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2006 Phys. Med. Biol. 51 R427

(http://iopscience.iop.org/0031-9155/51/13/R24)

INSTITUTE OF PHYSICS PUBLISHING PHYSICS IN MEDICINE AND BIOLOGY

Phys. Med. Biol. **51** (2006) R427–R453 doi:10.1088/0031-9155/51/13/R24

REVIEW

History of tomotherapy

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Received 23 February 2006, in final form 30 May 2006
Published 20 June 2006
Online at stacks.iop.org/PMB/51/R427

Abstract

Tomotherapy is the delivery of intensity modulated radiation therapy using rotational delivery of a fan beam in the manner of a CT scanner. In helical tomotherapy the couch and gantry are in continuous motion akin to a helical CT scanner. Helical tomotherapy is inherently capable of acquiring CT images of the patient in treatment position and using this information for image guidance. This review documents technological advancements of the field concentrating on the conceptual beginnings through to its first clinical implementation. The history of helical tomotherapy is also a story of technology migration from academic research to a university–industrial partnership, and finally to commercialization and widespread clinical use.

1. Background

Other than the creation of Co-60 and the development of the linac for radiotherapy in the 1950s, the decade encompassing the late 1980s and the early 1990s was perhaps the most creative in the field of radiation oncology. Much of the progress was driven by the availability of smaller and faster computers transforming radiation therapy treatment planning. Dose calculation algorithms were maturing rapidly including the convolution/superposition (Mackie *et al* 1985, 1988, 2000, 2001a, Boyer and Mok 1985, Ahnesjö *et al* 1987, Ahnesjö 1989, Papanikolaou *et al* 1993) and Monte Carlo algorithms (Rogers and Bielajew 1990, Mackie 1990, Rogers *et al* 1995). CT scanners were ubiquitous in radiation therapy and beginning to be used for treatment planning. In 1982, Anders Brahme showed that a non-uniform dose distribution could be optimal for treating a ring-shaped field surrounding a central avoidance structure (Brahme *et al* 1982). In 1987, Alan Cormack, one of the winners of the Nobel Prize for the development of the CT scanner, extended Brahme's solution to the non-circular symmetric situation. Brahme (1988) showed that non-uniform fields were in general the preferred solution to optimization of radiotherapy dose distributions.

It was in this very fertile period that I took a position at the University of Wisconsin (UW) in 1987. My main focus was to implement the convolution/superposition code into a

3D treatment planning system. In a grant written to support the convolution/superposition work the possibility of deconvolution to obtain optimal dose distributions was suggested. That idea proved to be unworkable. In parallel, the University of Wisconsin (UW) had started focusing on developing a linac-based stereotactic treatment planning and delivery system. There was no treatment planning system at the time, so along with biomedical engineer, Mark Gehring, we began working on one. This system was made clinically operational in the fall of 1988 by Minesh Mehta (Gehring *et al* 1991). This system was provided as 'shareware' to approximately half a dozen academic institutions. The clinical and technical refinements of this planning system turned out to be important to the future tomotherapy project.

2. Formulation of the basic ideas for tomotherapy

The concept of tomotherapy arose in the late 1980s, well before the phrase intensity-modulated radiation therapy (IMRT) was coined, as the result of the fortunate blend of people, resources and computer technology coming together at the UW. Students such as Timothy Holmes, Stewart Swerdloff and researcher Paul Reckwerdt all became part of my team at that time and a blizzard of ideas followed. One of the key elements was done by Swerdloff in fulfilment of a one credit Special Topics course. Under my supervision, Swerdloff, a PhD student in medical physics, investigated potential methods to deliver the non-uniform optimized beams of radiation predicted by Brahme (1988). The idea of using custom compensators was not investigated because we assumed that multiple field directions would be required to deliver the non-uniform fields and it would be too laborious. The methods investigated included using the

- collimator jaws of a conventional linac to form a slit beam, which would be translated by moving the jaws and then rotating the collimator jaws to form a radon-transform like delivery of one non-uniform intensity field;
- multiple shaped fields that defined the contour lines of equal intensity and
- slit field and modulating it using a bank of parallel fast-moving collimator leaves.

The rotating and translating slit beam method was abandoned because it would also require conventional field blocking to achieve regions of zero intensity. This method might be more practical with a modern conventional multileaf collimator. Multiple shaped fields would also require a multileaf collimator to be practical. At that time the only multileaf collimator equipped linac was a Scanditronics Microtron, although the first patent treated with a multileaf collimator dated to 1959 (Gscheidlen 1959). This method is now called step-and-shoot IMRT or static MLC IMRT. Swerdloff and Mackie concluded that a slit beam modulated by a bank of fast moving collimators would be the more practical solution. The bank of leaves so described is now called a binary MLC and is the basis for the intensity modulation of tomotherapy.

With Paul Reckwerdt and Tim Holmes, we developed the basic properties of collimator motion, geometrical configuration of the delivery system, dose calculation and optimization system. Holmes realized that a CT ring gantry would be ideal for tomotherapy, and with the inclusion of a detector system, it would also give the unit the ability to generate CT scans of the patient. However, the idea was nearly abandoned because of a flaw that the group perceived. Multiple rotationally delivered slit fields would require extraordinary precision in the couch translation to avoid severe hot or cold spots along the junction of the fields. In 1991, I was given the task of preparing specifications for a new CT scanner for the UW Radiation Oncology Clinic. In this investigation, the new developments in spiral CT (Kalender and Polacin 1991) became clear. Spiral (or helical) delivery would greatly reduce the potential

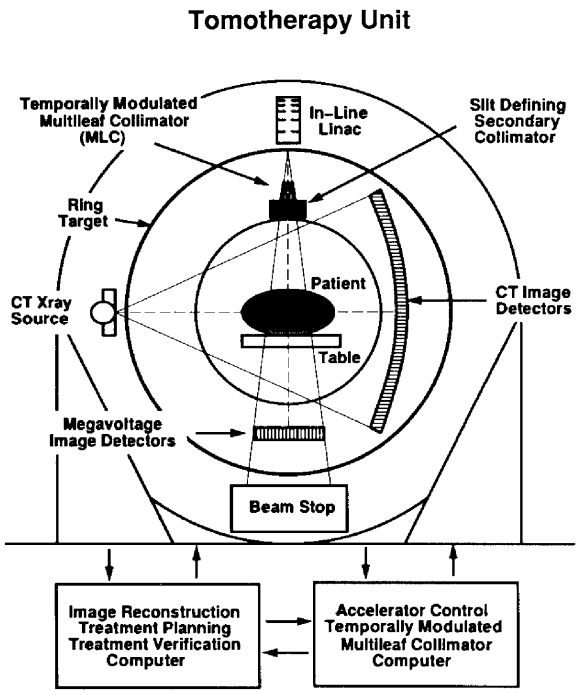

Figure 1. Conceptual drawing of a helical tomotherapy unit in the first tomotherapy paper (Mackie *et al* 1993).

for hot and cold junction artefacts. The first patent was filed in the spring of 1992 (Swerdloff *et al* 1994a, 1994b) and the first presentations given shortly thereafter.

3. Early work on patenting, presenting, publishing, and grant submission

The first paper on tomotherapy was submitted in July 1992 (Mackie *et al* 1993). It took nearly a year for the paper to be accepted likely because the idea was viewed with some healthy skepticism. From the time of submission to publication the paper took about 18 months. In that time David Convery and Michael Rosenbloom had published a paper (Convery and Rosenbloom 1992) on how to use conventional multileaf collimators for intensity modulating the field. The 1993 helical tomotherapy paper described most of the details of a modern unit. The use of a continuously moving slip-ring gantry for radiotherapy was introduced. It described how the modulating beam was formed using a fan beam and a temporally modulating collimator system that became known as a binary collimator. It described that intensity modulation would not require the use of a field flattening filter, and the spectrum across the beam would therefore be improved.

The first tomotherapy paper introduced several important concepts (see figure 1). It hypothesized that a ring gantry would be ideal for obtaining a CT image set before treatment to verify that the patient had been set up correctly. It described placing a separate kilovoltage (kV) CT scanner at right angles to the treatment beamline and even speculated on being able to CT scan the patient at the same time as the treatment. The possibility of reconstructing the dose delivered to the patient on the basis of the CT scan of the patient and the detected exit

beam was postulated. To quote directly from the paper, 'In principle, the CT image set and the dose reconstruction could be used to modify the treatment in subsequent fractions.' This is the first reference to both dose reconstruction and adaptation of radiotherapy on the basis of information obtained by CT imaging at the time of treatment. The paper also introduced the concept of using intensity modulation for a concomitant boost using the following example: 'it may be better to deliver both the primary field and the larger regional field for the full treatment duration to increase repair of normal tissues encompassed by the regional field or to provide more tumor cell killing at the same probability of normal tissue damage'.

