UT SOUTHWESTERN

THE TARGET

News from the Department of Radiation Oncology

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Ground-Breaking

A new state-of-the-art facility and the first Vero machine in the U.S. will reinforce UT Southwestern's leadership in radiosurgery.

Clinicians in UT Southwestern's Department of Radiation Oncology see more patients than any other provider in North Texas, but thanks to a physical expansion and the addition of state-of-the-art technology, the department soon will offer even more patients the most advanced radiation treatments available.

Renovations began in October to a 16,000-square-foot facility near University Hospital — St. Paul into which the department will expand and offer enhanced treatment options for patients. The building

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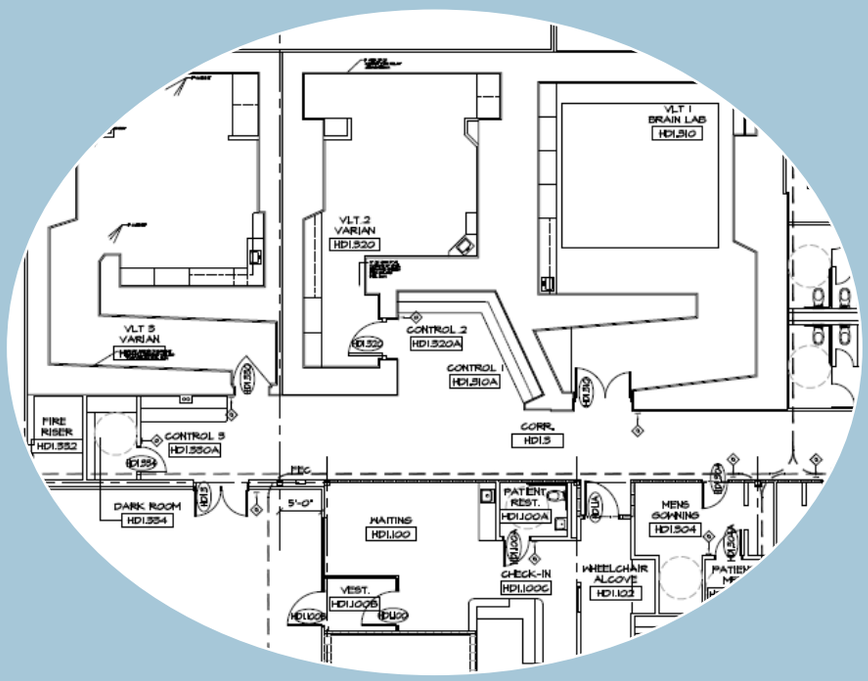
What's Inside



Department of Radiation Oncology expands

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"Vero is next-generation technology for clinics that are very progressive..."

– Timothy Solberg, Ph.D.

previously housed the radiation oncology department before it moved to its current home in the Moncrief Radiation Oncology Building on the North Campus.

As part of the expansion, UT Southwestern will be the first institution in North America to install Vero, an advanced system for delivering noninvasive radiation treatment to cancer patients. In addition to UT Southwestern, the Vero system has been installed in only a handful of facilities in Japan and Europe.

