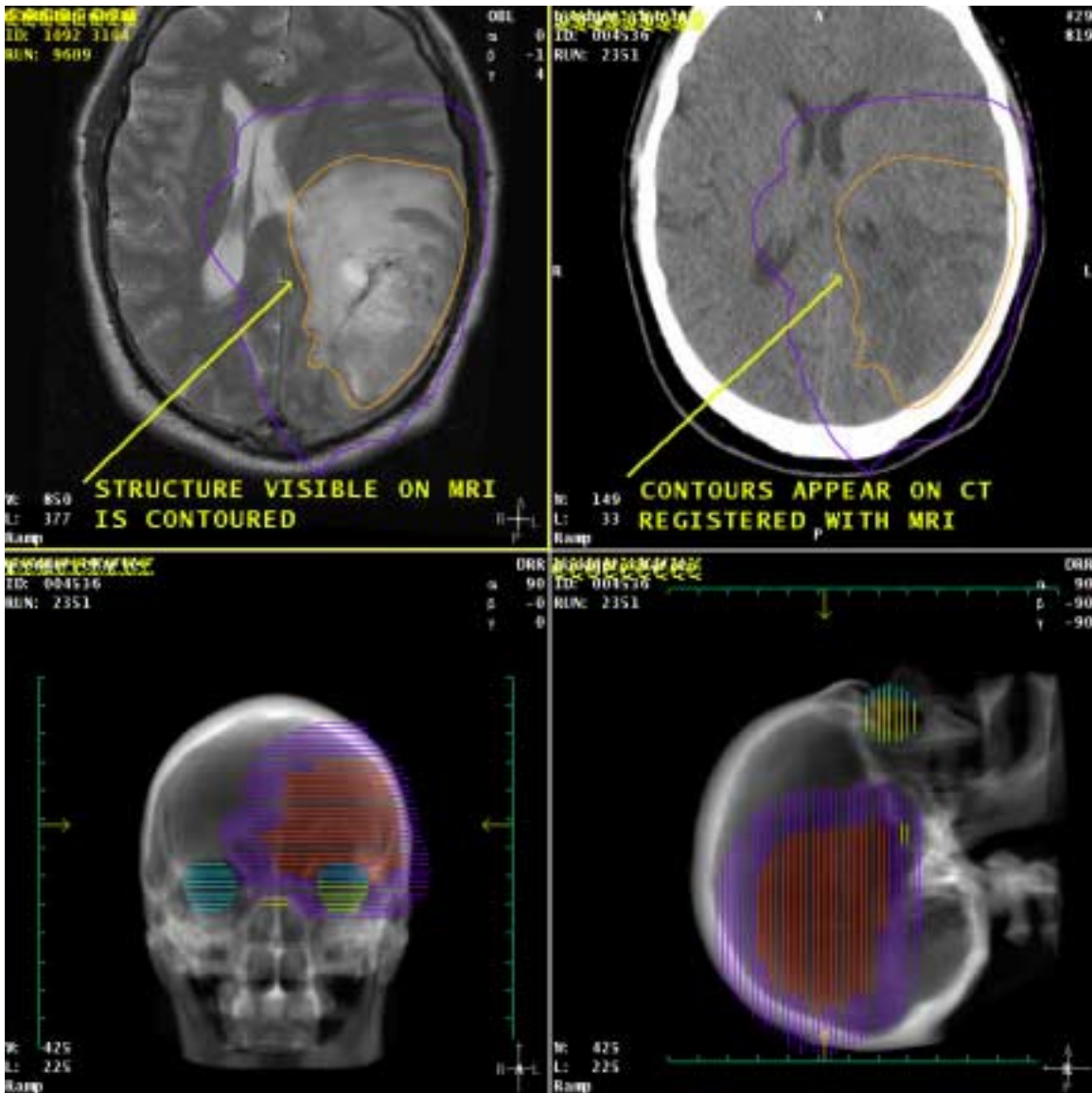


Figure 2. The use of MRI (upper left) for tumour localization compared to a CT scan (upper right) which is needed to perform radiation dose calculations. These are images of a cross section in the head through the brain region. The MR image on the upper left shows a tumour (light grey colour) while the CT image cannot discern the diseased region. However, CT gives the proper information for radiation dose calculations. Thus the MR data needs to be "fused" with the CT data to allow proper radiation therapy optimization. The lower two images are digitally reconstructed radiographs derived from the CT data in the anterior-posterior (lower left) and in the lateral (lower right) directions. The contours outlined are the target volumes and the eyes.

The recent development of IMRT on conventional linacs provided a major increment in radiation therapy dose delivery. However, the rate-limiting step in such highly precise treatments is not the delivery technology but rather the patient. A course of radical radiation treatment often consists of up to 40 daily treatment fractions. For each fraction, the patient must be repositioned. This repositioning has inherent uncertainties that relate not only to setting the patient up to external reference marks, usually laser alignment with marks positioned on the skin surface, but also to the movement of internal organs from day-to-day. To address the issues of highly conformal dose distributions as well as accounting for patient setup and organ motion uncertainties, a new technology, known as "tomotherapy", has been developed. Theoretically, it provides better targeting with a corresponding reduction in the dose to normal tissues. This allows a higher dose to the tumour which results in an increased probability of tumour control.



Figure 3. A multileaf collimator (MLC) on an Elekta linear accelerator (looking from the patient's perspective towards the radiation source).

