

THE TARGET

DEPARTMENT OF RADIATION ONCOLOGY

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+ Education & Training: The Foundations of Radiation Oncology

Top Story

By Ryan Daugherty & Mary Whitmore

UT Southwestern's Department of Radiation Oncology provides world-class care to approximately 200 patients each day and conducts groundbreaking research in clinical radiation oncology, medical physics, and molecular radiation biology. As an integral part of its mission, the Department also delivers high-quality education programs to train the next generation of medical practitioners and scientists.

“We will make continuous efforts and provide resources to offer vigorous training programs in all aspects of radiation oncology.”

The Department had no formal education or training programs, however, until Hak Choy, M.D., FASTRO, came on board as Chairman in 2003. After only a year under Dr. Choy's leadership, the Department had become the second largest academic radiation oncology department in Texas and was, and still is, recognized across the country for academic excellence.

Dr. Choy had a vision of growing educational and training programs for radiation therapists, medical

dosimetrists, and medical physicists. One of his top priorities was to create a residency training program in the Department's strong academic environment.

Over the past decade and a half, the Department has been committed to providing comprehensive and advanced educational programs and has implemented multi-year accredited training programs, such as the Radiation Oncology Residency Program and the Medical Physics Residency Program. The Department also provides continuing medical education for physicians.

Together, these programs ensure that the research in and clinical practice of radiation oncology will continue to advance in the service of patients with cancer.

Residency Programs

UT Southwestern has a long history of, and commitment to, training residents, with more than 80 accredited residency and fellowship programs currently operating. Affiliation agreements with the teaching hospitals of Parkland Memorial Hospital, UT Southwestern's William P. Clements Jr. University Hospital and Zale Lipshy University Hospital, and Children's Health offer a wide variety of learning

experiences. Many of our residents have received awards and special recognition for their work.

Our residency programs include:

Radiation Oncology Medical Residency

Accredited by the ACGME since 2005, our four-year Radiation Oncology Medical Residency is open to physicians who have completed their first post-graduate year. Led by Michael Folkert, M.D., Ph.D., Assistant Professor of Radiation Oncology and Director of the Medical Residency Program, and Kiran Kumar, M.D., MBA, Assistant Professor and Associate Director of the Medical Residency Program, our residents work with leading experts and use the most advanced technologies and research facilities in the world. Our Radiation Oncology Residency, which currently has 13 residents, has grown significantly over the past five years to become one of the top residencies in the country.

Many factors make medical residency training at UTSW unique. Our faculty's diverse backgrounds expose residents to a wide array of treatment approaches, and the range of radiation delivery systems used in our clinical practice is unmatched. In addition, our residency program provides access to onsite technical training and certification that is usually only available to attending physicians in practice, including:

- Training in SpaceOAR, a procedure where hydrogel is used to create a space between the rectum and the prostate, thereby reducing high-dose radiation to the rectum.
- The CyberKnife Training Program, which provides an overview of clinical logistics using the CyberKnife for full-body radiosurgery.
- The Gamma Knife Training Program, which provides an overall understanding and working knowledge of the technology.

Moreover, all residents receive and actively participate in extensive didactic training, with comprehensive radiation biology and medical physics lectures, simulation training, biostatistics, disease-site specific lectures, and many visiting professors throughout their residency.

In addition to clinical training, residents participate in clinical, biological, or physical science research, resulting in protocol development, national meeting presentations, publications, and competition for societal and foundation

funding. While most residents have 12 months of dedicated, protected research and elective time, we also support the Holman Pathway, a research-intensive track that allows even more research time. Residents have completed extensive laboratory research, developed clinical protocols, completed professional programs (MBA and MPH), served on numerous national committees, and conducted research in Japan through this opportunity.

As part of the Medical Residency Program, former Chief Resident Osama Mohamad, M.D., Ph.D., spent nine months in Chiba, Japan, where he conducted research on carbon ion radiotherapy, a new radiation modality that started in Japan in 1994. There are only a few centers in the world - notably in Japan, Italy, Germany, and China - that are conducting research on heavy ion therapy. While in Japan, Dr. Mohamad looked specifically at the risk of secondary cancer after carbon ion radiotherapy as it compares with the risk after photon radiation and surgery for patients with prostate cancer. The results were published in *The Lancet Oncology* this past March.

