TECHNOLOGY TRENDS

SRS, SBRT deliver promising results

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External beam radiation therapy has yielded promising results and improved patient outcomes in recent years, yet its accuracy and safety remain areas of concern. Side effects of radiation treatment include problems that occur as a result of the treatment itself as well as from damage to healthy cells in the treatment area.[1]

However, with improvements in radiation therapy delivery and planning, cancer patients today have more "targeted" treatment options, notably stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT).[2] Using SRS and SBRT techniques, high doses can be given in one to 5 fractions with acceptable toxicities to organs at risk.[2] In most cases, patients can resume all of their normal activities within 1 or 2 days.[3] This has led to widespread adoption of SRS and SBRT, and approximately 400 facilities are equipped to perform SRS and SBRT in the United States (U.S.).[3]

Promising results

Lung cancer is one of the deadliest and most common causes of cancer death in men and women in the U.S.[3] Although lobectomy is the standard treatment and offers the best chance of curing early-stage non-small cell lung cancer (NSCLC), a significant proportion of patients in the U.S. aging population are not surgical candidates at diagnosis.[4] In recent studies, SBRT has demonstrated excellent local control and cause-specific survival with minimal toxicity in early-stage NSCLC.[5] SBRT is considered a curative alternative to surgery not only for elderly patients with severe lung disease, but also for patients with severe heart disease, patients in poor health,[6] and patients with early-stage but inoperable NSCLC tumors.[7]

In a recent study[8] of SBRT of spinal cord lesions, a cohort of 500 cases of spinal metastases underwent radiosurgery. Long-term tumor control was demonstrated in 90% of lesions treated with radiosurgery as the primary modality, and in 88% of lesions treated for radiographic tumor progression. Long-term pain improvement occurred in 290 of 336 cases (86%). Twenty-seven of 32 cases (84%) with a progressive neurologic deficit before treatment experienced at least some clinical improvement.

These are just some of the many successful outcomes achieved with SRS and SBRT treatments, as there are many other treatment sites, such as primary and metastatic tumors to the liver, kidney, pancreas and prostate.[8]

Time and comfort contribute to accuracy

Two factors contribute to more accurate delivery of ionizing radiation: faster treatment times and patient comfort.

"We believe faster treatment in prostate cancer and patient comfort contribute to accuracy," John B. Fiveash, MD, Radiation Oncologist, Department of Radiation Oncology, Associate Professor and Vice Chairman for Academic Programs, University of Alabama at Birmingham, "With faster treatment… patients are more comfortable and less likely to move during the therapy."

In many cases, movement is a function of time. In prostate cancer, gas patterns or rectal or bladder filling can move the target, and a quicker treatment is more likely to be associated with more accurate treatment. The Assessing the Impact of Margin Reduction (AIM) study showed that prostate cancer patients treated with reduced margins and tumor tracking had lower radiotherapy-related morbidity than their counterparts treated with conventional margins.[9]

Study subjects received radiation treatment with the Calypso Beacon System, implantable electromagnetic transponders that are placed in or around a tumor and tracked continuously during external beam radiation therapy.

"The Calypso Beacon studies look at prostate studies as a function of time, and if you have look at motions over 3 mm, with treatments lasting 10 to 12 minutes, 25% of the patients will have motion of the prostate >3 mm. If you have a treatment that lasts a minute or 2, it's about 5% or less," indicated Dr. Fiveash. "A quick treatment with RapidArc or flattening filter free mode (FFF), if you're