SERIAL TOMOTHERAPY

Tomotherapy, literally translated, means "slice therapy". The first implementation of this concept was performed by NOMOS Corporation ^[3,4] and was provided as an add-on accessory to existing linear accelerators. The add-on feature consists of a set of multileaf collimators that provide a narrow "fan" beam shape (Figure 4) projecting a maximum width at the patient of about 20 cm. The fan beam thickness can be either 0.8 or 1.6 cm and each leaf projects a shadow of about 1 cm width at the patient. When the leaves are in the beam, that portion of the beam is fully shielded except for a minor (~0.5%) transmission component. Either the leaf is open or closed for that slice providing "binary" dose delivery, i.e., for that portion of the beam, the beam is either on or off. The open beam components are generally referred to as "beamlets" or "pencil beams". Radiation delivery consists of a machine that rotates around the patient while the beam is on and the leaves rapidly move in and out depending on whether that beamlet is aimed at the target or at normal tissues. After two simultaneous slices have been delivered, the patient is translated by two slice thicknesses and the next two slices are delivered until the total treatment volume is covered, hence the nomenclature, "serial tomotherapy". Figure 5 shows the NOMOS MIMiC system attached to the head of a conventional linac.

The determination of leaf sequencing is done by a computerized treatment planning system that uses image data as patient input information. The radiation oncologist defines the malignant target regions as well as the critical tissues. Thus, for example, in Figure 2

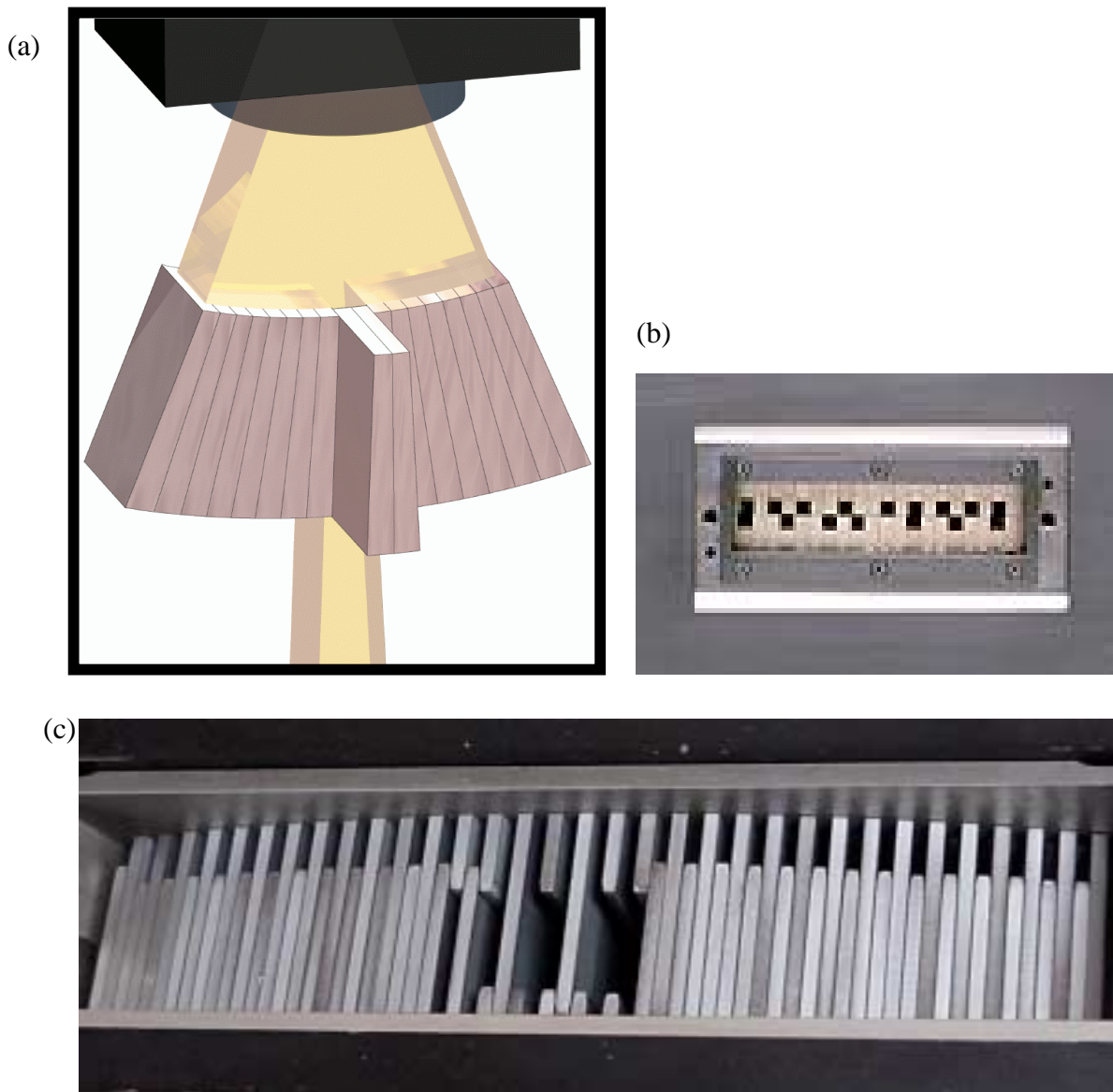


Figure 4. (a) Schematic of a binary multileaf collimator with a fan beam geometry. This schematic example shows leaves that move from one side. (b) Picture of NOMOS double slice multileaf collimator system (MIMiC) with two rows of leaves. (c) Picture of TomoTherapy single slice multileaf collimator showing the interdigitated leaves and how they move from both sides.

contours are generated by the radiation oncologist on multiple MR or CT slices. Furthermore, critical regions are outlined (e.g., eyes in Figure 2) and dose limits to these critical regions as well as the prescription dose are defined as objectives for the optimization. To date over 10,000 patients have been treated using serial tomotherapy at over 75 institutions.



Figure 5. The Nomos MIMiC multileaf collimator attached to a conventional linear accelerator at the Baylor College of Medicine/The Methodist Hospital, Houston, Texas.

HELICAL TOMOTHERAPY

General Design Considerations

Traditional linear accelerators are currently limited to serial tomotherapy due to the limited rotation possible ($\sim 370^\circ$) and the inability to move the couch smoothly and automatically during radiation delivery. Furthermore, serial tomotherapy is unable to image the patient in treatment position and, therefore, unable to assure the accurate placement of the high dose volume with respect to the malignant region. The tomotherapy unit under development at Madison, WI (TomoTherapy Inc.) seeks to remove these limitations^[5].