UT Southwestern is the first and only center in the U.S. to send a resident to Japan for heavy ion radiotherapy research, and, although the timetable is uncertain, there are plans to bring this research to a few centers in the U.S., including UT Southwestern.

"We are continuing to work on this with a group in Japan," says Dr. Mohamad. "We are conducting a randomized clinical trial for pancreatic cancer where patients are going to be flown to Japan to get treated; the data collected so far using carbon for this serious cancer type are very encouraging."

Yuanyuan "Faith" Zhang, M.D., Ph.D., a third-year medical resident, is a Holman Pathway fellow.

Through this track she is able to have additional research time to study how immunometabolism in tumor microenvironment impacts cancer therapy response. In her research, she uses molecular, biochemical, and metabolomic approaches to characterize tumor responses to radiation modulated by superoxide dismutase mimetic, GC4419 (currently fast-tracked for FDA approval as a normal tissue protector) using head and neck cancer models.

She is co-mentored by Michael Story, Ph.D., Professor and Vice Chair, and Director of the Department's Division of Molecular Radiation Biology and Ralph



DeBerardinis, M.D., Ph.D., Professor and Chief of the Division of Pediatric Genetics and Metabolism.

“Holman’s Pathway is a fantastic opportunity for me to develop key research skills and projects during my time in the residency program,” says Dr. Zhang. “It provides the protected time, mentorship, and resources to successfully transition into a physician-scientist career.”

Radiation Oncology Medical Physics Residency

The Medical Physics Residency, a CAMPEP-accredited, three-year program, is one of the largest in the world of its kind. The program emphasizes clinical excellence and academic career development in radiation oncology physics. The residency, overseen by Paul Medin, Ph.D., Professor of Radiation Oncology and Residency Director, Strahinja Stojadinovic, Ph.D., Associate Professor of Radiation Oncology and Residency Associate Director, and Yang Park, Ph.D., Assistant Professor of Radiation Oncology and Residency Associate Director, integrates two years of full-time clinical training and one year of research in medical physics.

Medical physics residents at UT Southwestern receive a uniquely diverse clinical training with access to state-of-the-art technology and hands-on experience with a full complement of special procedures. Since approximately half of the physics and engineering faculty focus primarily on research and are well funded by the National Institutes of Health, American Cancer Society, Radiological Society of North America, Cancer Prevention & Research Institute of Texas, and various corporations, they can provide residents with invaluable insight.

Postdoctoral Medical Physics Certificate Program

The Postdoctoral Medical Physics Certificate Program, accredited by CAMPEP and led by Jing Wang, Ph.D., Associate Professor of Radiation Oncology and Program Director, offers didactic course prerequisites to enter a CAMPEP-accredited medical physics residency program, including Radiological Physics and Dosimetry, Radiation Protection and Safety, Fundamentals of Imaging in Medicine, Radiation Therapy Physics, Radiobiology, and Anatomy and Physiology. The program offers one or two three credit-hour courses each semester.

“Our goal is to provide our postdoctoral fellows with the basic and applied scientific knowledge that is necessary for further education and research in medical physics and for entry into a medical physics residency – all leading to

a career in clinical medical physics,” says Dr. Wang.

Graduate Programs

Cancer Biology Graduate Program

The Cancer Biology Graduate Program offers training for students interested in pursuing a research career investigating the molecules, mechanisms, and pathways involved in the development and treatment of cancer. Cross-disciplinary collaboration – a hallmark of UT Southwestern’s approach to research – is crucial in cancer biology research because of cancer’s involvement in various biological systems.

Led by Rolf A. Brekken, Ph.D., Professor of Surgery and Deputy Director of the Hamon Center for Therapeutic Oncology Research, and 69 cancer faculty – including several from the Department of Radiation Oncology – the program is funded by three training grants and the State of Texas provides \$300 million per year for scientists in Texas to investigate cancer. This program is highly flexible and allows students to focus on their specific interests with a wide range of choices.