Several concepts described in the first tomotherapy paper were never implemented. The stationary 'hoop' target concept was abandoned because it would have increased the complexity of the collimation. The 'running start and stop' was never implemented because it required the jaws to be moving during treatment and optimization of beams near the 'bow' and the 'stern' of the tumour can limit the dose received there. The use of a segmented monitor on the entrance side of the beam was not required because the binary leaves proved to be very reliable and mechanically stable. There was no need to optimize the switching time of the leaves because the switching time proved to be so fast (typically it takes 20 ms to open and close a leaf on a modern binary collimator).

Some predictions in this paper were completely wrong. The paper said, 'Treatments to huge fields such as whole, hemi-body or total skin radiotherapy would be best carried out with large extended SSD fixed fields.' It has turned out that helical tomotherapy is particularly adept at long complex fields. In particular, total marrow irradiation enables a patient to be irradiated prior to a bone marrow transplant with reduced dose to avoidance regions such as the brain, thyroid, lungs, liver, lung, bowel, etc, as was first shown by Jim Welsh (Welsh *et al* 2002).

Tim Holmes' PhD work at the UW was on radiotherapy optimization. He began his work by examining the similarity between single photon emission computed tomography (SPECT) reconstruction theory and optimization methods (Holmes *et al* 1991, 1995 Holmes and Mackie 1994a, 1994b). He showed operationally, that SPECT acquisition is a physical projection of radiation through the patient while radiation therapy was a physical backprojection operation. SPECT reconstruction filters the projection data and mathematically backprojects it through the patient. He reasoned that optimization calculations should involve mathematical projections of energy fluence through the patient. The mathematical operation had to be done iteratively, because unlike SPECT, mathematical backprojections for radiotherapy could not backproject negative dose. Backprojection methods worked well for tomotherapy optimization algorithms because a large number of beam directions were used. At about the same time, Tomas Bortfeld using similar methodology showed that the same principles could be applied to a few beam directions if the backprojections were specially filtered. Holmes *et al* (1995) concluded that there would be negligible difference in the dose distribution in the target and abutting normal tissue as a function of beam energy. Truncating the negative values seriously perturbed the solution. With Holmes, Reckwerdt and McNutt, we began to explore other methods which involved directly ray-tracing across the phantom and determining which voxels required a higher intensity along the ray and which required less intensity (Reckwerdt *et al* 1997).

Funding, both Federal and industrial, was not easy to get at first. During a funding gap of more than a year, Tim Holmes graduated in 1993 and worked part time for a UW spin-off company, Geometrics Corporation, started by Mark Gehring, Paul Reckwerdt, Cameron Sanders and myself. Our corporation developed a 3D treatment planning system that had evolved from our 'UW Stereo' stereotactic planning system that was later renamed Pinnacle^{TM} and was marketed by ADAC Corporation (ADAC is now owned by Philips Medical). This company fulfilled the goals that I had come to the UW for, to implement clinically a 3D

treatment planning system that included the convolution/superposition (C/S) method. By this time the C/S code was mostly written by Paul Reckwerdt. The University of Wisconsin Radiation Oncology clinic, under the leadership of Timothy Kinsella, Mark Ritter and Minesh Mehta (Kubsad *et al* 1990, Mehta *et al* 1991) provided the ideal clinical outlet to validate and improve these software systems. Geometrics also proved to be an excellent education for product development and business that would prove invaluable later in the founding of TomoTherapy Inc.

With very little money at our disposal, the first tomotherapy tests were primitive but effective at refining our concepts. Paul Jursinic, a PhD fellow at the UW and Mary Martel from the University of Michigan produced the first tomotherapy irradiation pattern using Michigan's Scanditronix Microtron multileaf collimator system. The irradiation took many hours and consumed many films. For her efforts, Martel received a case of Wisconsin beer. The irradiation pattern looked terrible and was decidedly unpublishable but it was very valuable in that it proved that our optimization results were generally correct. James Yang, a PhD student at the UW, produced distributions using a single pencil beam produced from a standard linac. The irradiation was like 1st generation CT tests whereby a pencil beam was scanned by a phantom rotating on a turntable. The velocity of movement of the beam was inversely proportional to the intensity it delivered (Yang 1997). Todd McNutt proved that the dose to a portal dosimeter could be predicted (McNutt *et al* 1996a, 1996b) and that dose reconstruction was possible. The detector system he did this work on was a Varian Portalvision^{TM} liquid ion chamber electronic portal imaging system. Joseph Deasy, a postdoctoral fellow in my group, also looked at applying tomotherapy to particle beams and came up with distal edge tracking type of intensity modulated proton radiotherapy, which has been shown to give the lowest integral dose to surrounding structures for any type of proton delivery to deep-seated lesions (Deasy *et al* 1997, Oelfke and Bortfeld 2000).

Yang was the first to study the impact of motion on tomotherapy (Yang *et al* 1997). Periodic motion, such as the one produced by breathing, and the periodic rotation rate of the gantry produce sinusoidal variations in delivery. The amplitude can be severe if the two movements are in synchrony. However, he showed that they would be minor if the rotation period is much longer than the breathing period, which is invariably the case. Similar results were recently obtained by Michael Kissick (Kissick *et al* 2005b).

In 1993, Paul DeLuca, encouraged his research lab at the Physical Science Laboratory (PSL) in Stoughton Wisconsin to be used for tomotherapy research. A deuteron Van de Graff accelerator and a tritium target to produce neutrons had to be removed. David Pearson, a senior scientist with vast knowledge of radiation and material science, joined the tomotherapy group at this time. At about the same time as we moved into our PSL facility, on the second resubmission, we received Federal funding to study tomotherapy.

4. Serial tomotherapy

Contemporary with early conceptual design for helical tomotherapy at the UW, Medco, a company formed by neurosurgeon Mark Carol began developing what came to be called the serial (or sequential) tomotherapy concept (Carol *et al* 1993, Carol 1995). The concept also used a narrow rotating beam of radiation modulated by two sets of binary collimators so that twin slices could be irradiated at once. Rather than continuous translation with gantry rotation, serial tomotherapy rotates to deliver two slices at once and then has the couch translated by the distance subtended by the two slice widths to then deliver the next two slices. The delivery unit was designed to be added onto a conventional linac gantry. The system was called the

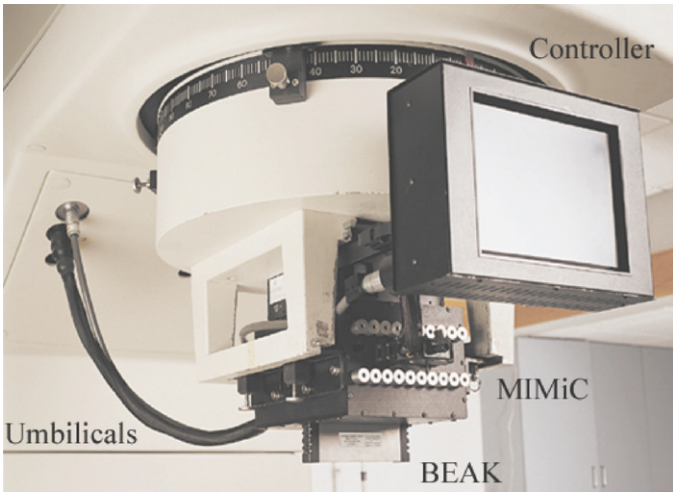

Figure 2. Photograph of the NOMOS Peacock serial tomotherapy system. Courtesy NOMOS Corporation.

Peacock™ (all of the Nomos product names had ornithological derivations) and the binary collimator was called the MIMiC™. The accuracy of translation of the couch was assured by the use of an external translation jig called the Crane™ (Carol *et al* 1996). The setup of the patient was assured using an invasive immobilization system called the Talon™ that was screwed into the patient's skull and docked rigidly to the imaging system and treatment couch. In 1994, the Peacock™ system was the first form of collimator-based IMRT to treat a patient.

The Peacock™ binary collimators were pneumatically powered and had two settings, nominally 1 cm and 2 cm but the actual opening was somewhat smaller. A later add-on device called the Beak™ could be added below the MIMiC™ collimator to reduce the slice width to about 4 mm for use in small stereotactic radiosurgeon applications (Salter 2001). The leaves were designed to project to a 1 cm resolution at the axis of rotation of the gantry.