As can be seen in Figure 6, the helical tomotherapy machine is a combination of a helical CT scanner and a linear accelerator. It uses the slip ring technology of diagnostic CT scanners and, therefore, the unit is capable of continuous rotation around the patient while the couch is moving into the gantry, thus providing smooth helical delivery as shown in Figure 7. Mounted on the rotating gantry and attached to the slip ring is a compact (~ 40 cm long) 6 MeV S-band (3 GHz) linear accelerator generating a 6 MV photon beam. The beam from the accelerator is collimated by a multileaf collimator (Figure 4c) consisting of 64 leaves each of which project a shadow of 6.25 mm at the patient generating a total fan beam width of 40 cm. By using a separate collimation ("jaws") system above the multileaf collimators, the "slice thickness" can range between 0.5 to 5 cm. Since it is a specially designed machine for helical, fan beam delivery, the

multileaf collimation system is specifically designed to minimize leaf transmission and interleaf leakage - important considerations for narrow beam, multislice delivery procedures.

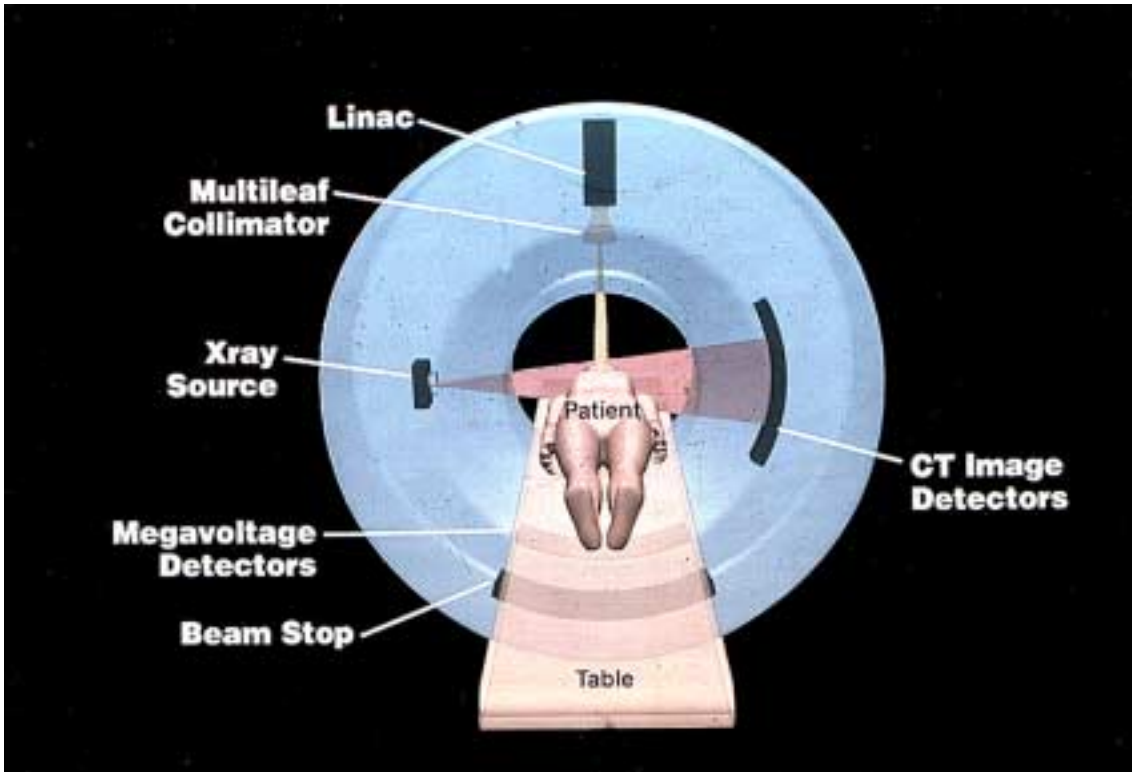


Figure 6. Schematic of helical tomotherapy unit. The first production models will not have the kilovoltage imaging system but will rely solely on megavoltage CT. (Courtesy TomoTherapy Inc. Madison, WI)

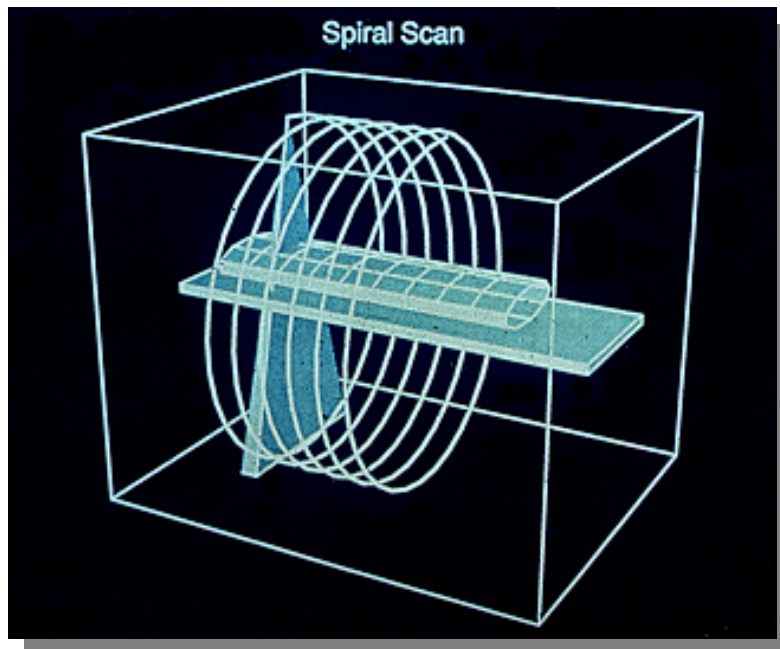


Figure 7. Schematic of tomotherapy's fan beam geometry and helical delivery.