Biomedical Engineering Graduate Program - Medical Physics Track

This program, led by Xun Jia, Ph.D., Associate Professor of Radiation Oncology and Program Director, is focused on the development of cutting-edge imaging and therapeutic tools to improve radiotherapy treatment. Offered to students with undergraduate training in physics, engineering, computer sciences, or related physical sciences who are looking to establish a career in medical physics research or clinical medical physics, the program covers:

- Medical image reconstruction and application in radiotherapy
- Radiotherapy treatment planning and adaptive replanning
- High-performance computing for radiotherapy, such as Monte Carlo radiation transport simulation
- Modeling of organ motion
- Developing advanced imaging and therapeutic approaches
- Modeling radiobiological phenomena and understanding the mechanisms
- Applying AI technologies in radiotherapy
- Coursework in radiological physics, imaging, and anatomy and physiology



- Seminars, journal clubs, and clinical rotations

SBRT Training Program

Created and led by Robert Timmerman, M.D., FASTRO, FACR, Professor and Medical Director, and Dr. Medin, the Department of Radiation Oncology offers a Stereotactic Body Radiation Therapy (SBRT) Training Program, the longest running training program of its kind in the U.S.

This two-day continuing medical education course is designed for radiation oncologists, medical physicists, medical dosimetrists, administrators, and radiation therapists in both large and small centers who are interested in properly implementing SBRT into clinical practice.

“Important therapies are those that are routinely performed at the point of care with efficiency and quality,” says Dr. Timmerman. “We’re eager to share our expertise and experience with this modern treatment that starts to tap the true potential of radiotherapy for curing cancer.”

In this program, oncology professionals learn about the evolution of SBRT, guidelines for conducting proper treatment, billing and compliance, physics, dosimetry, and the unique requirements of SBRT that go beyond conventional radiotherapy and intensity-modulated radiation therapy (IMRT). Also included are clinical

outcomes and treatment patterns in spine, liver, lung, GI, and GU cancers, as well as a description of various treatment platforms in clinical operation.

Gamma Knife Training Program

UT Southwestern’s Gamma Knife Training Program provides a comprehensive understanding of the radiosurgery system for both new and experienced users and is geared toward radiation oncologists, neurosurgeons, neuro-otologists, and medical physicists. The program offers two courses: a four-day new user course and a three-day upgrade course.

The program is led by co-directors Zabi Wardak, M.D., Assistant Professor of Radiation Oncology, Dr. Stojadinovic, and Toral Patel, M.D., Assistant Professor of Neurology and Neurotherapeutics. Dr. Timmerman and Bruce Mickey, M.D., Professor and Vice Chair of Neurosurgery, serve as program advisors.

“The latest model of the Gamma Knife, known as the Icon, has allowed us to treat patients with a frameless approach,” says Dr. Wardak. “This has expanded patient eligibility, allowing patients to benefit from the Gamma Knife’s unique capability to limit radiation to the normal brain, and has offered patients with multiple and/or larger metastases the option to be treated in a more potent, more convenient, and less neurotoxic way. The



course will help train future users of the Gamma Knife with these modern techniques.”

The course is structured to provide training based on the Department’s extensive clinical experience. “The traditional way of training new Gamma Knife users has been a predominantly didactic approach,” says Dr. Stojadinovic. “In contrast, our program is structured for hands-on learning experience by following radiosurgery patients in real time, which is essential for new users.”

The overall course includes hands-on didactic training with both frame-based and frameless radiosurgery of benign and malignant intracranial disorders and comprehensive training on the expanded utilization of the Gamma Knife Icon with frameless radiosurgery, including fractionated, distributed, and staged radiosurgery for benign and malignant intracranial disorders. In this program, participants will be able to:

- Understand principles of frame-based and frameless Gamma Knife radiosurgery
- Review radiosurgery indications, treatment parameters, and outcomes for benign and malignant intracranial disorders
- Gain proficiency in stereotactic frame application, GammaPlan treatment planning software, Icon-specific training with mask-based simulation and treatment, and the physics of Gamma Knife radiosurgery
- Learn about expanded patient eligibility with mask-based workflow for fractionated radiosurgery, distributed radiosurgery for brain metastases, and staged treatments for large arteriovenous malformations

CyberKnife Physician Training Program

UT Southwestern’s CyberKnife Physician Training Program is the world’s first CyberKnife training course not provided by the manufacturer. The program is geared toward radiation oncologists and provides an

overview of the clinical logistics of using the CyberKnife for full-body radiosurgery, including:

