TECHNOLOGY TRENDS

Updates in IGRT: The new, the improved, and the future outlook

Mary Beth Massat

When a 56-year-old liver transplant patient came to Henry Ford Health System, Detroit, Michigan, with a metastatic focus recurrence from hepatocellular cancer nestled between the porta hepatis, duodenum, stomach, and large colon, M. Salim Siddiqui, MD, PhD, had a plan. Rather than refer the patient for palliative care, the director of the Stereotactic Radiation Program opted for treatment.

"The soft tissue mass was surrounded by organs that move and expand at different rates relative to each other, so we couldn't rely on just cone-beam computed tomography (CBCT) because the mass could move," explains Dr. Siddiqui. Fortunately, Henry Ford Hospital had recently installed the Edge (Varian Medical Systems, Palo Alto, California), a new dedicated radiosurgery suite that offers real-time tumor tracking and motion management technologies, along with triggered imaging with beam-hold ability for planning and delivering radiosurgery treatments.

Three fiducial markers were implanted in the mass. Dr. Siddiqui and his team performed a 4D-CBCT simulation to create an internal target volume (ITV) motion envelope for tumor movement and for each fiducial. With this information they had a plane reference to capture any rolls, pitches, yaws and translations of the mass. With the integrated 6 degrees of freedom treatment couch, Dr. Siddiqui could quickly and easily adjust for those as well. The plan called for 5 fractions of 7 Gy, with only 2 mm expansion from the ITV to the planning target volume (PTV).

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"We used 4D-CBCT to capture and image the tumor within its motion envelope and precisely align to the planned soft tissue tumor, then used kV imaging to see if the fiducials fell within the corresponding ITV," he explains. "Then we used triggered kV imaging to track in real time the fiducials, delivering the treatment beam only when the fiducials were within the ITV and PTV expansion."

Without this technology, the patient could not have been treated. "This was just remarkable," says Dr. Siddiqui. "This was his only soft-tissue recurrence, and we gave the patient tremendous hope."

Advanced image-guided therapy systems are changing external-beam radiation treatment (EBRT) plans, enabling radiation oncologists to prescribe radiation therapy in areas of the body that were previously difficult to treat.

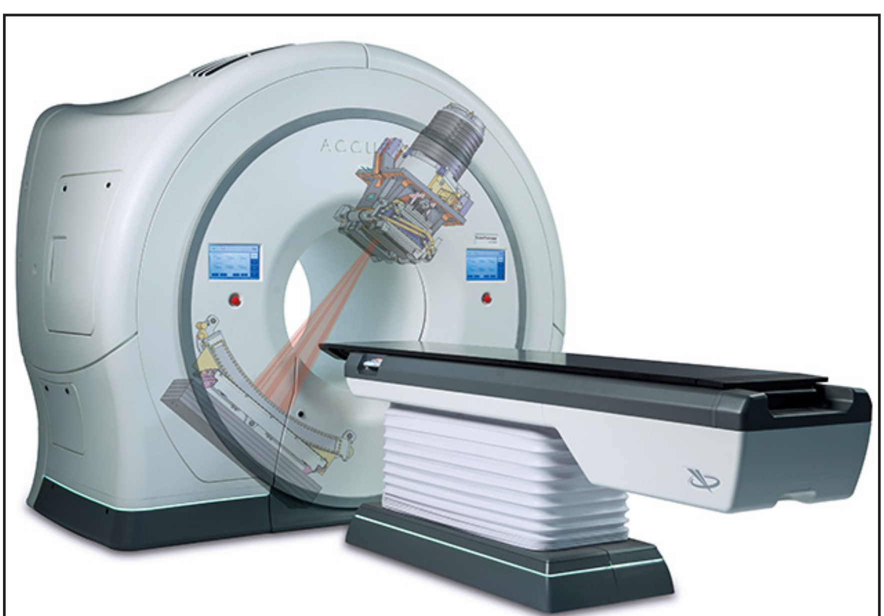
For Paul J. Kim, MD, medical director at Skyline Radiation Oncology, Tustin, California, the use of 4D imaging with Clarity (Elekta, Atlanta, Georgia) is improving certainty of the prostate gland's location during radiotherapy. By applying the ultrasound to the perineum, he can visualize and track the prostate's position continuously during each radiation treatment.