The Corvus™ (Greek for raven) optimization algorithm, used for the Peacock ™ system, was simulated annealing (Webb 1991a, 1991b, 1992). The optimization implementation was the first commercial optimization system and the Peacock™ system was the first commercial IMRT system (see figure 2). The first patients were treated with the system in 1994 by the team of Shiao Woo, Walter Grant and Brian Butler at Baylor College of Medicine in Houston (Woo *et al* 1996). The company changed its name to Nomos Corporation and received FDA (510k) clearance to market the Peacock IMRT product in 1996. Nomos licensed the binary MLC patent from the UW's intellectual property agent, the Wisconsin Alumni Research Foundation (Swerdloff *et al* 1994a, 1994b). Nomos supplied the UW group Serial Number 3, MIMiC™ binary MLC collimator. This unit was used extensively for proving the feasibility of helical tomotherapy on the UW benchtop tomotherapy unit.

In 1994, the marketing response from the radiotherapy vendors to the Peacock™ IMRT system and the Corvus™ treatment planning system was to downplay the importance of IMRT and optimization. However, at the same time they put their research and development departments in high gear to address the market opportunity for IMRT demonstrated by Mark Carol and the Nomos Corporation. There is no question that without the initiative and speed to market of Nomos, IMRT would have been delayed by many years.

Rather than integrating the binary collimator into a linear accelerator or developing helical tomotherapy (at our suggestion), Nomos developed the Corvus™ system for conventional multileaf collimators (Boyer *et al* 1997, 1999, Xing *et al* 1999). For many years, the Corvus™ system was the only system capable of producing optimized plans for IMRT for both binary and conventional MLC systems. While they updated and improved the Corvus™ system, the Peacock™ did not evolve much beyond its original inception. Some efforts were made to develop a 2D binary MLC based on filling columns with mercury metal but the idea was never clinically implemented (it was patented as *US Patent* 5,802,136)

Until very recently, the Nomos Peacock™ system had treated more IMRT cases than any other IMRT system. By 2003, more than 100 systems had been installed, predominately in the United States (Curran 2003).

5. Industrial partnership and engineering

After first talking to all of the other leading linear accelerator vendors, my group negotiated research support from General Electric Medical System (GEMS) in 1994. This was largely because of the vision of GEMS Global Radiotherapy Marketing Manager, Per Jonsson. This funding support included provision for a benchtop tomotherapy unit employing a GEMS Orion™ 4 MV linac and the gantry and couch system from a HiSpeed Advantage™ CT scanner to build a clinical prototype.

The three years of support from GEMS was productive, but trying. GEMS could devote little of their CT engineering resources to our project. In order to become familiar with their scanner technology our personnel had to spend time with their engineers. This could only be done if it did not cost GEMS any net time lost in their CT product development. We struck an informal deal whereby our group members would spend time at GEMS helping them with their CT Lightspeed™ scanner development. At times three or four of our group including Paul Reckwerdt, Guang Fang, Eric Schloesser and Brian Geiser were commuting 200 km through Wisconsin winter weather to the GEMS CT development facility in Waukesha, Wisconsin. During these times little progress was made on tomotherapy but a tremendous amount of knowledge was being gained on the theory and operation of CT (Fang *et al* 1997). At this time, we were also communicating with GEMS linac designers, principally Dominique Tronc, at their Buc France facility. The plan was for GEMS to develop a compact X-band linear accelerator specifically for tomotherapy. Unfortunately, the GEMS Radiotherapy business was troubled with low market share and the X-band accelerator never made it beyond the planning stage.

A major goal for the group was developing a benchtop tomotherapy system in the PSL bunker. The bunker as well as its associated shack was very primitive and it was kept in tolerable condition by collective action by one and all such as clean up and paint days where we would try to make it as habitable as possible. Things improved greatly when the group finally got a mobile home sized trailer to replace the mice infested shack. The facility was placed next to PSL's world-class design and fabrication facility, and our ability to get advice and access to tools and machining equipment. As shown in figure 3, our benchtop consisted of a 4 MV GEMS Orion™ linac was mounted such that the beam could only come out horizontally. The RF system was mounted on a wall beside the linac. The same phantom rotation and translation system used by James Yang was centred between the linac and a GEMS xenon CT scanner detector. John Balog began delivering unmodulated tomotherapy treatments to cylindrical phantoms and was the first to report the thread effect because of the helical junctioning of the slit beams (Balog 1998, Kissick *et al* 2005a). Balog also developed

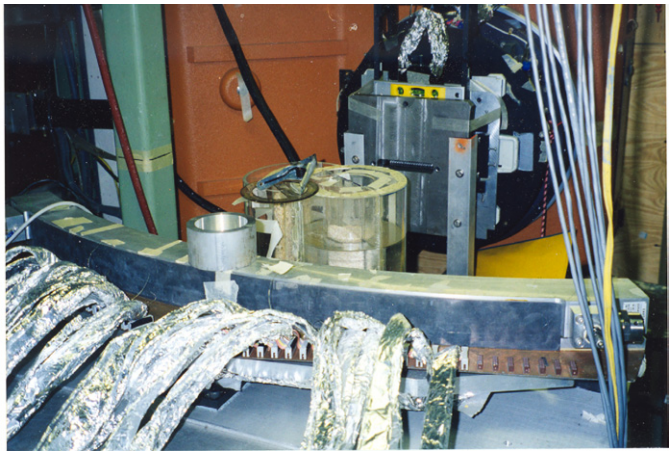

Figure 3. The University of Wisconsin Tomotherapy Benchtop system. Located at the Physical Sciences Laboratory (PSL) in Stoughton WI, this lab was the first operating helical tomotherapy prototype. A GEMS 4 MV linear accelerator (in the background) was placed in a fixed horizontal position and the beam emerged parallel to the horizon. A turntable rotated and elevated the phantom to mimic the gantry rotation and couch translation, respectively. A GEMS CT detector (in the foreground) and data acquisition system was used to produce CT images.

a simple model to predict the effect of neighbouring leaves to the fluence issuing from a leaf (Balog *et al* 1999b).

With the promise of support from GE, the UW group began to collaborate with the engineering group at PSL. Dan Wenman was the principal mechanical engineer for the design of the jaw system, binary MLC and weldment structure to attach to the GEMS CT gantry that held the RF, linac, and CT components. During this time, using calculation results from James Yang (Yang 1997), we optimized the head of the machine to minimize unwanted radiation at the same time reducing the source to axis distance (SAD) and maximizing the bore through which the patient would travel. For rotation therapy there is no dosimetric advantage to a long SAD. The incorporation of the jaws defining the field into the primary collimator enabled this combined component to be up to 23 cm of tungsten. This would enable the average leakage to be less than 0.01%, a factor of 10 lower than International Electrotechnical Commission guidelines (IEC 1998). Even with increased shielding we were able to reduce the SAD from the standard 100 cm to 85 cm and to have an 85 cm bore through which the patient travels, which is larger than the standard 70 cm CT gantry bore.

The design, manufacture and testing of the leaves were a challenge. With a leaf height of 10 cm of tungsten we felt that we could reduce the leaf leakage to less than 1%. John Balog explored the effect of a tongue and groove design to reduce the leakage (Balog *et al* 1999a). We chose a tongue that went 0.15 mm into a groove that was 0.3 mm thick. This allowed a tolerance in manufacture of no more than ± 0.05 mm for either the leaves or the leaf carriage fixture. Our design actually reduced the leakage to about 0.3% on average. Balog also developed a calculation to predict the energy fluence that takes into the account the opening state of neighbouring leaves (Balog *et al* 1999b). The shape of the leaf had to be longer than it was high in order for it to be guided with high precision. This would have made the leaf too heavy. To reduce the weight we decided to cut a large square hole in the leaf where it would never intercept the radiation and to use this space for placing cushioning to more gently stop the leaves. The leaves were tapered with the end near the source about 2 mm thick and

the end near the patient about 3 mm thick. The thinness of the leaves, their complex shape, their exacting tolerance requirements and the use of high purity tungsten resulted in great difficulties in their manufacture. The leaves had a tendency to 'potato chip' or curl slightly. The amount of curl was imperceptible but it would cause the leaves to bind in their fixture. It took the vendor of the first set of leaves more than one year to perfect their manufacturing process.