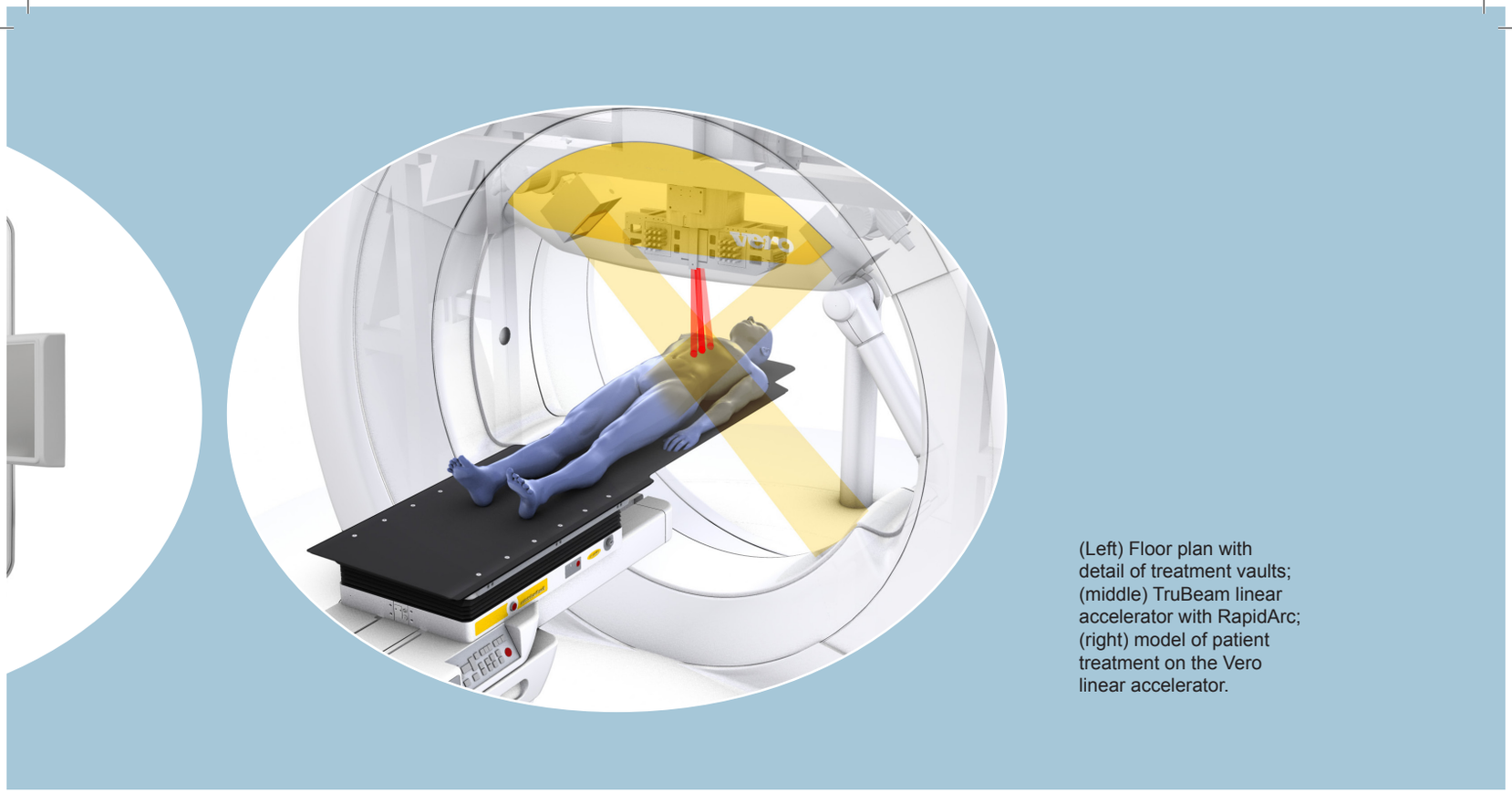
In partnership with Brainlab AG of Germany, the Vero device will be installed in the renovated facility in early 2011. The first patients to be treated with the device at the medical center could be seen as early as next summer.

The new building is intended to facilitate the department's training as well as therapeutic programs. As pioneers and recognized experts in the use of a type of cancer treatment called stereotactic body radiation therapy, or SBRT, UT Southwestern faculty in radiation oncology currently provide training in the technique to professionals, including physicians, medical physicists, radiation therapists, dosimetrists and others. The new facility's design includes a dedicated visitor conference room and a separate entrance from patients, which will allow medical professionals worldwide to observe the department's operations while maintaining patient privacy.

The department also will add to the facility two new Varian TruBeam linear accelerators, which also provide advanced radiation therapy.

"Our department is currently landlocked, so adding additional physical space, as well as additional treatment machines, will allow us to increase patient capacity," said Dr. Hak Choy, chairman of radiation oncology.

The Vero system integrates many state-of-the-art radiation therapy capabilities into one machine and is designed to locate tumors and meticulously direct radiation precisely where



(Left) Floor plan with detail of treatment vaults; (middle) TruBeam linear accelerator with RapidArc; (right) model of patient treatment on the Vero linear accelerator.

it is needed using SBRT. This noninvasive procedure delivers radiation beams to a tumor in a concentrated, precise manner, minimizing damage to healthy tissues and reducing the number of treatment sessions for patients.

SBRT typically is delivered to patients by one or more different machines, each providing its own specialized form of treatment. UT Southwestern's Department of Radiation Oncology currently treats cancer patients utilizing many of these advanced technologies.

"We have the reputation at UT Southwestern for delivering cutting-edge radiotherapy, and we have recognized experts, both physicians and physicists, who are capable of applying this new technology for the benefit of our patients," Dr. Choy said.

Radiation oncology and medical physics experts at UT Southwestern will evaluate the Vero system and develop clinical guidelines for its use.

The Vero machine combines several radiation treatment modes, including intensity modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT), and image-guided radiation therapy (IGRT), Dr. Choy said. Several different types of integrated imaging technologies, including X-ray, CT and fluoroscopy, allow clinicians to locate and track tumors in real time, even when the patient's body moves while breathing.