- Patient selection, setup, and alignment for different clinical applications
- Fiducial placement and evaluation on treatment console
- Simulation with different stereotactic setups
- Treatment plan evaluation on CyberKnife planning software
- Beam delivery with various tracking technologies, including skull, fiducial marker, spine, lung tumor, and respiratory-synchronized tracking
- Disease subsite-specific instruction given by expert radiation oncologists on stereotactic techniques, clinical applications, and evidence-based clinical lectures

The course, led by program directors Asal Rahimi, M.D., M.S., Associate Professor of Radiation Oncology, and Dr. Park, is designed for physicians to understand the capabilities of the CyberKnife, how best to use its functions in different clinical settings, and how to evaluate and approve treatment plans on the CyberKnife treatment planning system.

“The current manufacturer-provided course lacks experienced physician-lecturers, which could degrade its relevance to actual clinical practice,” says Dr. Park. “Because UT Southwestern is a leader in, and pioneer of, CyberKnife stereotactic treatments, our physician- and medical physicist-led program benefits all new users of the CyberKnife and gives them hands-on training for clinical application.”

SBRT/SAbR Physician Fellowship

Accredited by the Texas Medical Board, the SBRT/SAbR (stereotactic ablative radiotherapy) Physician Fellowship is a one-year training program that begins July 1 and ends on June 30. Led by Fellowship Program Director Dr. Folkert and Dr. Timmerman, the program’s clinical training focuses on applying SBRT to treat malignant and benign tumors of the brain, base of skull, head and neck, lung, spine, liver, pancreas, and prostate with an evidence-based approach.

Goals and learning objectives of the Fellowship are to provide advanced subspecialty training in stereotactic radiation therapy for both intracranial and extracranial stereotactic irradiation and to gain knowledge of the advantages and disadvantages of different radiation

treatment techniques, including external beam, 3D conformal, IMRT, and stereotactic radiotherapy and radiosurgery. The advantages of the Fellowship include:

- Multiple active protocols that provide prospective application of SABR to new disease sites, in combination with systemic therapies and immunotherapy
- Multi-vendor sites: both Elekta and Varian, as well as Gamma Knife, CyberKnife, and GammaPod
- Incorporation of SABR into all disease site teams
- The opportunity to complete both the CyberKnife and Gamma Knife training courses, as well as the potential to serve as an instructor in those courses during the latter half of the Fellowship

“Our SABR Fellowship is unique because of the incredibly diverse applications of the technique to practically every disease site and stage, as well as the range of delivery systems we use every day,” says Dr. Folkert.

Affiliation agreements with multiple teaching hospitals offer a wide variety of learning experiences.

Observerships

Our Department also offers two new one-month observerships that allow physicians and physicists to observe and learn about the various aspects of patient care under the supervision of sponsoring faculty.

Our Clinical Observership allows exposure to several treatment techniques, including:

- SBRT/SABR treatment – Observers are exposed to treatment planning, contouring, positioning, implementing, and observing malignant and benign tumors.
- HDR and LDR brachytherapy – Observers are exposed to intraoperative and outpatient brachytherapy procedures.
- Gamma Knife and CyberKnife radiosurgery – Observers are immersed in the patient set-up, treatment planning, simulation, and other aspects of both Gamma Knife and CyberKnife radiosurgery systems.

Our Medical Physicist Observership provides observers with many different educational opportunities, including exposure to state-of-the-art equipment such as GammaPod, Gamma Knife Icon, various Varian linear accelerators, and CyberKnife.

UT Southwestern Radiation Therapy Program

The Master of Radiation Therapy Program is the only program in the Southwest located at a major academic medical center that grants a master’s degree. It combines academic and clinical experience for a comprehensive, well-rounded education and provides world-class training that prepares radiation therapists for a career in high-tech cancer treatment.

There are two tracks in the program. The main track provides didactic and clinical education that meets standards for accreditation by the Joint Review Committee on Education in Radiologic Technology. Upon completion of this program graduates will be eligible to sit for the American Registry of Radiologic Technologists examination.

The second track is available for individuals who are already practicing in the health care setting as registered radiation therapists. Students in both tracks will select among several types of research options to meet the degree’s research requirement.