The on-board megavoltage CT detection system is from a conventional, commercial diagnostic scanner using xenon detectors. Similarly, the patient couch is also from a commercial scanner. The CT detection system can be used for: (1) patient set-up verification and repositioning, if necessary, (2) verification of leaf positions during treatment, and (3) reconstruction of the actual dose delivered to the patient with the possibility of making corrections in subsequent fractions. Although megavoltage CT images generally have inferior tissue contrast compared with kilovoltage CT, research to date demonstrates that imaging using megavoltage photons may be adequate for set-up verification, delivery verification and dose reconstruction purposes ^[6,7]. To improve image quality and reduce the dose to the patient, when used for imaging purposes, the linear accelerator is slightly detuned leading to a maximum electron energy at the target of 3.5 rather than 6 MeV. While the schematic in Figure 6 shows both megavoltage and kilovoltage imaging capabilities, the first helical tomotherapy units will not incorporate the kilovoltage capabilities. These will only be added if a clinical need is demonstrated.

Status of Helical Tomotherapy

In the late 1980s, the University of Wisconsin Radiotherapy Research Group began to explore methodologies for intensity modulation of radiation therapy beams. They concluded that the simplest method would be to move a bank of temporally modulated collimators into and out of a narrow fan beam provided by a slice-by-slice delivery, i.e., tomotherapy ^[7]. Subsequently, MEDCO Corporation (later to become NOMOS Corporation) implemented serial tomotherapy using the temporally modulated multileaf collimation system licensed by the Madison group. The Madison group was discouraged by a belief that this rotate-then-translate, slice-by-slice delivery would produce discontinuities at the junction between the slices and, thus, shelved the concept. However, with the introduction of helical CT scanners, tomotherapy was re-examined and it was argued that a fan beam continuously rotating about a patient would eliminate beam-junctioning artifacts ^[5,7]. The Madison group then developed a benchtop prototype research unit using a 4 MV accelerator for experimental purposes. In the meantime, TomoTherapy Incorporated was created in Madison as the company to produce commercial versions of this treatment modality. The clinical prototype, helical tomotherapy machine (alpha unit) is installed in the University of Wisconsin Medical Centre and is scheduled to treat the first patient in early 2002. The first two clinical beta test machines will be installed in Canada, one at the London Regional Cancer Centre, London, Ontario and the other at the Cross Cancer Institute, Edmonton, Alberta. Each of these two clinical beta test machines is expected to treat the first patient at the same time in the summer of 2002. At the present time there is very significant interest in this new radiation treatment modality throughout the world. Subsequent machines are likely to be installed in the U.S. as well as other parts of the world although, at the time of writing, specific sites remain to be designated.

The Process of Helical Tomotherapy

Due to the integration of several technologies into a single piece of equipment, helical tomotherapy allows the development of a number of processes that are either very difficult or simply not possible with other radiation therapy devices. A summary of the

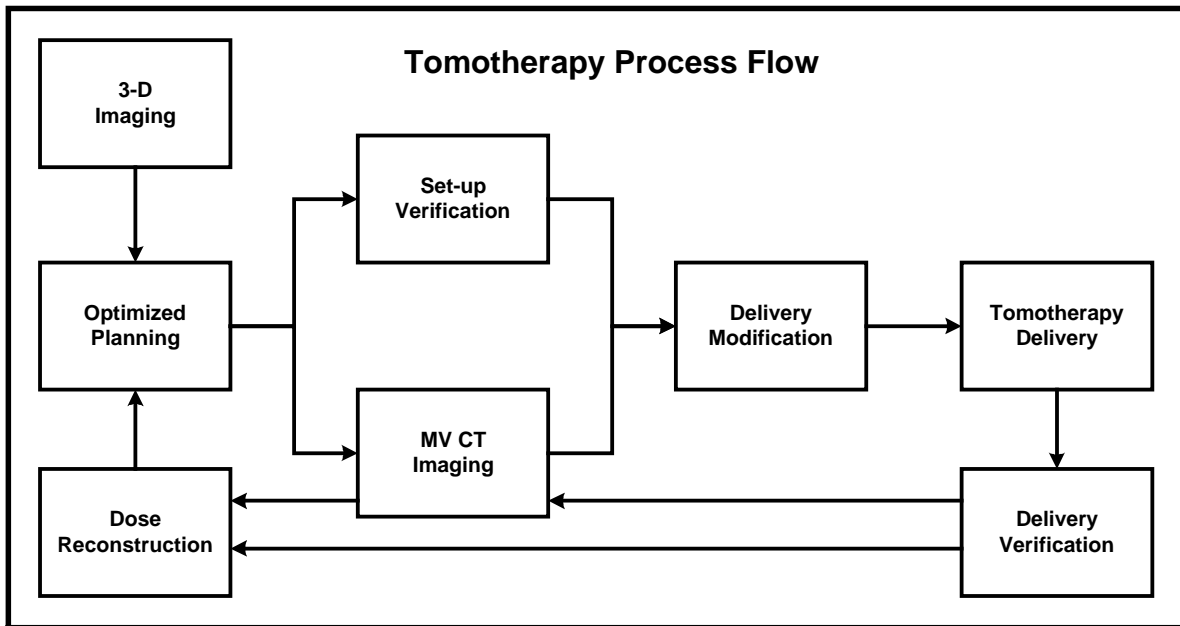


Figure 8. A schematic flow diagram illustrating the various steps of the helical tomotherapy process.

major components of the tomotherapy processes is illustrated in Figure 8. What follows is a somewhat more detailed description of the steps in the tomotherapy process.