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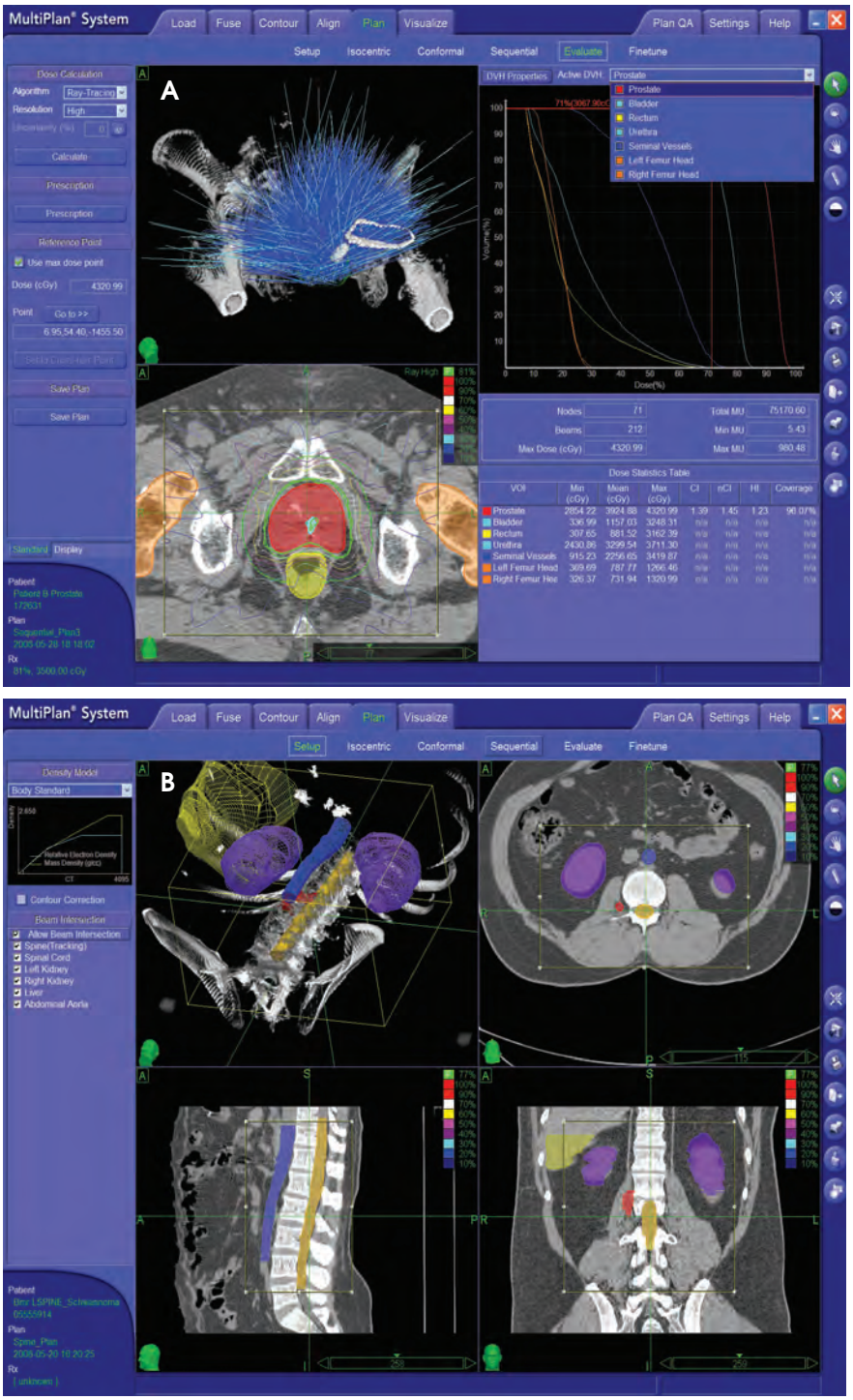

FIGURE 1. *The MultiPlan Treatment Planning System for Cyberknife is designed specifically for radiosurgery, allowing for the simple and efficient creation of even the most complex treatment plans. (A) shows a treatment plan for the prostate and (B) shows structure delineation.*

doing stereotactic treatments, in particular, has an advantage for accuracy, or you need a way to do real-time monitoring, such as with Calypso."

When the radiation oncology department at the University of Alabama at Birmingham opened a new radiotherapy facility, the primary goal was to broaden and grow its SBRT program and to do hypofractionated frameless SRS treatments with single and multifraction. The physicians also wanted better image-guidance for more efficient treatments elsewhere in the body. Already equipped with a TomoTherapy system, recently acquired by Accuray Inc., a Gamma Knife (Elekta AB), and a RapidArc system by Varian Medical Systems (Varian), the department selected Varian's TrueBeam system.

"We chose TrueBeam for frameless SRS treatment, for its more efficient administration of body radiosurgery, and to have better integration of the image guidance systems," said Dr. Fiveash.

TrueBeam rotates around the patient and can deliver radiation from multiple angles, while the operator uses advanced imaging techniques to control the beam shape and strength, and it synchronizes the beam delivery with a patient's breathing pattern. TrueBeam also features a high-intensity mode, which can deliver dose up to 4 times faster than conventional linear accelerators.

"The greatest time savings is in higher dose-per-fraction cases, which is why we wanted TrueBeam," said Dr. Fiveash. "We used to schedule patients for lung or liver surgery in 60- to 90-minute time slots to deliver a very-high-dose treatment. Now, we are scheduling 30-minute time slots, and that's a resource advantage for the machine, for the physician, and it's much more comfortable for the patient."