Upon completion of the six-semester program, students will have the skills and experience to simulate patients for treatment and administer treatment to adult and pediatric patients, perform dosimetry calculations, fabricate beam modification devices, observe brachytherapy procedures, perform total body irradiation with electrons and photons, and use various image-guided modalities. Students will also gain experience with key treatment technologies, such as the Gamma Knife ICON, CyberKnife M6, Varian VitalBeam and TrueBeam, Elekta Versa, Active Breathing Coordinator (ABC), and 4D CT with bellows.

For more information about our programs and courses, visit www.utsouthwestern.edu/education/medical-school/departments/radiation-oncology/education-training/.



A View of Cancer from Both Sides

PATIENT STORY

By Ryan Daugherty

Rob Tenery, M.D., 76, of Waxahachie, Texas, has devoted his life to helping others – a trait that runs in the family.

The son and grandson of general surgeons, “Robbie” first started making rounds with his father at the local hospital when he was 5 years old and began working in the laboratory when he was 9. Just three years later, he began helping take X-rays.

“Those were my summer jobs; I was always involved in medicine one way or the other,” he says. “I can’t be more thankful for the influence my father and grandfather had on me.”

Dr. Tenery attended medical school at the University of Texas Medical Branch at Galveston, which led him to UT Southwestern Medical Center, where he completed his internship at Parkland Memorial Hospital. He returned to UT Southwestern in 1974 and completed his residency in ophthalmology.

Dr. Tenery has practiced as an ophthalmologist at Medical City Dallas Hospital for 45 years; during that time, he also taught at UT Southwestern as a clinical professor.

In 2009 things suddenly changed when Dr. Tenery found himself in the role of the patient. During preparation for a mitral valve repair, a chest X-ray revealed a spot on his lung. In 2011, he was diagnosed with epithelial growth factor receptor-positive lung cancer and underwent surgery to have the upper lobe of his left lung removed.

Two years later, a biopsy revealed that cancer had returned in his rib. His doctor referred him to David Gerber, M.D., Professor of Internal Medicine at UT Southwestern. Dr. Gerber told Dr. Tenery that his chest cancer was an uncommon type that was thought to have a genetic component, and he started treating Dr. Tenery with erlotinib (Tarceva),

an oral chemotherapy drug. Tarceva controlled the disease for another two-and-a-half years.

“I felt that Dr. Gerber was not only going to take care of me, but that he and his staff genuinely cared about me, too,” says Dr. Tenery. “I can’t begin to tell you how much of a difference that made.”

In October 2017, a PET scan revealed four metastatic lesions: two on his ribs, one on his scapula, and one on his cervical spine. A thoracic multidisciplinary tumor board discussed his case and recommended that he be evaluated by Hak Choy, M.D., FASTRO, Professor and Chairman of Radiation Oncology.

Very few physicians have Dr. Choy’s expertise in treating lung cancer with chemotactic-radiation therapy. Under his leadership, UT Southwestern has quickly become one of the leading institutions in the country in treating patients with advanced radiation oncology technology and techniques, including SBRT. These innovations improve the quality of care for patients like Dr. Tenery because planning margins can be reduced and surrounding healthy tissues can be spared even as the treatment dose is escalated.

“When I met with Dr. Choy, he gave me hope,” says Dr. Tenery. “He said, ‘I think we can get it.’ That was all I needed to hear from such a knowledgeable and optimistic physician.”

In that initial meeting with Dr. Choy, it was decided that the four lesions would be treated with 13 sessions of palliative radiation over a three-week period.

Dr. Tenery responded well to the radiation treatments and to a change from oral to IV chemotherapy. However, in November of 2018,



a scan showed a new lesion on his right adrenal gland. To treat this new tumor, he received five more radiation treatments over a two-week period, which he tolerated extremely well.

Moving forward, Dr. Tenery will continue to see Dr. Gerber monthly for chemotherapy, and Dr. Choy will treat future metastatic lesions as they arise. Thanks to innovations in radiation oncology technology and techniques, these lesions can be targeted precisely with high doses of radiation, while surrounding tissues are spared. Also, advances in technology and techniques will improve patients' quality of life.

"With modern technology and treatments available, we can improve quality of life and offer patients hope," says Dr. Choy. "It's incredible to see that Dr. Tenery is doing well 10 years after his diagnosis. This is a testament to our Department's success and the field's innovations."

