Assistant Professor of Radiation Oncology Raquibul Hannan, M.D., Ph.D., is leading the new i-SABR trials (combining immunotherapy and stereotactic ablative radiotherapy).

UT Southwestern is launching two innovative trials for metastatic prostate and renal cell cancers that will combine either a personalized cancer vaccine or an immuno-stimulatory agent with stereotactic ablative radiotherapy (SABR, also known as SBRT). SABR itself is known to generate a systemic immune response. The new trials will evaluate whether these two approaches can work synergistically to teach the patient’s own body to rid itself of cancer.
Collectively known as the i-SABR trials (immunotherapy + SABR), the studies led by Assistant Professor of Radiation Oncology Raquibul Hannan, M.D., Ph.D., are an effort to capitalize on the fact that tumors treated with radiation remain inside the body, leaving a source of tumor-specific antigens from the dying tumor cells. These dying tumor cells can essentially act as an in-place cancer vaccine, attracting dendritic cells that may notify the body’s immune system to seek out and destroy cancer cell metastasis elsewhere in the body.

The so-called “abscopal effect,” in which radiation delivered to a primary site of cancer results in shrinkage or elimination of cancer in the metastatic sites, is primarily noticed with the high radiation dose levels given in SABR. Radiation delivered to a primary site of cancer results in shrinkage or elimination of cancer in the metastatic sites, which radiation delivered to a primary site of cancer results in shrinkage or elimination of cancer in the metastatic sites.

The systemic part of the treatment—sipuleucel-T, which is for prostate— is also the first and so far only immunotherapy approved by the FDA for any type of cancer.

“There have been multiple phase III randomized clinical trials of sipuleucel-T with adequate follow-up, so we know there is a survival benefit to its use,” Dr. Hannan says. “Our goal is to see if we can make the therapy even more potent by combining it with the immunogenic effects of SABR.”

This spring, UT Southwestern Radiation Oncology, along with colleagues in the Departments of Urology and Medical Oncology in the Simmons Cancer Center, opened a phase II clinical trial combining the prostate cancer vaccine sipuleucel-T with SABR for patients with metastatic, castrate-resistant prostate cancer.

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—Raquibul Hannan, M.D., Ph.D.

Eligible patients may have any number of metastatic lesions; however, a maximum of six lesions will be treated with SABR in the trial. “The lesions that get priority are larger lesions, which we already know are more difficult for a systemic treatment alone to eradicate,” Dr. Hannan explains. “We will also give priority to treat lesions causing pain or symptoms, as well as lesions that could cause debilitation, such as an impending fracture or spinal cord compression.”

After their initial consultation and eligibility verification, patients would first go to an approved blood center to undergo leukapheresis, a process in which white blood cells are harvested. Those cells are sent to Dendreon, the maker of sipuleucel-T (trade name Provenge), which has a proprietary method of incubating a patient’s dendritic cells with a prostate cancer antigen combined with an immunostimulant, creating an autologous cancer vaccine. The patient then returns to Simmons Cancer Center a few days later to receive an infusion of his own cells, which are now trained to be active against the prostate cancer.

The process is repeated twice over five weeks; meanwhile, radiation is delivered in one to three fractions, depending on the tolerability of the site, beginning with the second week of treatment.

“The idea is that while the activated dendritic cells from the vaccine are in circulation, stereotactic radiation therapy will kill cancer cells, making countless additional patient-specific tumor antigens available for cross-presentation and priming of the immune system, leading to a synergistic therapeutic effect between the two treatments,” Dr. Hannan says.

The metastatic renal cancer trial, expected to open later this summer, is also a phase II study combining high-dose interleukin-2 (HD IL-2) with SABR.

This FDA-approved, nonspecific immunostimulant is given as an IV infusion every eight hours for a total of three weeks (including a one-week break) but must be given in an ICU setting because of its toxicity. This cycle is typically repeated once more if patients respond.

Although not an ideal treatment, HD IL-2 “gives the only chance of a cure for metastatic kidney cancer patients, as it results in a durable, long-term response in about seven to nine percent of patients,” Dr. Hannan says. “But that’s not very high, especially compared to its toxicity. Our goal is to increase this response rate by combining it with SABR.”