A great deal of thought and effort went into the system engineering of the MLC. Much earlier we had investigated several motive systems for the leaves including relays, linear motors, rotating cams, hydraulics, pneumatic pistons and even steam pistons! We re-evaluated all of these options again and once more opted for pneumatic pistons because of the relatively long movement distance, compactness, speed and robustness of pneumatic pistons. We first built a single leaf prototype of the binary collimator to investigate bearing mechanisms, shock cushioning and lifetime. The single leaf unit had a crude but effective cycle counter so that we could leave it operating for weeks at a time to determine wear and tear on the leaf and its transport mechanism. There were several iterations in design through the better part of a year until a suitable design emerged. The single leaf unit used a commercial pneumatic piston. Assembling 64 individual pistons was impractical. We chose to build the MLC around two piston blocks each with 32 pistons. The two blocks were identical but designed so that when they faced off from each other they would be shifted by $\frac{1}{2}$ leaf spacing. Similarly, two leaf carriage fixtures were designed to hold 32 leaves each so that the odd and even leaves would slide by each other without touching. To maintain accuracy, the leaf carriage fixtures were cut from single pieces of tool steel using the electrical discharge machining process. The leaf carriages were curved so that each leaf was at a constant distance from the source ensuring that the face of each leaf pointed back at the source. On top of each block were two optical sensor boards to verify if the leaves were in their correct state. Each leaf was controlled by an individual electrical relay and valve which enabled the leaf to be pulled open or pushed closed. The rated mean time to failure for the valves was a billion cycles (which represented more than 100 years of normal use). Instead of hoses, the valves and pistons were connected by channels cut into aluminium plates. The design and testing of the MLC system took several man years. As a testament to its design, the current MLC in the commercial unit is minimally changed from the original one designed at PSL.

Lee Greenler at PSL led the design of the air-cooled closed-loop water system. Because the gantry was continuously rotating we could not easily vent the water reservoir to the atmosphere. We built into the system a purging system for gas that would enter our system.

At this time, the plan was to mount the gantry containing the linac behind a conventional CT scanner. This configuration of two gantries would have been similar to a modern CT-PET configuration. To solve the problem of transporting between the two gantries Murray Thompson, a Professor from the UW Physics Department and a former Director of PSL, designed an elegant conveyor belt couch.

A chapter in the AAPM Summer School on Medical CT and Ultrasound reviewed our ideas on tomotherapy (Mackie *et al* 1995). For the first time the concept of conformal avoidance was described as the complement to conformal therapy and useful when the extent of the gross tumour volume (GTV) and clinical target volume (CTV) were uncertain but the position of normal tissues that would limit the dose was well defined. The term conformal avoidance has entered the lexicon of radiotherapy but its original intent is still not widely understood. Its most important tenet is that treatment margins should be as large as necessary but the dose accurately constrained to avoid normal tissue. If the extent of the targets becomes uncertain the margin defining them should extend but avoidance of irradiating critical structures may become paramount. This concept was more fully elucidated in a later review article

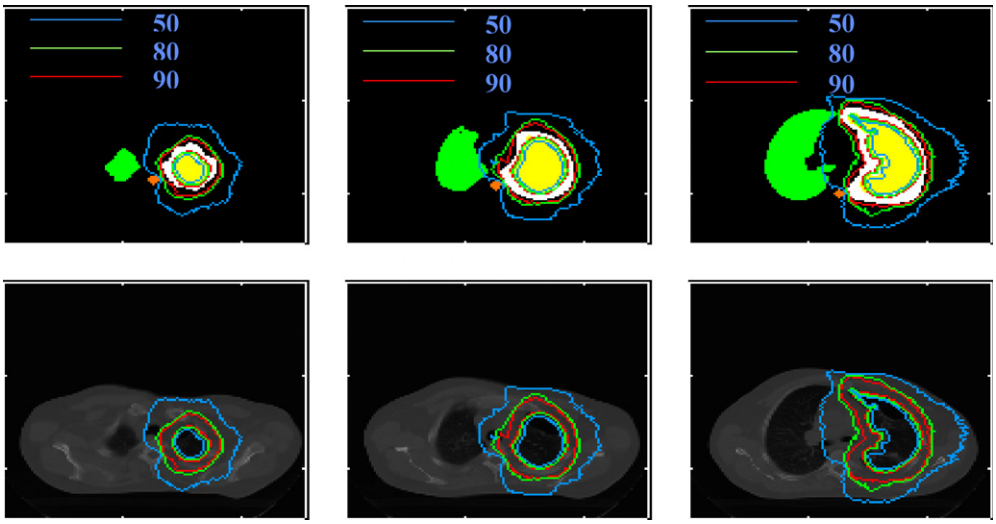

Figure 4. An early treatment planning example of a mesothelioma case. Avoidance of the contralateral lung was assigned high importance. The characteristics of a helical tomotherapy plan are evident; very high conformation to the target volume even when it has an avoidance region within it. The plan was constructed in 1999.

(Mackie *et al* 1999) and Stacy Aldridge would develop the idea further in her PhD at the UW (Aldridge 1999).

The tradeoff between treating the tumour to a homogeneous dose and avoiding dose to critical structure is the central tradeoff in radiotherapy and with the advent of tomotherapy there is more control over this than ever before. Figure 4 illustrates a mesothelioma plan that illustrates that the avoidance of structures (in this case lungs and spinal cord) is as important as the homogeneous irradiation of normal tissues.

A tremendous amount of headway was made in developing several algorithms. Following the original suggestion by Paul Reckwerdt, several tomotherapy group investigators including Ed Fitchard, Stacy Aldridge, Weiguo Lu, and Gustavo Olivera developed the mathematics of setup verification from projection space (Fitchard *et al* 1998, 1999a, 1999b, Aldridge 1999, Lu *et al* 1999). The main idea is that the translations and rotations of rigid objects are encoded in the radon projections. By comparing the projections of a planning image with the projections at the time of treatment the information to provide shifts to move the patient to the beams or the beams to the patient could be made. Jeff Kapatoes found another approach to dose reconstruction. Instead of iterative projection and backprojection used by McNutt (McNutt 1997), the detector could be calibrated to determine the energy fluence incident on the patient by only knowing the patient thickness and the distance from the patient to the detector (Kapatoes *et al* 1999, 2001a, 2001b, 2001c). Later, Ke Sheng also found yet another way to perform dose reconstruction (Sheng 2004, Sheng *et al* 2005). In turn, with knowledge of the energy fluence incident on the patient and the CT taken just before treatment the actual dose distribution delivered to the patient could be inferred. A test of dose reconstruction is documented in figure 5.

Gustavo Olivera and David Shepard both contributed a great deal to our understanding of tomotherapy optimization. Olivera showed that our algorithm that adjusted the energy fluence to deliver from a beamlet at each iteration cycle was equivalent to a quadratic objective

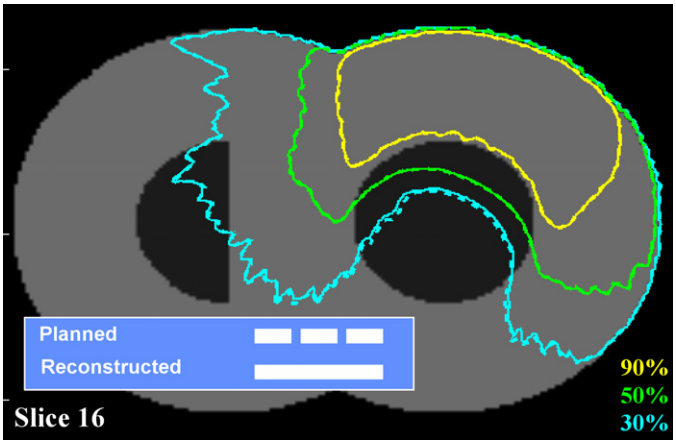

Figure 5. Comparison of the dose distribution measured in a simulated breast phantom using film and dose reconstruction. The unit density tissue was water and the lung equivalent material was dry oatmeal encased in polystyrene. The UW benchtop unit was used for this test. The phantom is shown on the benchtop in figure 3. From Kapatoes (2000).

function (Olivera *et al* 1998, 1999, Shepard *et al* 2000). Using a very simple but flexible model, Shepard showed that the dose becomes more homogeneous and the dose is reduced to small avoidance structures near the tumour if more beam directions are used (Shepard 1999, Shepard *et al* 1999a, 1999b). He also showed that the quality of the delivery was not impacted by having the tumour shifted from the rotation centre. This showed that simultaneous treatment of multiple targets was possible. The model was also used by other investigators (Sauer *et al* 1999). Jennifer Smilowitz formalized the calibration of tomotherapy based on energy fluence emitted by the machine rather than dose in a phantom (Smilowitz 2002). The chapter 'Tomotherapy' in Van Dyk's book *The Modern Technology of Radiation Oncology* (Olivera *et al* 1999) was a tour de force review of the algorithms and processes of tomotherapy at that point in time.