"Vero is next generation technology for institutions that are very progressive in their clinical approach," said Dr. Timothy Solberg, director of medical physics and engineering in UT Southwestern's Department of Radiation Oncology. "The medical community and industry look to us as a premier cancer center for research and clinical care to pave the way for a new technology that will truly benefit patients."

In addition to the renovated facility, radiation oncology clinicians will continue to see patients in the Moncrief building as well as in the Annette Simmons Stereotactic Treatment Center at University Hospital — Zale Lipshy. The radiation oncology department also is the primary referral center for Children's Medical Center Dallas and oversees one of the largest pediatric brain tumor programs in the country.

"We are very fortunate to have many different technologies at our fingertips. When our physicians determine individualized treatment plans for our patients, they are not limited by the availability of technology," Dr. Choy said.

"Having the Vero system here at UT Southwestern will provide another powerful weapon in the fight against cancer," said Dr. James K. Willson, director of the Harold C. Simmons Comprehensive Cancer Center at UT Southwestern. "As our recent designation as a National Cancer Institute indicates, advanced cancer research and patient care are our utmost priorities, and the ability to offer patients access to care they may not be able to get elsewhere is key." ♦

New doctors to focus on patient care, research

Three physicians recently have joined the patient care team of the Department of Radiation Oncology.

Thomas Boike, M.D., assistant professor of radiation oncology, earned his medical degree at Wayne State University School of Medicine in Detroit, Michigan, and is the first physician to join the faculty from the department's own residency program.

Dr. Boike has developed an expertise in prostate cancer and recently contributed to the article "Down-regulation of human DAB2IP gene expression in prostate cancer cells results in resistance to ionizing radiation." (*Cancer Research*, 2010 Mar 23). In addition to treating prostate cancer, Dr. Boike also sees pediatric patients.

Puneeth Iyengar, M.D., Ph.D., and Kevin Choe, M.D., Ph.D., are both assistant professors of radiation oncology and graduates of the medical scientist program at Albert Einstein College of Medicine in New York.

Dr. Iyengar completed his residency training in radiation oncology at M.D. Anderson Cancer Center in Houston, where he also worked in the Department of Genetics studying tumor suppression mechanisms, DNA damage signaling, and the biochemical pathways involved in radiation and chemotherapy resistance. His focus at UT Southwestern will be on the treatment of lung cancer and the formation of a research team to study inflammation, cachexia and the biology of lung cancer radiation resistance.

Dr. Choe completed a medical internship at Yale University Hospital in Connecticut, followed by a radiation oncology residency at University of Chicago Hospitals. He has received several prestigious funding awards for his research, including a Howard Hughes Medical Institute research grant and an ASTRO Young Scientist/Investigator Award. His areas of interest include the treatment of brain and other central nervous system cancers, as well as prostate cancer.

"Our new faculty members are all dedicated scientific researchers and extremely capable physicians," said Department Chairman Hak Choy, M.D. "They will help implement our mission of providing quality patient care while investigating new treatment options with the potential to eradicate cancer." ♦

At left, from top to bottom: Thomas Boike, M.D.; Kevin Choe, M.D., Ph.D.; Puneeth Iyengar, M.D., Ph.D.

Richardson clinic offers specialized care

UT Southwestern physicians recently began offering stereotactic body radiation therapy (SBRT) at Methodist Richardson Cancer Center in Richardson, Texas.

The addition of SBRT to the Richardson program allows doctors to treat tumors that may not be treatable by other means, including surgery. Inoperable lung cancers and previously treated spinal cord tumors are among the conditions that can be successfully treated with SBRT.

In addition, SBRT is typically completed in three to five sessions, as opposed to daily treatments lasting two to six weeks.

Since 2007, the Department of Radiation Oncology has partnered with the Richardson cancer center to professionally staff its radiation oncology practice, expanding the ability of both institutions to provide an advanced level of cancer care in the region. ♦

Study: Can SBRT ablate liver metastases with a single treatment?

Jeffrey Meyer, M.D.

Although the development of liver metastases is often associated with an incurable prognosis, certain patients, particularly those with colorectal primary cancers, can become long-term, disease-free survivors with resection of their liver lesions.

Numerous institutional reports support the concept of curative-intent metastasectomy, again, usually in patients with colorectal primary tumors with liver metastases their only known site of metastatic spread.

Although open surgical resection remains the 'gold standard' approach to managing liver metastases, there is significant interest in minimally or noninvasive tumor ablation techniques.