An important part of both trials will be correlative laboratory studies. “We are going to do extensive studies to explore the specific biological aspects of how SABR interacts with immunotherapy,” says Dr. Hannan, whose earlier laboratory studies have shown that SABR initiates and augments a tumor-specific immune response by altering the tumor microenvironment. “Fully understanding how this process works will enable us to design more effective i-SABR treatment combinations for all cancer patients, not just prostate and kidney.”

Optimized for stereotactic treatments, the Vero linear accelerator at UT Southwestern—the first in North America—is often used to treat metastases.

Dr. Hannan explores the biological basis for SABR’s immune response.
**Endowed chair honors longtime leader**

Professor of Radiation Oncology David Pistenmaa, M.D., Ph.D., was honored with a dinner on March 14 to celebrate the elevation of the endowed position that bears his name. Established in 2005, the David A. Pistenmaa, M.D., Ph.D., Distinguished Professorship in Radiation Oncology is now a university-designated Distinguished Chair with an endowment of $1 million. Dr. Pistenmaa, who chaired the Department of Radiation Oncology from 1996 to 2003, was presented with a chair and scroll at the event by UT Southwestern President Daniel K. Podolsky, M.D. Dr. Pistenmaa graduated from West Point and received his medical degree in 1969 from Stanford Medical School and his Ph.D. in medical physics from the University of California at Berkeley.

He completed an internship in medicine at Cornell University Medical School and then returned to California and Stanford for a three-year residency in radiation therapy. He was invited to join the Stanford faculty in Radiation Oncology and followed that with a stint at the National Cancer Institute (NCI) as chief of the Radiotherapy Development Branch. He led the NCI for private practice and headed the largest radiation oncology private practice group in the Washington, D.C./Virginia area.

Dr. Pistenmaa was recruited to UT Southwestern in 1992 to help form the new Harold C. Simmons Comprehensive Cancer Center. He was named Chair of the Department of Radiation Oncology in 1996 and led the planning and design efforts that resulted in the 2003 opening of the UT Southwestern Moncrief Radiation Oncology Building. Dr. Pistenmaa is a Fellow of the American College of Radiology and he has consistently been on “Best Doctor” lists for Dallas.

Graduates of UT Southwestern’s Radiation Therapy Program (jointly operated by the university’s School of Health Professions and the Department of Radiation Oncology) successfully completed that two-year program, earning either a Bachelor of Science degree or a post-baccalaureate certificate in radiation therapy. Congratulations to all our trainers!

**Radiation oncology professionals complete training**

This spring a new batch of health professionals graduated from each of the department’s specialized radiation oncology programs. Senior medical residents John Anderson, M.D., and Sheena Jain, M.D., have successfully completed four years of residency training in radiation oncology, and are now qualified to seek board certification.

In the Department’s division of medical physics and engineering, medical physics resident Brian Hrycushko, Ph.D., was awarded his diploma for completing the two-year medical physics residency program. And finally, six students in the Radiation Therapist Training Program (jointly operated by the university’s School of Health Professions and the Department of Radiation Oncology) successfully completed that two-year program, earning either a Bachelor of Science degree or a post-baccalaureate certificate in radiation therapy.

Congratulations to all our trainers!

**Superficial voltage system excels at treating skin cancer**

The Department of Radiation Oncology’s new superficial voltage system is geared to precisely treat small areas on the surface of the skin, including skin cancer, cutaneous lymphomas, and keloids, providing more pleasing cosmetic outcomes for patients.

“Just like its name, superficial voltage delivers the maximum dose right at the surface to a depth of about one centimeter, so we are able to limit the dose to the underlying tissue,” says Assistant Professor Susie Chen, M.D.

It’s a treatment that has come full circle in the history of the development of therapeutic radiation devices.

Low-energy superficial voltage (5-200 kilovolts) and orthovoltage (200-500 kilovolts) machines were originally the first radiation therapy devices used to treat all kinds of cancer prior to the invention of linear accelerators and the onset of cobalt-60 units. Orthovoltage and superficial voltage were then relegated to treating superficial tumors.

When electron beam therapy came into use, it supplanted both of these older technologies. But more recently, some have been reconsidering the use of orthovoltage and superficial voltage.

“The margin we treat is much tighter with superficial voltage due to the physics of it,” Dr. Chen says. “This is a very specialized technology for skin that many other centers do not yet have.”