(1) **3-D Imaging.** This step of the process is analogous to the generic first step of radiation therapy planning as shown in Figures 1 and 2. This imaging is generally performed with standard diagnostic imaging equipment or CT-simulators. Under special circumstances or emergency situations (e.g., out of regular working hours), the megavoltage CT capabilities on the tomotherapy unit could be used to generate this image data for treatment planning and dose delivery purposes on short notice.

(2) **Definition of Target Volume and Organs at Risk.** With this 3-D image data set, the radiation oncologist needs to contour the target volume as well as the organs at risk. This could be done at the CT-simulator or on a conventional 3-D treatment planning computer after the image data set has been transferred to the treatment planning system.

(3) **Data Transfer to Tomotherapy Planning Computer.** The 3-D data set along with the contours of the target volume and the organs at risk are transferred to the tomotherapy treatment planning computer which will perform the delivery optimization calculations.

(4) **Optimized Planning.** To calculate an optimized treatment plan, the radiation oncologist needs to define the planning constraints or objectives, e.g., the prescribed dose to the target volume and the dose limitations to various organs at risk. The tomotherapy treatment planning system provides "inverse planning" capabilities and determines the leaf positions for all the gantry angles and couch positions. The computation is carried out until all the constraints are satisfied or have been optimized. A typical tomotherapy treatment will involve the delivery of tens of thousands or even hundreds of thousands of pencil beams of radiation. Each of these pencil beams also affects many thousands of

volume elements in the patient. Thus, each optimization involves processing an enormous amount of data - clearly, this is a very complex computational process. The present version of computer hardware associated with tomotherapy optimization calculations involves an array of 32 parallel processors. Even then the optimization takes approximately one hour of computation time.

(5) **Creation of Verification Data.** Verification information for tomotherapy consists of the expected beam intensity at the detector array for each gantry angle and couch position. This intensity pattern is referred to as a "sinogram" because each point irradiated in the patient maps a sine wave pattern at the CT detector as the gantry revolves. Sinograms can actually be obtained for various processes including a CT sinogram as described above, an MLC sinogram, a registration sinogram, a verification sinogram and a planned detector sinogram. Conceptually, they are very similar; however, each is implemented in a very specialized manner to address a specific task. For example, the registration sinogram is a 2-D array containing the signal measured by the detector when a loose helical scan is performed of the patient (Figure 9). This sinogram is used to register the position of the patient and aids the determination of the patient position for each fraction and whether or not dose delivery adjustments are required. Verification data can also be generated for a specific measurement phantom situation which can be used to assess the accuracy of the MLC delivery configuration that is intended for a particular patient treatment. This allows measurements to be made in the phantom to confirm the accuracy of the dose intended for the patient.

(6) **Transfer of Planning Data to the Treatment Unit.** Once the multileaf delivery configuration has been established by the treatment planning optimization calculation, the leaf positions for each gantry angle and couch position are transferred to the tomotherapy unit for delivery implementation.

(7) **Phantom Verification.** This step of the process is described above under Creation of Verification Data and involves treating a phantom with the clinical multileaf collimator configuration and performing the actual measurements to verify its accuracy.

(8) **Pre-Treatment Megavoltage CT.** A pre-treatment CT scan is performed for the verification of the patient position and the location of the internal anatomy. This allows for the relocation of the patient or for the replanning of the multileaf collimator configuration to ensure dose delivery to the right tissues within the patient.

(9) **Delivery Modification.** Modification of the treatment configuration is performed dependent on the information obtained from the pre-treatment megavoltage CT. Automated delivery modification which involves the actual recalculation and resetting of leaf positions is not implemented in the first releases of tomotherapy, partly because this requires additional approval by the U.S. Food and Drug Administration and Health Canada.

(10) **Tomotherapy Delivery.** Once the above steps confirm the accurate location of the patient and the internal anatomy, the dose is delivered according to the planned multileaf

configuration with the leaves moving in and out while the beam is on, the gantry is rotating and the couch is moving simultaneously.

(11) **Delivery Verification.** While the patient is being treated, the detector array is actively measuring the radiation transmitted through the patient (for each pulse of the linac). This is used to determine actual radiation incident on the patient and can be used to verify dose delivery during or after treatment.

(12) **Dose Reconstruction.** Using the incident radiation fluence delivered to the patient and the CT information that was obtained before the treatment, the dose actually deposited in the patient can be computed and compared to the planned dose. If necessary, corrections can be made to subsequent fractions.