"If the prostate moves away from the beam, we can stop, adjust and resume," says Dr. Kim. "Because real-time tracking has improved our certainty of the prostate's location during the treatment, we have the opportunity to reduce our treatment planning margins. It's non-invasive and does not require placement of any fiducial markers, thereby improving patient acceptance of the treatment."

While the length of treatment remains the same, the treatment delivery is of a higher quality. "We are hitting the target with less volume of surrounding tissues, such as the rectum or bladder, receiving high doses of radiotherapy," he adds. "This is where real-time imaging technology is helping, to track moving targets and enable us to more safely deliver treatment."

Certainly, image guidance in EBRT has come a long way, adds Sandra Zaky, MD, DABR, from Palo Verde Cancer Center-Scottsdale in Scottsdale, Arizona. One advantage is the ability to deliver higher dose levels to the tumor, which can result in better disease control, while at the same time reducing margins around the tumor to protect

Hybrid imaging is achieved by acquiring Elekta's Clarity images at the same time as the CT acquisition procedure with the patient in the same RT setup position. This allows CT and Clarity images to be automatically fused for seamless integration into simulation and planning workflows. Clarity's software-assisted segmentation technology supports clinicians in rapidly contouring 3D soft-tissue targets and anatomy prior to treatment planning.



Accuray's TomoHDA™ System is the latest innovation in the TomoTherapy product portfolio and is equipped to deliver helical and direct-angle IMRT. With a unique combination of features including daily CT image guidance, VoLO Treatment Planning and TomoEDGE Dynamic Jaws, the system offers radiation oncologists fast, accurate and flexible treatment planning and delivery for patients, regardless of location, size and complexity of the tumor.

critical structures and reduce side effects. She sees a tremendous difference in the quality of treatment from a reduction in margins, particularly in head and neck cancers.

"Many patients receive chemotherapy concurrent with radiation, and it can be very toxic for the patient," Dr. Zaky explains. "Before we had the ability to acquire CT images throughout the course of treatment, we used larger margins so that we weren't missing the disease. Now, because we can use these daily images for more precise patient positioning and monitoring of treatment progress, we can reduce our margins. As a result, the dry mouth, skin changes, oral ulcers and other irritation in the mouth is reduced. With smaller margins, there are fewer side effects for the patients."

Dr. Zaky and her colleagues use the TomoHDA System (Accuray, Sunnyvale, California) with VoLO Planning to create treatment plans with tighter margins that spare healthy tissue and organs. The system's integrated imaging and flexible radiation delivery modes help keep treatments on track, and allow for more aggressive approaches, such as stereotactic procedures, that can be completed in fewer treatment sessions.

"Image guidance has changed stereotactic radiotherapy," she says. "We can confidently pinpoint the tumor with accuracy and deliver high doses at each treatment."

With the system's CT scanner-like design, Dr. Zaky can seamlessly image and treat larger fields compared to conventional linacs with smaller set size image fields, she explains. For example, she can image the entire leg with the CT while the patient is in the treatment position, and then deliver the therapy.

Intra-operative imaging

Advanced image guidance is also being used for brachytherapy in an intra-operative environment. At the University of Virginia School of Medicine

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The Siemens SOMATOM Sensation Open sliding gantry can be used for in-room imaging within an intra-operative setting. It enables clinicians to slide the CT to the anesthetized patient to capture imaging during a surgical procedure, such as brachytherapy treatments.

During treatment, the ViewRay system continuously monitors the patient's anatomy and adjusts for motion in real time, delivering the dose only when the tumor is located exactly where it should be. Continuous MRI and soft-tissue targeting assure accurate treatment delivery and minimize the dose to critical structures and surrounding healthy tissues.

in Charlottesville, Timothy Showalter, MD, assistant professor in the Department of Radiation Oncology, and Bruce Libby, PhD, associate professor, Radiological Physics, and chief of Clinical Brachytherapy Physics, are using a SOMATOM Sensation Open CT sliding gantry in a brachytherapy suite.

"To do brachytherapy in the intra-operative setting, you need several components all in one room," explains Dr. Showalter. "This includes shielding for [high-dose-rate] HDR brachytherapy, as well as in-room imaging, and the ability to perform a lumpectomy or surgical procedure. It's a unique arrangement, and having the CT scanner in the room enables us to slide the CT across the floor toward the anesthetized patient who has just received a lumpectomy—without moving the patient—which is really critical."