6. Formation of TomoTherapy, a UW spin-off company

In 1997, we were informed that GEMS would sell its radiotherapy business to Varian. That came as a terrible blow as the project was directly or indirectly supporting about 20 people. However, the autumn before, our treatment planning spin-off company, Geometrics, merged with ADAC. Paul Reckwerdt and I, although restricted from selling our ADAC shares, knew that we would have the capital to start a company to commercialize helical tomotherapy. The main motivations for forming TomoTherapy Inc. in the late fall of 1997 was to save the research group, to continue development of the clinical helical tomotherapy prototype and to commercialize the concept. I became managed by a potential conflict of interest committee and obtained a letter from the Wisconsin Attorney-General to give me permission to work on commercialization of tomotherapy. Reckwerdt and I began licensing negotiations with WARF to obtain exclusive rights to helical tomotherapy technology.

The 18 months from the end of 1997 to the summer of 1999 were very uncertain. The project was in limbo. It was obviously too big to be a university project with no commercial funding. Paul DeLuca secured interim funding, largely from funds derived from WARF, but

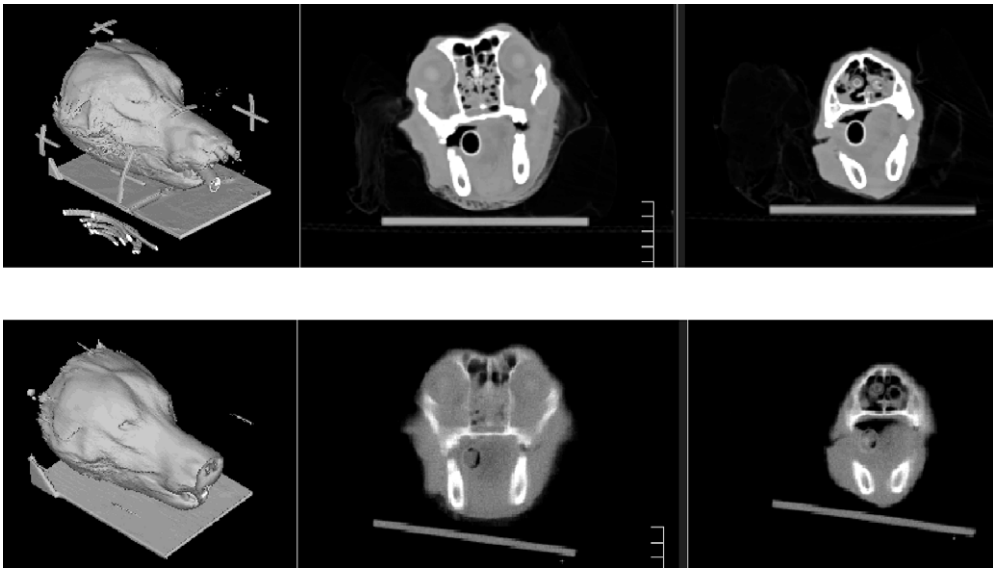

Figure 6. CT scans of a dog cadaver head. The upper panel is from a conventional kilovoltage CT scanner. The lower panel was acquired on the UW Benchtop Tomotherapy unit at PSL shown in figure 3 (from Ruchala (1999)).

also with significant contributions from the University of Wisconsin Comprehensive Cancer Center, the Departments of Medical Physics and Human Oncology, which enabled most of the bills to continue to be paid during this trying period of time.

The design for the first prototype was scaled back. Most notably, we dropped the idea for a kV CT scanner for reasons of cost, but also Guang Fang and Ken Ruchala had by then showed that it was possible to get high quality megavoltage CT images (see figure 6) using the GEMS xenon detector (Ruchala *et al* 1999, 2000a, 2000b). The reason for the good image quality was the high quantum efficiency of the detector (Keller *et al* 2002 and Hinderer 2003) and the large number of CT scan views. The GEMS detector had tungsten electrodes that also served to limit the scatter crosstalk between elements when used at kilovoltage energies. At megavoltage energies the photons were mainly interacting in tungsten via the Compton effect and the recoil electrons leaked out into the xenon gas where they caused ionization and were therefore detected (Keller *et al* 2002). The GEMS CT detector was operated such that every linac pulse was detected. This per-pulse operation also made it possible to use the detector as secondary verification that the leaves were opening as shown in figure 7 (the primary verification is optical sensors attached to the binary MLC).

Scaling back the scope of the project did not necessarily mean that the performance of the design was compromised. Olaf Meding modified a less expensive but highly accurate conventional GEMS CT scanner couch instead of the conveyor couch. Since we had never gotten the X-band linac from GEMS we obtained a robust and simple 6 MV S-band linac and an RF system from Siemens Oncology Care Systems. The Siemens linac employed an innovative target that rotated; driven by the water flow that cooled it. This meant that on the target the beam spot was distributed around a circle instead of always hitting the same spot. This enabled the focus spot to be about 1 mm, much smaller than usually employed in radiotherapy, which also helped to enable high quality megavoltage CT images.

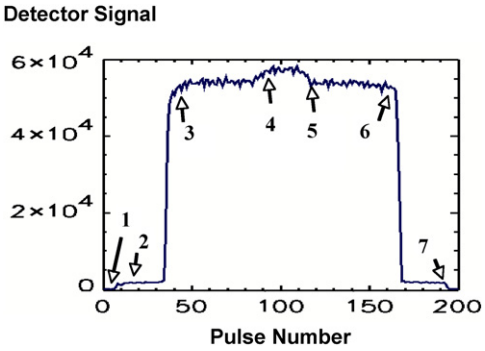

Figure 7. The pulse-by-pulse signal detected by one ion chamber element of the GEMS 9800^{TM} CT detector used in both the original prototypes and current Hi-Art^{TM} helical tomotherapy units. The detector is distal to a phantom that is being irradiated by the binary MLC. The detector element is centred about the exit beam from a single leaf. When that leaf and its neighbours are closed (1) the detected signal is due to leakage through the leaves which is very small. When one of the adjacent neighbouring leaves of the leaf that is aimed at the detector is opened (2) there is a small signal due to scatter from the phantom. When the centred leaf is opened (3) the signal increases significantly. Note that the rise time is indicative of the length of time that the leaf opens and it takes seven linac pulses with the linac running at 300 Hz to open a leaf, corresponding to an opening time of 23 ms. The other adjacent leaf is opened (4) and there is another increase about equal to that in (2). The adjacent leaf that opened last is closed (5). The centred leaf is closed (6) with a closing time nearly equal to the opening time. The adjacent leaf that opened first is closed (7) leaving all three leaves closed. The pulse-to-pulse variations in output are typical of all linear accelerators.

Finding capital for TomoTherapy was not easy. We were raising money at the height of the 'dot com' bubble. Some of the quotes from venture capitalists are priceless, 'We like your idea, but you will have to do it in California to be a success,' or, 'You're too concerned with the old economy, profits aren't important, the new economy is all about equity valuation,' or, 'Why should we invest in you when we can invest in a dot com and make 500 times our return on our investment.' In 1999, two Midwest venture capital firms (Venture Investors of Wisconsin, Madison WI and Avalon Technology, originally Ann Arbor MI) took a chance and TomoTherapy Inc. became staffed with eight ex-employees of my UW research group. Shortly afterwards the company hired its first employees not associated with the research group and so we started our transition to a business-like company. WARF took an equity interest in the new company. I went down to a 75% appointment at the UW and started working in the capacity of Chairman of the Board 25% of the time. I passed the title of Chief Executive Officer (CEO) to Paul Reckwerdt who would lead the company day-to-day until John Barni, a former CT executive from Marconi Medical, took the reins in September of 2000.