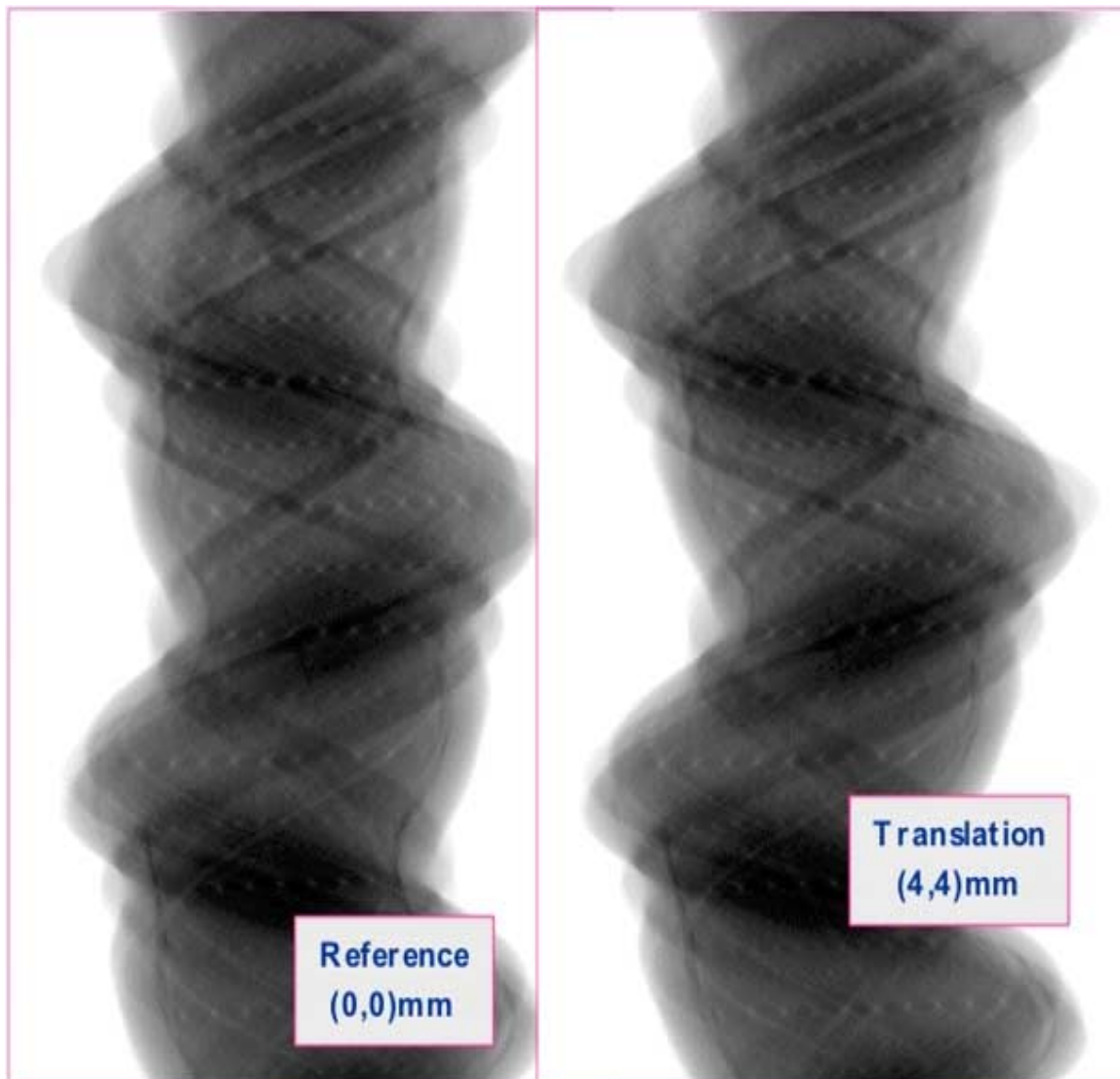


Figure 9. Example sinograms for the registration of the patient in projection space. Two sinograms are shown, one shifted with respect to the other. A sinogram is an array of pencil beam intensity values as a function of gantry angle (vertical axis in this Figure). Each horizontal row corresponds to one angular view (first view from the bottom). The columns label each detector in the array. A point object that is straight and parallel to the z-axis will appear as one cycle of a sinusoidal curve when the gantry revolves by 360 degrees. The amplitude and phase angle of the sinusoid depend on its distance and direction of the point from the isocentre, respectively. Darker grey scale level indicates greater attenuation.

Table 1 provides a comparison between the present capabilities on existing linear accelerators and the capabilities provided by tomotherapy [6].

Table 1. Comparison between conventional radiation therapy and tomotherapy. (Adapted from reference [6])

Process or Technique	Conventional Treatment	Tomotherapy
Conformal radiation therapy	3-D treatment planning	Inverse treatment planning
Set-up verification	Laser alignment Port films or electronic portal imaging	CT projections to obtain detailed anatomical information
Delivery modification	Repositioning of the patient	Adapt delivery according to patient displacement
Beam alignment verification	Port films or electronic portal imaging	Acquire CT scans before, during or after treatment
Delivery verification	Electronic portal imaging	Compute the energy fluence actually delivered to the patient on a pulse-by-pulse basis
Dose reconstruction	None	Superimpose on a CT representation the dose actually deposited in the patient during treatment and compare to the planned dose
Conformal avoidance	Relatively simple shielding	Highly precise delivery while minimizing the dose to organs at risk.

Dose Delivery Capabilities

A few examples will be used to illustrate the kinds of dose distributions that can be delivered using the tomotherapy technology. Figure 10 is a schematic example of a "U"-shaped target that encompasses a critical normal tissue. This could represent a nasopharyngeal tumour around the spinal cord. Figure 11 shows a more realistic clinical example for a cancer of the tongue. The dose distribution illustrates the conforming of the isodose lines around the target regions as well as the sparing of the parotids and the spinal cord. It should be noted that patient anatomy and the corresponding dose distribution change dramatically in the third dimension.

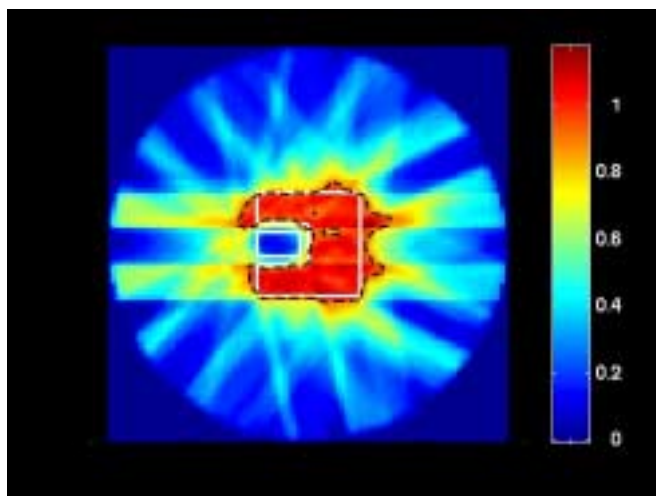


Figure 10. A schematic example of a "U"-shaped high dose region (red) surrounding a critical structure that receives a low dose (blue).