In any setting, moving a patient comes with a risk. Dr. Libby shares a story of a patient who had applicators and needles placed in the OR, only to have one of the applicators perforate the uterus when she was moved to the brachytherapy treatment room. Bringing the scanner to the patient, he adds, is safer for the patient and provides added flexibility.

"The whole combination of equipment ensures maximum flexibility, not just for breast patients, but also for our gynecological patients," Dr. Libby says. "If we are not happy with how the applicator is placed, we can take the applicator out and place it properly without moving the patient to a different room for placement. So the image guidance part of it is really important."

Plus, there's an added advantage of a more efficient workflow. According to Dr. Showalter, an ambulatory brachytherapy procedure for cervical cancer is extremely efficient in the image-guided brachytherapy suite.

"We can complete a tandem and ovoid case in less than an hour and a half," Dr. Showalter says. "That's in contrast to care delivered at radiation oncology centers without an integrated suite, [where] each step has to be completed in a different room or location. This might take 3 to 5 hours for a tandem and ovoid brachytherapy treatment.

"The rapid workflow allows us to offer new programs like the breast intraoperative radiation therapy, something that is innovative and not available elsewhere," he adds. "This alone will not necessarily improve cure rates, but it certainly will improve patient satisfaction."

MRI image guidance

For years, radiologists have realized the superiority of MRI for imaging soft tissues in the body, including the brain, spine and joints. In radiation therapy, using MRI for image guidance in treatment planning is no longer a vision—it's reality.

The Siteman Cancer Center, part of the Washington University School of

Varian's EDGE Radiosurgery Suite is a fully integrated, dedicated system for performing advanced radiosurgery using new real-time tumor-tracking technology and motion management capabilities.

Medicine in St. Louis, Missouri, is the first site to implement the ViewRay (Oakwood Village, Ohio), the only commercially available MRI-guided radiation therapy system. With it, Jeffrey R. Olsen, MD, assistant professor of radiation oncology, can image soft tissue anatomy in real-time to keep the radiation beam on target when the target moves during treatment. Dr. Olsen is performing research to apply this technology to cancer situations—including pancreatic cancer—to reduce treatment side effects.

Radiation alignment is traditionally performed using 2D X-ray images or CT imaging. Although such techniques allow visualization of bony anatomy, the use of MRI allows alignment based on the soft tissue tumor and critical structures not visible with traditional localization techniques such as X-ray imaging. The ability to capture real-time MR images means that as the position of critical structures move, or the shape of the tumor changes, the radiation beam can be adjusted to allow a more targeted treatment field. These changes allow treatment modification, called adaptive radiotherapy, based on a patient's individual anatomy. However, adaptive treatment presents a new logistics issue that the treatment team at Washington University is working to resolve—the quality assurance (QA) process. To reduce side effects, that's a problem Dr. Olsen doesn't mind having.

With traditional radiation therapy plans, the patient is imaged one day, and then treated the following day based on the QA process. The challenge is to implement a QA process so the patient can be imaged, planned and treated on the same day. It's a process where the patient receives repeat MR scans to make adjustments based on changes in anatomy. Allowing daily adaptation and planning revision can reduce the amount of normal tissue receiving radiation dose.

"We have seen increased motion and variability in some tumors, and we've been able to act on that information," says Dr. Olsen. "MRI changes the information we have and provides the initial foundation for moving forward with image-guided adaptive treatments. This is something that has the potential to improve outcomes and reduce toxicity."

Furthermore, as radiation oncologists use imaging such as MR or positron emission tomography/CT (PET/CT) to monitor patient progress earlier in the treatment cycle, adaptive treatments may allow for changes based on early response. If the patient is responding favorably to treatment, the oncologist can reduce dose or stay the course; if there is an unfavorable response, the dose might be escalated or the patient can be moved to another type of therapy. The key is that treatment can be tailored to the individual patient.

Three trends resonate across different sites: 1) treating cancers once considered untreatable; 2) providing new options that enhance quality of life post-treatment by reducing toxicity to healthy tissues and critical structures; and 3) using advanced imaging to personalize treatments based on patient response to treatment and the individual nature of the specific cancer. Even in the same body area, no two cancers are necessarily alike.