The first goal of TomoTherapy was to finish building the UW prototype. During the summer of 1999, TomoTherapy took an office at the UW Research Park. That space was far too small even for a company of fewer than ten people and that fall, the company took a lease on a former onion powder factory in Middleton Wisconsin, which is a suburb of Madison. The smell of onion powder never left the building! A bunker was fabricated of highway construction retaining blocks with concrete flooring slabs for the roof (see figure 8). The blocks were designed with a tongue and groove and were laid in a staggered pattern to minimize leakage. The first prototype unit was moved from PSL to this facility. As soon as we had a radiation beam the unit was moved in the fall of 2000 to the UW Hospital and Clinic. This took an act of courage by Minesh Mehta, the Chairman of Radiation Oncology,

Figure 8. Designed by Dave Pearson, TomoTherapy Inc.'s first test bunker constructed of highway retaining wall concrete blocks and pre-fabricated concrete flooring planks located in a former onion powder factory in Middleton WI. The building was leased and so the bunker was designed to be easily dismantled. Ken Buroker, TomoTherapy's Vice President for Regulatory Affairs, is in the picture.

and Bhudatt Paliwal, the Chief Physicist, as they had to allow the decommissioning of an existing treatment vault in a busy clinic with no certainty that it would be put back into service with a clinically working tomotherapy unit. They were early believers in the technology and took the plunge (Mehta *et al* 1995).

7. Clinical implementation

The fabrication of the UW unit was completed in early 2001 and a long software integration and validation process followed (see figure 9). The same convolution/superposition code developed at the UW was modified by Paul Reckwerdt, Julie Zachman and Ray Macdonald for helical tomotherapy (Mackie *et al* 2000, 2001a). In fact, the algorithm is even more suited to tomotherapy than for conventional radiotherapy. One of the most difficult aspects of the algorithm is modelling the source distribution. In a conventional linac, the field flattening filter makes up about 15% of the energy fluence at the isocentre. In tomotherapy, there is far less contribution from extrafocal radiation, and so a single source model is sufficient (Liu *et al* 1997). There is no need for an off-axis softening correction due to differential hardening of the beam caused by a field flattening filter. Similarly, the absence of the possibility of wedges or compensators eliminates considerable complication. There is also no need to take into account the influence of curved leaf ends in tomotherapy's convolution/superposition implementation.

Even though the first dose calculation and optimization ran on a single CPU, it was soon obvious that it would be impractical to use the convolution/superposition method for helical

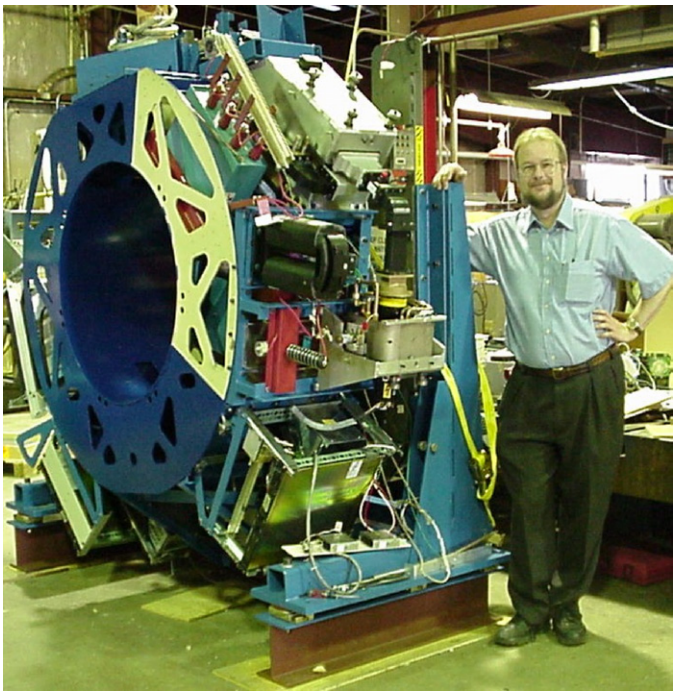

Figure 9. The author, Rock Mackie, beside the first clinical helical tomotherapy prototype. The unit was largely hand built and assembled by Dave Pearson and Eric Schloesser. The photograph was taken in May 2000 at UW PSL, during assembly. The unit is built around a GEMS HiSpeed Advantage^{TM} CT gantry.

tomotherapy on a single processor. That is because helical tomotherapy typically needs to compute the dose from tens of thousands of beamlets. Furthermore, hundreds of iterations of the optimizer are needed to converge towards a solution. In a conventional optimizer each iteration involves redoing the dose computation. This would have made the dose computation for helical tomotherapy much too long. The problem was solved in two ways. In order to speed up the optimization process we used a cluster of 32 CPUs each CPU with one GB of RAM on the same rack as the database computer. This allowed the dose calculation to be stored in 32 GB of RAM so that recalculation of dose would not have to be done each iteration cycle of the optimizer. Secondly, the convolution/superposition calculation was sped up significantly by Weiguo Lu without compromising the accuracy of the model (Lu *et al* 2005).

It took several years from planning to completion of the tomotherapy software systems which was largely designed by David Murray, Eric Schloesser, Guang Fang, Paul Reckwerdt, Ken Ruchala, Gustavo Olivera and me. On the Pinnacle^{TM} treatment planning system we had used Solaris Unix, C, and X-Windows. Instead of a database on Pinnacle^{TM}, we had used binary and ASCII files in a hierarchical directory structure. We were aware of the limitations in our previous choices and adopted Microsoft Windows, Java for the graphical user interface (GUI) and C and C++ for the computation code. Since we knew the unit would produce copious amounts of data we used a commercial database system, DB2^{TM}, from IBM that was robust and extensible. A CORBA interface was layered on top of DB2^{TM} which communicated to the planning, treatment console and treatment machine. CORBA also communicated to the outside world using DICOM. We wanted the planning system GUI to be much more simple

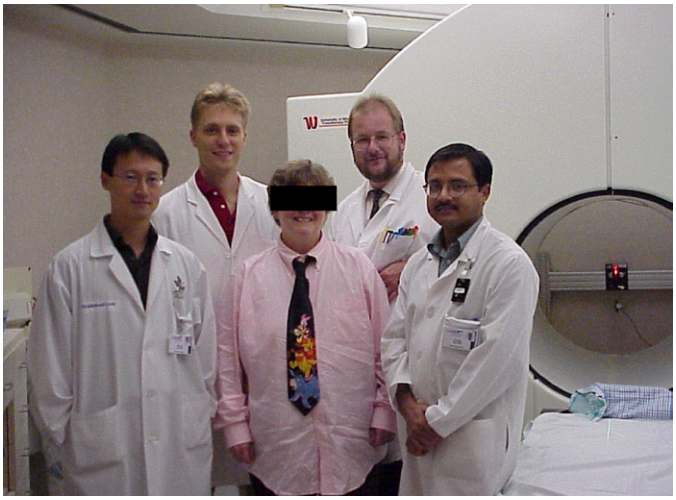

Figure 10. Treatment of one of the first patients at the UW. In back (left to right), Jeffrey Kapatoes and the author. In front were Michael Lock (from the London Regional Cancer Centre in London Ontario), the patient, and Susanta Hui, now at the University of Minnesota. The prototype tomotherapy unit in its covers is in the background.

and intuitive to use as compared with Pinnacle^{TM}. The operator consol software had to contain a GUI to control the CT scanning, patient registration and beam delivery system. Stephen Coon developed a separate hardware interface for the operator system to accommodate a key interlock system. The registration software included both automated registration using a modified mutual information algorithm (Ruchala *et al* 2002) and a manual registration that included visualization of the MVCT registered on the planning CT (Forrest *et al* 2004, Welsh *et al* 2004).

The first patient undergoing an MVCT scan was a client dog referred by veterinarian Lisa Forrest in the closing weeks of 2001. On 29 January 2002 we received FDA clearance to market the Hi-Art^{TM} helical tomotherapy system. In the spring of 2002 we initiated the first MVCT scans of a human under an IRB-approved protocol, which ultimately led to the publication of the first controlled clinical trial of MVCT evaluation (Welsh *et al* 2004). In the late spring of 2002 we treated a dog with a sinus tumour. On 21 August 2002, Jim Welsh, at the UW treated the first human patient. She had bone metastases and the capabilities of MVCT imaging, setup verification and correction were accomplished. Figure 10 is a photograph of an early patient treated in 2002.