"We also save a lot of time for brain treatments," he added. "We are treating patients in just over 10 minutes for

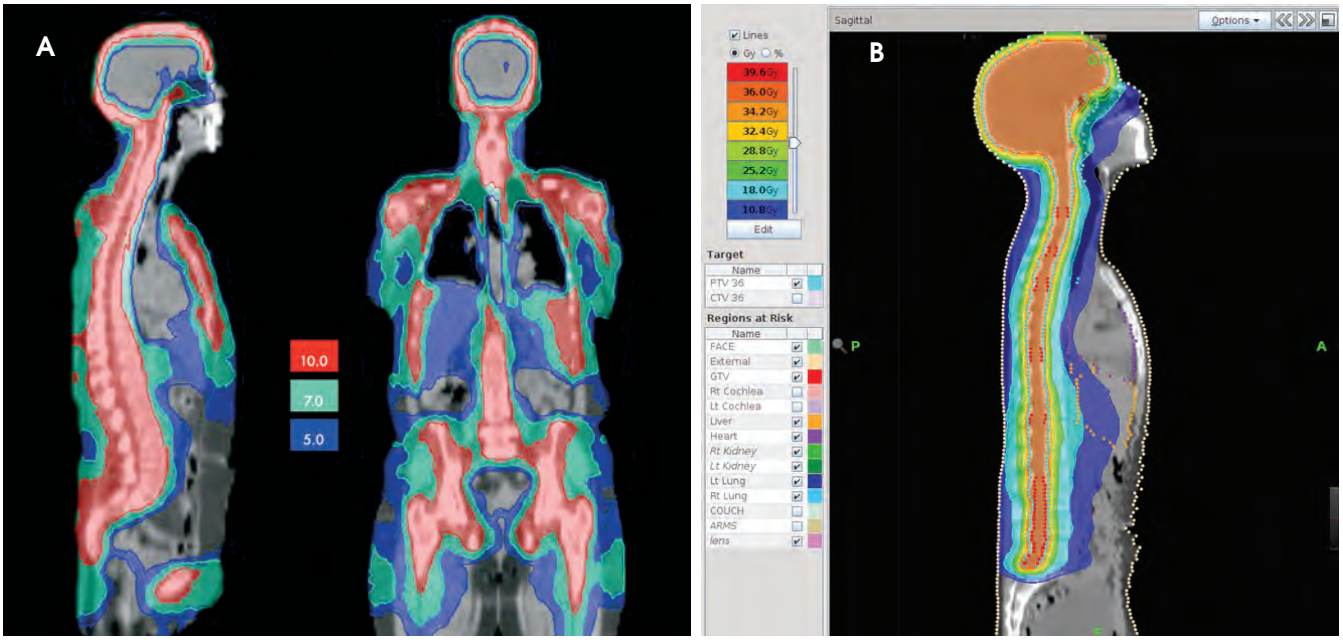

***FIGURE 2**. A treatment plan for total marrow irradiation (A) and for the cranio-spinal region (B) on a TomoTherapy System.*

single-fractionated or hypofractionated SNS treatments, which is much quicker than other delivery devices. You can combine RapidArc with flattening filter free mode (FFF) or High Intensity Mode and do beam time in <5 min. For multiple targets, it's a big time saver. If you are treating multiple tumors, like metastases, it could take 2 to 4 hours on a Gamma Knife, and we can do that in 15 min—there is more patient comfort and time advantages."

While time is important, it isn't everything. Frameless systems provide for greater patient comfort. "The Gamma Knife is especially effective for treating multiple metastases, such as 3 or more lesions in the brain, said Sandra S. Vermeulen, MD, a radiation oncologist at Swedish Cancer Institute in Seattle, WA. "We treat multiple lesions in the brain better with Gamma Knife than Cyberknife because it has a faster platform and better limits scatter radiation to other parts of the brain. But if you have 1 to 3 lesions, we can use the Cyberknife (a frameless radiosurgery system). Many patients don't want a frame-based system because it's uncomfortable."

The system has several distinct advantages over frame-based systems, including improved patient comfort, increased treatment degrees of freedom, and the potential to target extracranial lesions more easily.[10]

Contouring cuts treatment times

A recent advance in beam-shaping technology has led to the reduction in beam delivery time by as much as 41%. The newly released Agility is a 160-leaf, multi-leaf collimator (MLC) developed by Elekta for its Volumetric Modulated Arc Therapy (VMAT) system. The new MLC uses twice the number of leaves found on many standard MLC's, and is designed to sculpt delivered radiation to the distinctive contours of the tumor while reducing the risk of exposure to healthy normal tissues. On the VMAT, single or multiple radiation beams sweep in one or more uninterrupted arcs around the patient, reducing treatment times significantly.