Many of these treatments take the form of thermal ablation, wherein extreme heat (usually with radiofrequency ablation [RFA]) or cold (cryoablation) generated by probes placed directly into tumors lead to tumor cell kill. A large body of clinical experience with RFA has shown both its promise and its limitations in treating liver tumors. Larger tumors and tumors near large blood vessels are often not completely ablated by RFA, leaving the patient at significant risk for tumor recurrence.

Radiation traditionally has had a minimal role in the treatment of liver tumors as a result of the high sensitivity of normal liver tissue to radiation. However, with the advent of image-guided therapy and highly precise and accurate radiation targeting, selected discrete liver lesions can be treated to very high, ablative, radiation doses while sparing the normal surrounding tissue.

Stereotactic body radiotherapy (SBRT) applies the principles of intracranial radiosurgery to extracranial tumor targets, including liver tumors.

Several studies, including one performed at UT Southwestern, have demonstrated that high-dose radiation delivered with SBRT techniques to liver metastases can, at least, rival the tumor control results obtained with thermal ablation approaches. As an example, a recent multi-institutional phase II study showed two-year actuarial local control of 94 percent in selected liver metastases. SBRT is not hindered by the heat-sink effect seen with RFA and may ultimately provide an alternative to invasive surgery for selected patients.

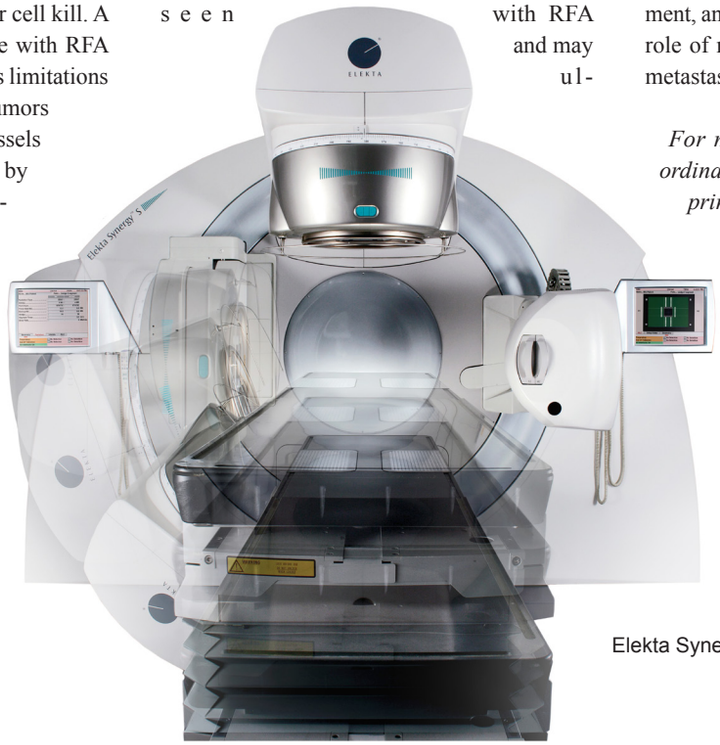
SBRT courses usually last from three to five fractions. An even more appealing option is true radiosurgery: single-fraction therapy. If shown to be safe and effective, liver radiosurgery may provide the advantage of convenience for patients and the advantage of seamless integration with systemic therapies for clinicians.

At UT Southwestern we have recently opened a clinical study evaluating the tolerability of high-dose radiosurgery for patients with liver metastases.

Patients with up to five hepatic metastases, including those with extrahepatic disease, are eligible (as long as a critical liver volume constraint can be met). Patients must have a life expectancy of at least six months. The starting radiation treatment dose is 35 Gy.

With our study design we hope to establish the tolerability as well as efficacy of this treatment, and to further refine the highly promising role of radiosurgery in the treatment of liver metastases. ♦

For more information, contact study coordinator Irma Smith at 214-648-5531, or principal investigator Dr. Jeffrey Meyer at 214-645-8525.



Elekta Synergy-S used for SBRT liver treatment

Radiation oncology researchers garner over $2 million in research grants

Real-time, adaptive radiotherapy and new strategies to improve prostate cancer treatment are among the projects that recently have attracted over $2 million in funding to investigators in the Department of Radiation Oncology.

The newly formed Cancer Prevention and Research Institute of Texas bestowed the largest grant, for $1.1 million, on a project created by Weihua Mao, Ph.D., for personalized, online, adaptive radiotherapy treatment.

Dr. Mao proposes to replace the conventional 3-D cone beam imaging typically used during radiation therapy to verify tumor location. Instead, 2-D images are captured and a computer model compares the points with the previous day's volumetric image to generate a new 3-D image of the tumor. The treatment plan will be evaluated on a daily basis and replanned if necessary.