UT Southwestern’s superficial device is expected to be put to use most often in the facial area, where cosmetic results are better due to the system’s limited field size and penetration. The tumor or other target will be outlined on the skin, and the information transferred to a sheet of lead in which a hole is cut out to match that shape. A cylindrical cone, with sizes ranging from 1.5 cm to 15 cm in diameter, is selected to cover the area and direct the radiation.

While it will not replace electron beam therapy, which is still extremely useful for large field sizes, superficial voltage will enable physicians in the Department of Radiation Oncology to choose from the widest range of tools available to best treat patients with superficial lesions of the skin.

**Superficial voltage system**

The new superficial voltage system was installed this spring at the Harold C. Simmons Comprehensive Cancer Center–Radiation Oncology clinic.

Department Chair Hak Choy, M.D. (left), with honoree David Pistenmaa, M.D., Ph.D.

**Cylinders of different sizes shape the size of the radiation beam.**
A phase III trial of accelerated whole brain irradiation (PBI) for early-stage breast cancer

A phase II randomized, double blind, placebo-controlled, vehicle-pressing esophageal adenocarcinoma

A phase III prospective randomized trial of standard versus accelerated hypofractionation plus concurrent radiation therapy and standard androgen deprivation therapy (ADT) with a GnRH agonist vs. dose escalated radiation therapy and enhanced ADT with a GnRH agonist and TAM-700 for men with high-risk prostate cancer

A randomized phase III study of standard or accelerated hypofractionation plus concurrent radiation therapy for locally advanced rectal adenocarcinoma

A phase III trial of accelerated whole brain irradiation (PBI) for early-stage breast cancer

A randomized phase II study of repeat breast radiosurgery/SBRT for localized spine metastasis

A randomized phase III study of image-guided radiation therapy (SIBRT) for localized spine metastasis

A randomized, double-blind, vehicle-controlled pilot study of the efficacy and safety of HuCara™ in the treatment of acute skin changes in patients undergoing external beam radiotherapy for tumors of the breast

A phase I study of CyberKnife® partial breast irradiation (PBI) for early-stage breast cancer

A phase II study of a novel anti-angiogenic agent in combination with bevacizumab and radiation therapy for the treatment of stage II and III rectal adenocarcinoma

A randomized phase III trial of subcutaneous lamivudine and TAK-700 for men with high-risk prostate cancer

A phase I/II study of nab-paclitaxel, carboplatin, and cetuximab with concurrent radiation therapy (IMRT) /- cetuximab for locally-advanced rectal adenocarcinoma

A phase I study of CyberKnife® partial body irradiation for patients with metastatic castrate-resistant prostate cancer (mCRPC)

A phase II study of stereotactic body radiation therapy (SBRT) for patients with metastatic castrate-resistant prostate cancer (mCRPC)

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A phase I study of CyberKnife® partial breast irradiation (PBI) for early-stage breast cancer

A phase II study of repeat breast preserving surgery and 3D-conformal partial breast re-irradiation (PBI) for local recurrence of breast carcinoma

A phase III trial of accelerated whole breast irradiation with hypofractionation plus concurrent versus standard whole breast irradiation plus sequential boost for early-stage breast cancer

A phase II study of repeat breast preserving surgery and 3D-conformal partial breast re-irradiation (PBI) for local recurrence of breast carcinoma

A phase II study of repeat breast irradiation (PBI) for early-stage breast cancer

A randomized phase II trial of stereotactic body radiation therapy (SBRT) for early-stage, centrally located non-small cell lung cancer (NSCLC) in medically inoperable patients

A phase I/II study of nab-paclitaxel, carboplatin, and cetuximab with concurrent radiation therapy (IMRT) /- cetuximab for locally-advanced rectal adenocarcinoma

A randomized phase III study of standard versus accelerated hypofractionated image-guided radiation therapy (SIBRT) in patients with stage II-II non-small cell lung cancer and poor performance status

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A phase III study of subcutaneous lamivudine and TAK-700 for men with high-risk prostate cancer

A randomized phase III study of image-guided radiosurgery/SBRT for localized spine metastasis

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Physicians who would like to make a referral may call the Department’s main clinic number at 214-645-8525 or UT Southwestern’s physician referral line at 214-645-8300 (toll-free 866-645-5455) for adult patients, or 877-445-1234 for pediatric patients.

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