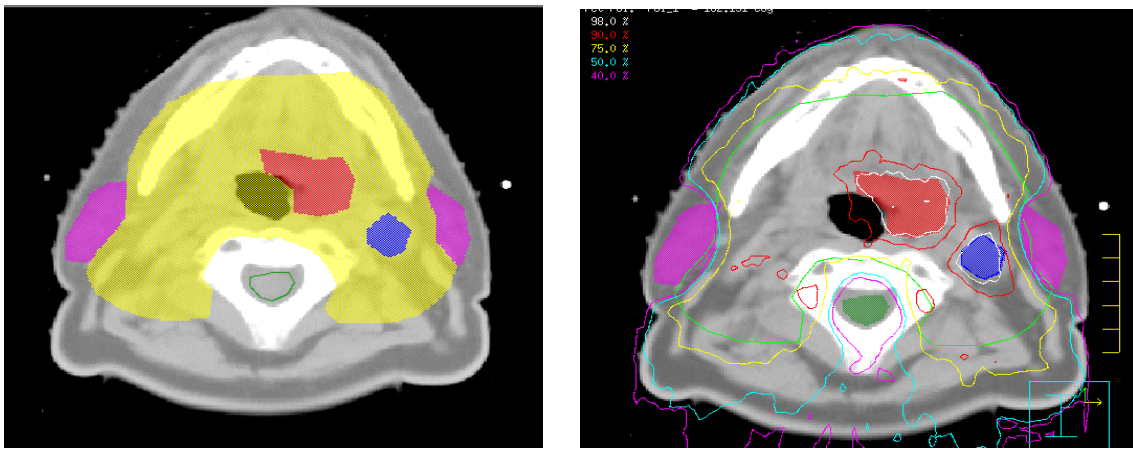


Figure 11. CT images of a head and neck region for a stage 4 cancer of the base of the tongue. On the left image, the orange demonstrates the primary tumour. The blue illustrates an involved node. Both the primary tumour and the node are to receive a high radiation dose. The yellow shows the region of potential microscopic spread and should receive a significant dose although not as high as the primary and the involved node. The grey region surrounded by white represents the spinal cord within the vertebral body and should receive a minimal dose. The magenta regions on the right and left are the parotid glands which should receive minimal dose. The dark area left of the primary tumour represents air in the trachea. The right image demonstrates the resulting dose distribution using tomotherapy delivery.

Figure 12 compares a dose distribution for a cancer of the lung patient using a conventional treatment technique to a tomotherapy distribution. Clearly, the distribution is improved significantly using tomotherapy not only in the plane of this image but also in adjacent planes.

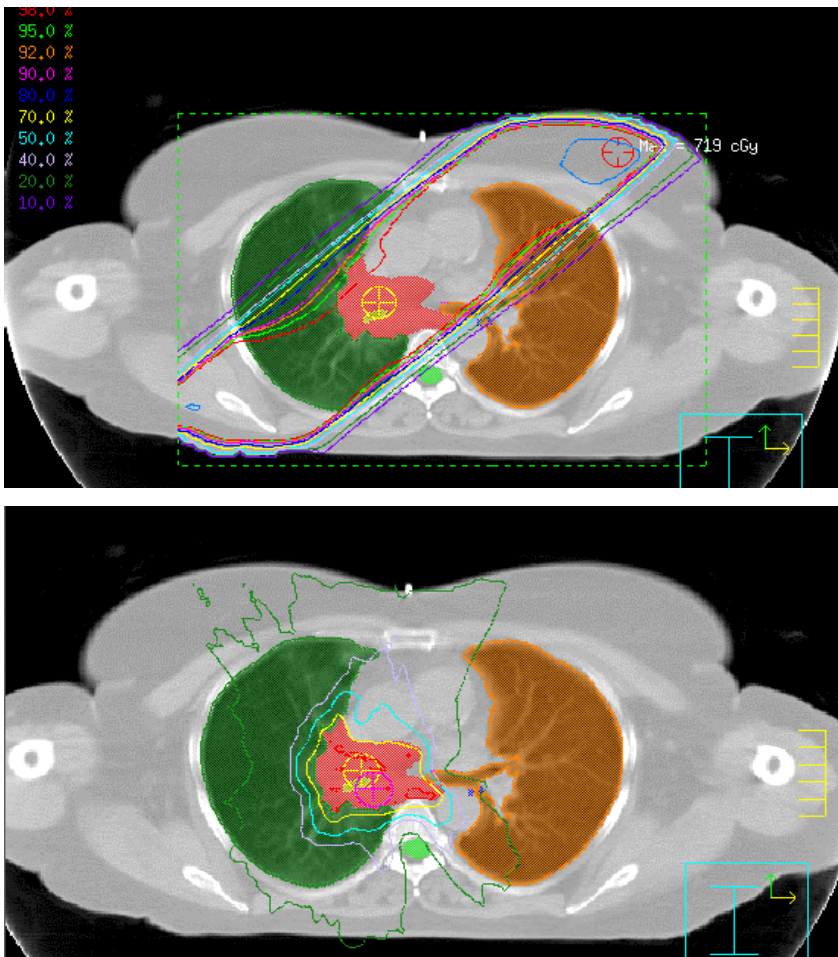


Figure 12. CT scans in the thorax for a cancer of the lung. Upper image illustrates a dose distribution for a conventional treatment while the lower figure illustrates a tomotherapy dose distribution.

CT Imaging Capabilities

The tomotherapy process relies heavily on the in-built capability of the system to acquire CT images for set-up and dose verification. This is realized in the present system by megavoltage CT imaging. As can be seen in Figure 13, the image quality is likely to be adequate for the objective of aligning the target. The dose delivered using the detuned linear accelerator is of the same order of magnitude as the one required for a diagnostic CT scan. Using a dose of around 50 mGy, the contrast resolution is better than 0.5% and the spatial resolution of a high contrast object is better than 1 mm.