By combining accelerated beam shaping and beam delivery, doctors at The James Cook University Hospital in Middlesbrough, England (UK), were able to cut 57 sec off the beam delivery time when treating a 61-year-old male with prostate cancer. The patient received his first treatment fraction, a single, 200-degree VMAT arc, in just 83 sec. In comparison, a 3-field, 3-dimensional (3D) conformal treatment would have taken 140 sec. This demonstrated a 40.7% reduction in beam delivery time with Agility/VMAT.

"The treatment speed not only reduces the likelihood that the patient will move and that the internal organs will shift position, but it also contributes to faster patient throughput, which is key. With Agility and VMAT, we expect to be able to treat 5 patients per hour," said Christopher Walker, Head of Radiotherapy Physics at The James Cook University Hospital.

Respiratory motion

One of the biggest challenges in radiotherapy is breathing, which causes the lungs, liver, prostate, and other organs to move during beam time.

One of the primary reasons for using SRS is to minimize radiation-induced normal tissue damage.[11] SRS and

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SBRT use image-guided radiation therapy (IGRT), which relies on medical imaging to confirm the location of a tumor during the delivery of radiation to improve the precision and accuracy of the treatment.[12]

At Swedish Cancer Institute in Seattle WA, doctors have Accuray's CyberKnife VSI, the Gamma Knife, and TomoTherapy system to treat prostate, lung and breast cancer, and colorectal carcinoma and melanoma.

Since Cyberknife uses individually targeted "pencil-beams" instead of arcs, the treatment isodose contour takes shape without using individual isocenters, and theoretically could be planned to exclude critical structures entirely.[10]

"You can fractionate with the Cyberknife platform because it is not a frame-based system," said Dr. Vermeulen. "If you have a tumor encompassing a sensitive location like near the eye, the optic nerves or chiasm, you can't treat it on Gamma Knife, but you can on Cyberknife because you can fractionate the dose to protect surrounding sensitive tissues."

Working with the CyberKnife is the Synchrony Respiratory Tracking System, which enables the radiation beam to track tumor movement in real time and allows patients to breathe normally during treatment. The patient wears the Synchrony vest, and the robot correlates chest motion and breathing patterns with the tumor position.

"The more accurate you can be, the higher the the dose can be delivered, which translates into higher tumor control rates," noted Dr. Vermeulen. "With conventional radiation, lung cancer local control rates are 60% to 70% and higher doses would damage adjacent normal tissue. However, with the targeting precision of Cyberknife we can now deliver 30% higher doses." She added, "This results in 90% local control for lung cancer, which is a phenomenal achievement."

Another breakthrough doctors at Swedish Cancer Institute are witnessing is in early-stage prostate cancer. These doctors started the radioactive seed implant program nearly 20 years ago, and today they are using Cyberknife to treat these patients with higher radiobiologic doses and seeing even fewer side effects than with seed implants.

Dr. Vermeulen said she is now working with Cyberknife to re-treat patients with metastatic disease of the spine, who had undergone conventional radiation and no longer had control of spinal metastases. "We could never do that before. This eliminates the crippling sides effects of the recurrent disease," she said.

Another valuable tool in the hospital's armamentarium is the TomoTherapy System, which uses helical, continuous, 360-degree delivery of IMRT. Tens of thousands of narrow beamlets are used, all of which are targeted directly at the tumor and individually optimized to contribute to the total tumor dose. By delivering beamlets from more angles than any other form of IMRT, the TomoTherapy System provides precise conformal radiotherapy. The advantage with TomoTherapy is that you can treat a larger area.

"If you have disease that has metastasized into the lymph nodes, you need to treat a quadrant or lymph node chain, the TomoTherapy application is exquisite," Dr. Vermeulen said. "Tumors which seed the spine like high-grade ependymomas and medullobalstoma require craniospinal irradiation. Where conventional radiation would have to include a significant amount of adjacent normal tissue leading to unwanted side effects, TomoTherapy can restrict the radiation to the craniospinal contents like protons can without the excessive cost to the consumer."

In the next issue of Applied Radiation Oncology, *Tech Trends will feature "Where protons meet photons," an in-depth evaluation of the pros and cons of proton and photon radiation therapy.*

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