Two other units, nearly identical to the first UW prototype, were built for the London Regional Cancer Centre (LRCC) in London, Ontario and the Cross Cancer Institute (CCI) in Edmonton, Alberta. These units were used to explore the principles of operation of tomotherapy by the large medical physics research groups at these institutions. Grigorov from LRCC found that the criteria for the RTOG 0126 prostate trial could always be met with a 5 mm margin surrounding the prostate (Grigorov *et al* 2003). Yartsev, also from LLRC, found that helical tomotherapy produced the most conformal dose distributions for brain tumours for a variety of common treatment techniques and resulted in a similar integral dose as other photon techniques. In a cranio-spinal planning study, Bauman found that helical tomotherapy produced ‘excellent target coverage, homogeneity, and organ sparing as compared with a conventional linear accelerator based craniospinal irradiation’ (Bauman *et al* 2005). Kron

et al (2004) and Kim *et al* (2005) investigated the use of helical tomotherapy for lung cancer. They concluded that tomotherapy provided good dose conformity and a loose helical (with pitches >1 instead of <1 as helical tomotherapy is normally delivered) approach could be used to treat them. Thomas at the CCI published an analysis of steps to make helical tomotherapy compliant with the AAPM TG-51 protocol (Thomas *et al* 2005a, 2005b). They showed that with some corrections to the formalism, their unit could be calibrated to an uncertainty of 0.1%.

The issues of implementing tomotherapy have continued to be explored at the UW. In 2001 the UW Department of Human Oncology, under the leadership of Minesh Mehta, received a Program Project grant from the National Cancer Institute to apply the concepts of adaptive radiotherapy and conformal avoidance. In 2005, now in the 5th year of the P01, almost 500 protocol patients have been enrolled with enormous progress in lung, prostate and head and neck cancers, and the team has been extremely productive with over 100 publications. Some of the projects deserve special mention as they represent many 'firsts'. Mark Ritter developed a hypofractionation protocol for prostate that was based on Jack Fowler's hypothesis that prostate cancer had a low α/β ratio and suggested that dose per fraction could be increased (Fowler *et al* 2003), in order to improve local control without an increase in complications. This protocol became so popular that several other institutions have enrolled and contributed patients to it, representing the first multi-institutional clinical research effort involving tomotherapy. In a prostate planning study Hidefumi Aoyama (Aoyama *et al* 2006) showed that helical tomotherapy offers reduced dose to critical tissues and about the same integral dose to normal tissue as conventional radiotherapy even with higher energy beams. Minesh Mehta is also exploring hypofractionated treatments to lung cancer based on the hypothesis that, when more of the treatment can be delivered before rapid proliferation occurs, the treatment will be more effective (Mehta *et al* 2001, Welsh *et al* 2004). In a planning study, Rufus Scrimger, a visiting fellow from the Cross Cancer Institute in Edmonton, Alberta, showed that helical tomotherapy produced more favourable dose distributions for lung tumours (Scrimger *et al* 2003). Raphael Manon confirmed in a larger study that tomotherapy can provide excellent normal lung sparing (Manon *et al* 2005). This dose-per-fraction escalation strategy required the integration of concepts including clinical proof of the accelerated radiotherapy concept (Fowler *et al* 2004), incorporation of PET/CT planning (made possible by the installation of the first hybrid PET/CT scanner in a radiotherapy department), motion detection, Bayesian statistical designs, etc. This work led to the natural extension into extreme dose-per-fraction escalation of early stage lung cancer (Fowler *et al* 2004), representing the first extracranial stereotactic radiosurgery application for tomotherapy. Paul Harari developed a conformal avoidance head and neck cancer protocol that was designed to reduce the dose to the parotids, auditory canal and uninvolved mucosa (Hong *et al* 2005). A related protocol for sinus tumours in dogs was also led by UW veterinarian radiation oncologist, Lisa Forrest. This unique protocol on client dogs with spontaneously arising tumours has resulted in excellent proof in the conformation possible with helical tomotherapy and the avoidance of critical structures such as the eyes. Almost every other technological development in radiotherapy has occurred outside the clinical trial mechanism, but this P01 produced rigorous scientifically verifiable and methodical clinical data for a new technology.

In parallel with the construction of the first helical tomotherapy prototypes based on GEMS CT gantries, an engineering project at TomoTherapy was designing a dedicated gantry, power distribution unit and couch. Led by David Murray, Eric Schloesser and Richard Schmidt, this system was designed to be easier to manufacture and service. It also would use an innovative solid state RF modulator from English Elective Valve (e2v) instead of a line modulator and a thyratron to produce the electrical pulse to the magnetron. The control for the original

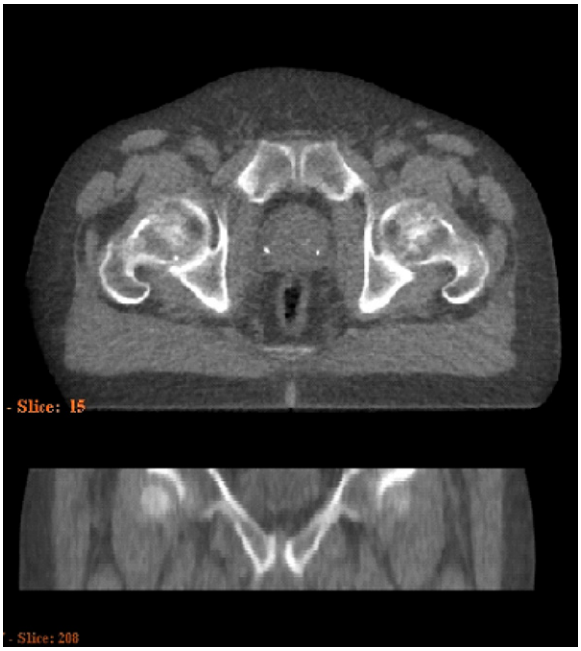

Figure 11. MCVT image of a prostate before treatment. The prostate gland with implanted markers is clearly seen. The rectal wall is clearly distinguished. The definition between muscle and fat is clearly distinguished. The dose was about 1 cGy.

unit was based on a robust GEMS architecture but it was not extensible. MD Anderson – Orlando received the first of these units although it was the Thompson Cancer Survival Center in Knoxville Tennessee that treated the first patient with this new system.

The beamline on the new gantry system was nearly identical to the original beamline. By this time measurements and detailed Monte Carlo simulation had shown that our original design parameters had been acceptable (Jeraj *et al* 2004, Glass 2003). The exception was that our first prototype had a tongue and groove design on the jaws that define the slice width, which was eliminated because it made the beam profile in the longitudinal direction asymmetric.

The image quality of the MVCT was improved in several ways even though the same detector was used. A new Analogic Corporation data acquisition system (DAS), used on modern CT systems, was adopted. This DAS had a low electronic noise and a dynamic range 20 bits deep. The linac energy was detuned from 6 MV for the therapy beam to lower than 3 MV for the imaging beam and the gun characteristics optimized for the finest spot size. An example of an MVCT image from a current Hi-Art^{TM} unit is shown in figure 11.

8. Recent concepts

With the Program Project grant in place at the UW much of the focus turned to the concept of adaptive radiotherapy, which is a collection of processes to ensure that the course of treatment is proceeding according to plan and to modify it if it is not (Olivera *et al* 1999). Harold Keller investigated implications of control theory on measurement error in setup uncertainty and the action levels that trigger a correction to the setup (Keller *et al* 2003, 2004). He showed that independently of the action level chosen, daily corrections were always advantageous in

improving the setup for the population. However, there will be a certain number of patients for which corrections will actually make individual setups worse. This has a higher chance of happening if the measurement uncertainty is a large fraction of the action level. As a practical matter, changes of setup should not be done if the shift is on the order of the measurement uncertainty. There is no practical need to change the setup uncertainty if it is much less than the PTV margin. Chuan Wu studied the issues involved with re-optimization in adaptive radiotherapy (Wu *et al* 2002, 2003a, 2003b, Wu 2002). For example, if dose reconstruction determines that there are cold spots in the tumour, it is possible to re-optimize, even using the original prescription, to achieve an improved dose distribution for the whole course of therapy. He showed that the prescription for re-optimization depended on whether the dose per fraction was to remain as close as possible to the original intent or the total dose was to be delivered as close as possible. He also showed that treatment plan modification could be made more flexible if voxel-based weights or dose prescriptions are used (Wu *et al* 2003a, 2003b).

Weiguo Lu developed a deformable registration algorithm (Lu 2001, Lu *et al* 2004). Deformable registration produces a one-to-one non-affine transform that maps from one image set to a second image set. Deformable registration is the basis for several important technologies used in tomotherapy. Adaptive radiotherapy will require the ability to map the regions of interest and dose distributions from daily CT scans to same volumes and distributions in the planning CT set in order to evaluate and modify the treatment. Lu's registration was originally two-dimensional but he has since implemented an improved three-dimensional deformable registration algorithm during his employment with TomoTherapy Inc.