This approach has the advantage of reducing patient exposure to additional X-ray radiation while allowing physicians to monitor and address changes in the tumor target.

"This methodology will significantly improve the efficacy of cancer treatment through more accurate tumor targeting and sparing of sensitive and dose-limiting normal tissues," says Dr. Mao.

Two other grants from the Department of Defense are aimed at improving prostate cancer treatment.

Kwang Song, Ph.D., obtained a training grant to study gold nanoparticles as a molecularly targeted radiation dose enhancer for prostate cancer. As shown in previous theoretical and experimental studies, gold nanoparticles can produce a dose enhancement factor of more than 2 at certain concentrations, and have other properties that may make them suitable for molecular targeting.

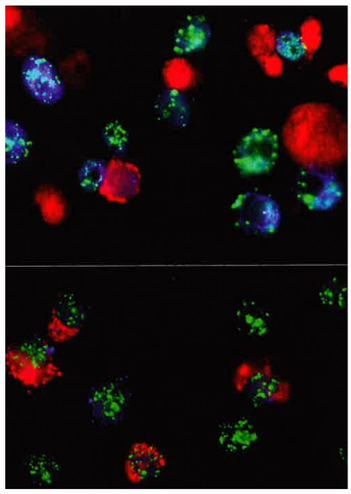
Debabrata Saha, Ph.D., also received a grant to explore the enhancement of radiation therapy for prostate cancer using a novel class of compound (NU7441). NU7441 may help suppress aggressive and metastatic cancer progression in prostate cells lacking a particular tumor suppressor gene. The Saha laboratory also received an industry grant to study radiosensitization of non-small cell lung cancer cells using combined modal therapy.

Finally, the National Institutes of Health (NIH) awarded a grant to Timothy Solberg, Ph.D.,for the purchase of an image-guided irradiator to be shared with other NIH investigators for preclinical testing of stereotactic body radiation therapy procedures. ♦

Fighting cancer at the cellular level

UT Southwestern researchers recently identified another important factor in the DNA damage response and double-strand break repair. The human gene MOF is now thought to play a critical role in DNA repair due to its several activities, including the acetylation of histone 4.

The picture at right, featured on the cover of the July 2010 (Vol 30, Number 14) issue of *Molecular and Cellular Biology*, shows the depleted acetylation of histone 4 by MOF (top frame), causing the retarded appearance of ionizing radiation-induced foci of phosphorylated H2AX (green). Depletion of another histone acetyltransferase (bottom frame) does not elicit the same response. ♦



Clinical social worker helps patients overcome treatment hurdles

What do you do if you're too sick to drive to your therapy appointment? Or can't afford your medication? Or just feel really depressed?

Cancer poses extreme challenges on patients, both physical and mental. Licensed clinical social worker Dinah Foster works full-time in the Department of Radiation Oncology to help patients manage those challenges that may complicate their treatment.

Getting the help you need

One of the most common problems patients face is just getting to their appointments.

"Radiation treatment takes place on a daily basis, often over a course of several weeks," observes Ms. Foster. "A lot of people have trouble with that, whether they're too sick to drive, elderly, live far away or they don't drive."

Her solution is to partner the patient with community resources or arrange a network of family, friends, neighbors or church members to help make the trips.

Ms. Foster can also:

- Advise patients how to apply for Social Security disability benefits
- Connect patients with basic needs resources such as food and clothing
- Make a referral to a private counselor for counseling

"A lot of people are apprehensive when they first come here about what radiation will do and what they need to know," says Ms. Foster.

"The nurses and I work together to talk with them about it. We use written materials as well as our education room to make sure patients can find what they need, whether it's information about radiation, wigs, support groups or side effects."

Patients are not automatically scheduled with the social worker; however, anyone can request a free consultation at any time during treatment. Nurses and radiation therapists also refer patients to Ms. Foster when they believe someone may need help.

Ask questions

Sometimes patients find it intimidating to talk with their doctors, in which case the clinic's social worker provides another avenue for communication.

"Patients can be hesitant to ask certain questions or they don't want to take up their doctor's time," explains Ms. Foster.

Dinah Foster, LCSW

"I encourage patients to keep a notebook and make sure they're writing things down, whether they're questions for the doctor or questions for me," she continues. "Sometimes when you're going through treatment there's a lot on your mind and it's easy to forget things."

"A large part of my job is knowing what resources are available to our patients," she says. "I tell them, 'bring in your book and we'll go through your questions. If I can't answer them we'll find somebody who can.' " ♦

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