Hypofractionation, quantitative imaging, radiomics and more

Real-time imaging and adapting therapy to changes in motion, anatomy and tumor shape/size—these are today's innovations. But what does the future hold?

"There is a clear movement toward hypofractionation," says Corey Lawson, senior director, TomoTherapy Brand Management, Accuray. "Most importantly, it appears that shorter treatment courses can have a positive impact on outcomes for a variety of disease types…there are obvious quality-of-life benefits for patients as well, including reduced travel time and time spent in the treatment room." He also believes that with shorter treatment courses, hypofractionation can help increase capacity on a radiation therapy system, providing opportunities for centers to use the technology more effectively and efficiently.

"The key to hypofractionation is the ability to deliver dose aggressively to the tumor to achieve better control, without incurring increased toxicities or side effects," Lawson adds.

For Mike Saracen, senior director of marketing at ViewRay, now that MRI is used in conjunction with treatment, the next step is making personalized treatments a reality. "There is an untapped opportunity to leverage MRI technology, whether that is through the use of different sequences, contrast enhancement, or even functional MRI," he says. "I can see a future where, instead of looking at 4 frames per second, it becomes faster, maybe even 12 frames per second. Or instead of slices, the clinician is looking at a whole 3D volume. MRI offers that possibility."

At Elekta, Kevin Brown, global vice president of scientific research, says that the company is also pursuing the integration of high-field MRI with state-of-the-art radiotherapy. "The goal is to sharpen soft-tissue visualization to the extent we can—to maximize dose to the target and minimize the dose to surrounding tissues—and to improve the ability to image moving targets, such as those in the lung."

Brown also believes that quantitative imaging can help oncologists assess the tumor's response during the patient's radiation course. By extracting quantifiable features from medical imaging, such as PET or other functional imaging, oncologists can more precisely assess response based on functional or cellular changes rather than qualitative changes in the tumor shape or size.

Corey Zankowski, Varian Medical System's vice president of product management, envisions the emergence of radiomics, or the extraction of more information from medical imaging for further analysis, as an emerging frontier in image-guided radiation therapy. Looking at the characteristics of a tumor, such as size, shape and texture, as well as complex wavelet transformation, can help stratify patients into categories to help predict treatment response.

"Enabling clinicians to see the texture of the tumor and where it is invading can help characterize aggressiveness of the tumor," Zankowski says. "This can help guide and personalize the treatment, and I think that will drive a lot of what we will be doing in the future."

He also believes that optical monitoring (e.g., multiple cameras in different positions that look at the patient's surface and detect small shifts) will give clinicians added confidence in patient positioning and the delivery of treatment near organs that move.

One thing is certain for Cecile Mohr, PhD, director of global product marketing at Siemens Radiation Oncology, Malvern, Pennsylvania: Multi-modality imaging is becoming more important for devising the treatment strategy. Specifically, the use of advanced imaging, such as MRI and PET, helps significantly in many cases, including stereotactic radiosurgery and stereotactic body radiosurgery. It also further advances therapy planning beyond these specialties. "In brachytherapy, clearly CT and MRI are significantly helping with local control," says Dr. Mohr. "These modalities provide more precision in the treatment homogeneity, and the whole treatment pathway is changing."

Siemens is also exploring PET/MR. "With PET/MR, clinicians can access multi-parametric images and look at the biology of the tumor for planning and treatment response. This is a promising and active area of research," says Dr. Mohr, noting that many questions remain.

With the extent that CT is used today in conjunction with treatment planning, Aenne Guenther, vice presient of Marketing & Sales, Siemens Radiation Oncology, anticipates that dual-energy CT will be utilized in the near future. Dual-energy CT takes images at different energy levels, providing information on tissue composition.

"Dual-energy provides more diverse information from the CT scanner," Guenther explains. "It could potentially improve contrast-to-noise ratio for more reliable contouring, provide patient-specific electron density and atomic number, and improve dose calculations in both proton and brachytherapy procedures."

There is no question that imaging in radiation therapy treatment planning continues to play an essential role. New technologies and techniques are quickly evolving, providing the ability for clinicians to view the organs, structures and tumor in real time for more accurate planning that spares healthy tissue and better targets the disease. Imaging can also help determine the response to treatment earlier in the cycle, so clinicians can better personalize therapy to the individual patient—an inspiring goal in the fight against cancer.