Tiezhi Zhang (Zhang *et al* 2004) developed a fully four-dimensional model for delivering tomotherapy called synchronized breathing delivery. The idea is to record the breathing pattern of a patient getting a 4D CT scan. For every gantry angle the recorded pattern is used to select the correct 3D representation of the patient for a particular breathing cycle. The dose that will be deposited in the patient from beamlets from this direction are deformably registered to one of the breathing phases so that the iterative dose evaluation can be done on a common phase. Iterative optimization proceeds as usual. When the treatment is delivered the patient has to breathe in the same pattern as closely as possible to the original 4D CT on which the planning was based.

Tomotherapy research has become more clinically focused in recent years. John Fenwick developed a comprehensive approach to quality assurance of a helical tomotherapy unit (Fenwick *et al* 2004, 2005). He stressed the importance of tests of synchrony of the moving parts of a tomotherapy unit. Stewart Becker examined the issues related to treatment of accelerated partial breast irradiation in the prone position with tomotherapy (Becker 2006). He concluded that helical tomotherapy is more homogeneous and can avoid normal tissue nearly as well as brachytherapy. Susanta Hui also reported similar results (Hui *et al* 2004). Sarah Boswell quantified the accuracy that can be expected with automatic and manual image registration using daily megavoltage CT and concluded that tomotherapy can achieve registration to within 1 mm 95% of the time. She showed that outlier results are possible with automated registration if the setup of the patient is far off and there are periodic structures present in the images. Similar results for positioning re-treatments of vertebral tumours were reported by Mahan *et al* (2005). They found that the dose gradient between the target volume and the cord was $10\%/\,\mathrm{mm}^{-1}$ necessitating high setup accuracy and that the cord dose was 25% of the target volume dose. They reported that the spine could be positioned to within 0.6 mm in the lateral direction and 1.2 mm in the longitudinal direction. Langen *et al* (2005a) found that markers in the prostate can improve the accuracy of alignment. They also found that in the absence of markers the use of anatomical registration was better than simply placing contours on the daily CT images. Meeks *et al* (2005) studied the clinical performance of MVCT and

concluded that while the low-contrast detectability was not as good as conventional CT, many soft tissue structures are visible and it was sufficient for improving the patient setup. Kupelian *et al* (2005) and Ramsey *et al* (2006) reported that gross lung tumour volume imaged with MVCT shows that the tumour shrinks significantly during treatment. Ramsey *et al* (2006) speculate that if the target volume could possibly be shrunk as the treatment progresses in order to better protect normal lung.

The use of tomotherapy for completely new types of treatments has been documented. One of the first concepts to be tested was the use of 'extended field irradiation'. This was initially employed clinically at the UW, by Jim Welsh for multiple bone metastases and by Mark Ritter and Kristin Bradley for extended nodal irradiation including the pelvic and para-aortic lymph nodes for pelvic tumours. Susanta Hui described the feasibility of total marrow irradiation (TMI) whereby the bone marrow is irradiated to a treatment dose and the normal structures are set as avoidance structures thereby reducing the dose to them substantially (Hui *et al* 2005). However, it was Jeffrey Wong's team, at City of Hope in Duarte CA, which delivered several TMI treatments with minimal side effects (Wong 2006). The conformal avoidance of the hypocampus when targeting multiple brain metastases to avoid long-term neurocognitive deficits was proposed by Depak Khuntia (Khuntia *et al* 2006). Alonso Gutiérrez, along with Lisa Forrest, developed a minimally invasive surgical technique to implant inflatable bags in patients to separate the tumour from sensitive organs. The saline and iodine-contrast filled bags have sufficient contrast to be detectable on the MVCT images before treatment. The work has been piloted on bladder tumours in dogs with the goal to protect the small bowel. It is anticipated that the work might also be applicable in human bladder tumour or in even more difficult tumours that are limited by normal tissue toxicity, such as pancreatic tumours.

The Hi-Art^{TM} helical tomotherapy system has several innovative features not found in other radiotherapy systems. Only two of these features will be highlighted. The planning system has a built-in delivery quality assurance system. After planning is completed, a CT scan set of a phantom, in which the delivery quality is to be measured, is selected. The dose in the phantom is computed from the same intensity pattern to be used to treat the patient. The phantom is irradiated with a sheet of radiographic film and/or ion chambers in place. The ion chamber is read out and the film is scanned. The data are brought back into the analysis tool on the planning system and evaluated. Evaluation tools include comparison of calculated and measured isodose curves, plots of dose comparisons along an arbitrary direction, gamma plots (Low *et al* 1998), gamma histograms and comparison of point calculated dose versus the ion chamber measurements. Recently Thomas (Thomas *et al* 2005a, 2005b) reported that mean per cent discrepancy for high dose regions was $-0.5\% \pm 1.1\%$. The Hi-Art^{TM} system has adaptive radiotherapy features that includes dose computed in the daily megavoltage CT scans (Olivera *et al* 1999, Mackie *et al* 2001b, 2003a, 2003b). Langen *et al* (2005a), (2005b) have recently shown that the daily dose assessments based on MVCT are as accurate as the original CT plans performed on conventional CT scans. These actual dose distributions can be compared to the planned dose distributions using isodose plots, dose volume histograms, dose difference maps, and dose difference volume histograms. Contours can be adjusted to take into account changing anatomy due to patient weight loss or tumour shrinkage. The patient registrations can be made and the dose from multiple fractions summed to determine the dose delivered thus far. This information can be used to judge whether the treatment is proceeding according to plan. If it is not, the information can be used to re-optimize the dose distribution to improve the dose delivered to the remaining fractions. This adaptation tool can also be used to plan boosts taking into account the actual dose delivered to the patient.

Figure 12 is a photograph of the Hi-Art^{TM} helical tomotherapy unit at the UW Radiotherapy Clinic.

Figure 12. Photograph of Minesh Mehta, the Chairman of the UW Department of Human Oncology, in front of the UW Hi-Art^{TM} helical tomotherapy unit about to treat one of his patients.

9. R&D and mature operations of TomoTherapy Inc.

The research and product development groups at TomoTherapy Inc. have grown continuously since 1999. Today, the research group, led by Gustavo Olivera, currently has more than 20 scientists working on advanced concepts in adaptive radiotherapy, autocontouring, dose computation, optimization, image reconstruction, stereotactic radiosurgery and radiation detectors. TomoTherapy also supports several customers in basic and clinical tomotherapy research. A new concept for improving the efficiency of tomotherapy for emergency or palliative patients was researched by the group. It involves being able to scan, plan and treat the tumour in one session so that the patient can as quickly as possible get under treatment. The concept of 'topotherapy', first proposed by Holmes (1993), is the use of a fixed gantry but moving couch to deliver highly modulated single field plans. Topotherapy may be ideal for treating breast cancer in the manner of conventional tangents. At the beginning of 2006, the Product Development Group, led by Eric Schloesser, has more than 70 employees who are responsible for implementing their ideas and innovations suggested by customers and TomoTherapy's research group, thereby continuously improving the product. At the end of 2005 the company released their first version of adaptive therapy that included displaying and analysing the dose delivered to the daily CT image. This software is capable of taking into account the delivered dose when the plan is altered to account for observed deviations in dose.

Now, led by Fred Robertson MD as CEO, TomoTherapy Inc. has rapidly grown from its university research and development roots to a disciplined profitable corporation. The company now occupies a 5800 m^2 building and has over 400 employees. At the end of 2006 they will occupy nearly double that space and have nearly 500 employees. The success thus far of the concept is best expressed by the more than 75 helical tomotherapy units in clinical use on three continents. In a review article, Andy Beavis (2004) asked: is tomotherapy the future of IMRT? It is certainly *a* future of IMRT, whether it will be *the* future is as much up to the success of business as much as technology.

Acknowledgments

I would like to thank the dozens of dedicated individuals, both discussed in this article and unfortunately not discussed for reasons of brevity, who contributed to the design and implementation of helical tomotherapy. I would like to thank Jeff Kapatoes, Julie Zachman, Eric Schloesser, Gustavo Olivera, Ken Ruchala, and especially Paul Reckwerdt, Michael Kissick and Minesh Mehta for detailed editing and useful suggestions. I would also like to thank the University of Wisconsin, the Wisconsin Alumni Research Foundation, General Electric Corporation, Siemens Corporation and the National Cancer Institute, and last but not least, TomoTherapy Corporation for support and encouragement in bringing this new radiotherapy modality to life. I received partial support from NIH P01-CA088960, NIH T32-CA09206, and NIH P30-CA14520. I disclose that I have financial interest in TomoTherapy Inc.

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