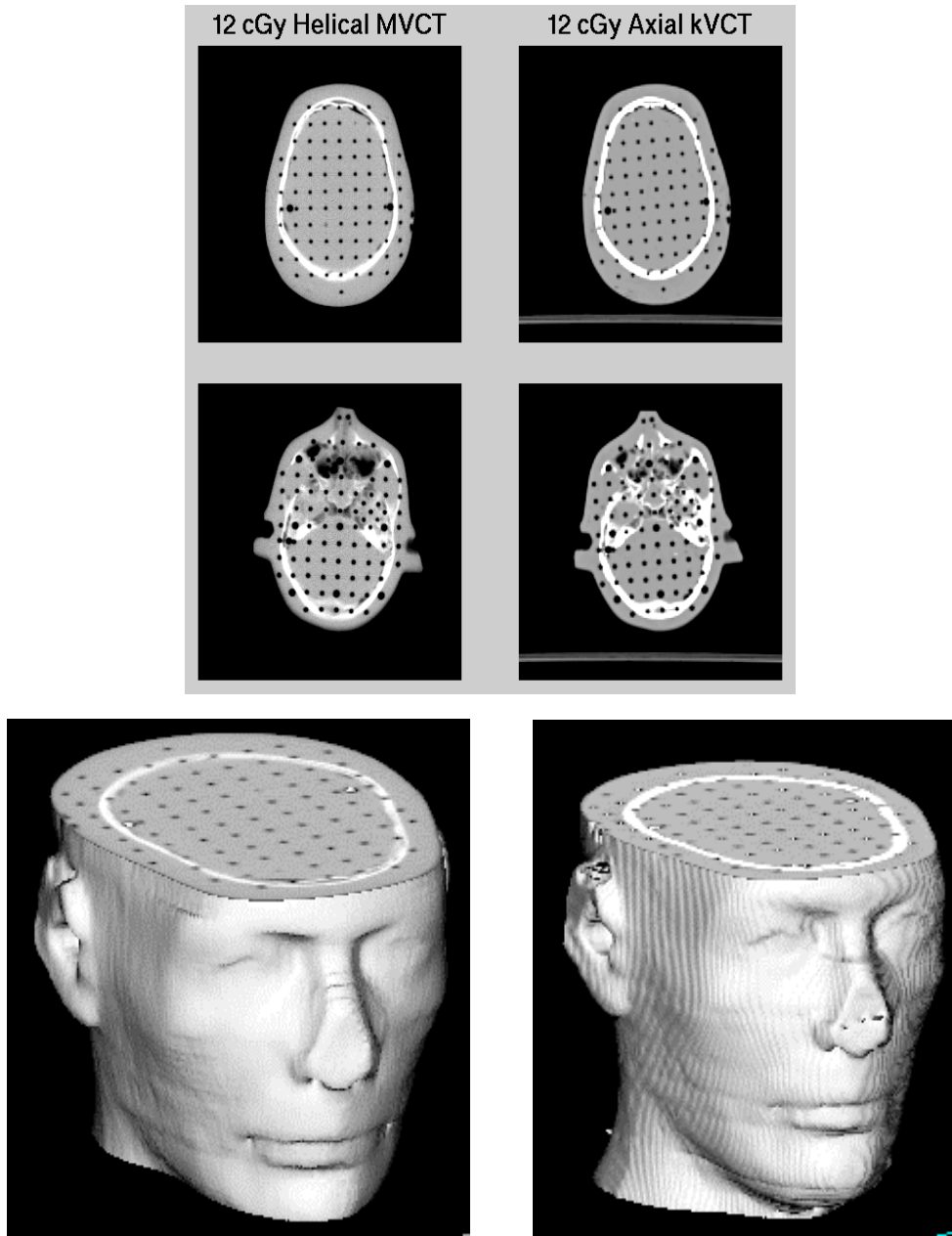


Figure 13. Each figure shows images of a Rando phantom which is usually used for radiation dose measurements; hence, the location of the regularly distributed holes for dosimeter placement. The upper figure compares transverse slices for MV CT (left) and for kV CT (right). Similarly the lower figure shows a 3-D reconstruction and rendering using MV CT (left) and kV CT (right).

SUMMARY

Helical tomotherapy mounted on a ring gantry provides significant advantages over today's state-of-the-art radiation treatment. First, it provides on-line imaging which allows for treatment adaptation on a daily basis accounting for the tissue locations on each set-up. The dose reconstruction capabilities provide an ability to determine the dose actually delivered to the patient, also on a daily basis. The tomotherapy unit fits into a significantly smaller room compared to modern linear accelerators since it does not involve a couch rotation. Because of the CT detectors with an added beam stopper and the ring mounting, the primary beam is virtually fully attenuated, thereby reducing the shielding requirements of the treatment bunker. Both the reduced room size and the reduction of shielding will provide significant cost savings in the implementation of this technology. Because tomotherapy is a single energy linac, fully integrated with a treatment planning system, it is expected that once the technology becomes routine, it will be significantly easier to commission in comparison to today's multi-energy and multi-modality (photons and electrons) linacs.

The technology of radiation oncology is evolving at a rapid rate, primarily as a result of the evolution of computer applications and their integration into diagnostic imaging and radiation therapy dose delivery equipment. The ring-mounted helical tomotherapy concept combines state-of-the-art imaging and treatment capabilities. Perhaps the tomotherapy development represents the greatest advance in radiation therapy since the first use of cobalt-60 in the 1950s. Indeed, the London Regional Cancer Centre recently (27 October 2001) celebrated the fiftieth anniversary of the first patient in the world treated with cobalt-60. The London Regional Cancer Centre is again pleased to be part of the tomotherapy developments in radiation therapy. It is also exciting to note that two Canadian centres, Edmonton and London, will be the first in the world to install helical tomotherapy units, other than in Madison where the system is being developed. These advances will provide a radiation treatment technology that allows daily adaptation of the treatment technique to match the location of the tumour and the normal tissues. With the better ability to focus the radiation beams, higher doses can be delivered to the tumour resulting in higher cure rates. In addition, lower doses will be delivered to normal tissues resulting in lower complication rates. The net result should be an overall improvement in the quality of life of the cancer patient.

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