Although the road hasn't always been easy, Dr.

Tenery has maintained a positive outlook along the way. The aspects of his life that have helped the most with his cancer treatment are his faith in God, the prayers of friends and prayer groups, and the support of his family.

"The process has been easier knowing that prayers are heard, having my fears pushed aside, and knowing His hand is always there for me," he says. "And, of course, Janet, my wife of 54 years, as well as my family, and especially our grandson, Mason, have supported and encouraged me."

Dr. Tenery also hasn't lost passion for his work. He explains that treating patients, as well as being one, brings him to a closer understanding that we are all in this battle together, alongside God and the good doctors at UT Southwestern.

"I don't know that I can say I'm a better doctor, but fighting cancer has made me a much more compassionate one," he says.

+ NEW FACULTY

Department News

MOLECULAR RADIATION BIOLOGY



Medhat Elhalawany, Ph.D.
Instructor

Dr. Elhalawany received his Ph.D. in molecular and cellular biology from Nagoya University in Japan. During his postdoctoral training at Cluster in Biomedicine in Italy, University of British Columbia, Calgary University, and Cancer Biology Institute in Egypt, he worked with research groups that focused on molecular aspects of problems in biomedical sciences. He will work in Dr. Aguilera's lab researching the tumor biology of pancreatic cancer. He will also focus on secondary data analyses of publicly available data to understand the similarities and differences across diverse tumor types and to explore the effect of genomics variants on protein functions.



Deepak Gurbani, Ph.D.
Instructor

Dr. Gurbani received his bachelor's and master's degrees in biology from Kanpur University in India and his Ph.D. in biotechnology from Council of Scientific & Industrial Research Institute of Toxicology Research, Lucknow and Jamia Hamdard University in New Delhi, India. During his postdoctoral training at UT Southwestern Medical Center, he led experimental efforts toward the development of several reversible and irreversible inhibitors for different cancer-associated kinases serving as useful pharmacological probes. With his expertise in X-ray crystallography, biochemistry, cancer biology, and structure-guided

drug development, Dr. Gurbani continues to lead compounds targeting other cancer-associated kinases for development of new targeted cancer therapies.



Zhaogang Yang, Ph.D.
Assistant Professor

Dr. Yang received his bachelor's degree in pharmaceutical sciences and master's degree in pharmaceuticals from Peking University in China. He also received a master's degree in pharmacology and a Ph.D. in pharmaceutical sciences from Ohio State University. He completed his postdoctoral research training at both the Mayo Clinic at Rochester and Ohio State University. Dr. Yang's research interests focus on developing novel nano-platform for cancer diagnosis and therapy.

PHYSICS



Tom Banks, Ph.D.
Assistant Professor

Dr. Banks received his bachelor's degree in physics from Cornell University and his Ph.D. in nuclear physics from UC Berkeley, where he also worked as a postdoc and an assistant researcher in neutrino physics. In 2015 he transitioned to medical physics and spent a year studying at the University of Victoria, BC, followed by a two-year residency in therapeutic medical physics at Stanford University. Dr. Banks' research interests include developing novel clinical techniques in partnership with physicians, and applying new technologies to improve clinical operations.

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GRANTS & PARTNERSHIPS

Department News

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Research Highlights

Engineering New Approaches to Immune Suppression

By Jonathan Feinberg, Ph.D.

Tumor cells' ability to evade detection and eradication by the body's innate immune system is one of the hallmarks of cancer. Tumor cells accomplish this, in part, by suppressing phagocytosis, the process by which certain immune cells engulf foreign substances and present them to other immune cells to initiate a systemic immune response throughout the body. Discovering the mechanisms by which tumor cells suppress phagocytosis will help researchers to develop new therapies that can activate the immune system to fight cancer.

Wen Jiang, M.D., Ph.D., Assistant Professor of Radiation Oncology, approaches the problem of phagocytosis suppression from a unique perspective that bridges medicine and engineering. Before attending medical school at Stanford University, Dr. Jiang earned a Ph.D. in bioengineering at the University of Toronto, where he developed nanostructures and nanomaterials for cancer diagnostics and therapy. His dual expertise allows him to investigate the biological mechanisms of phagocytosis suppression and develop the technology to target those mechanisms.

Supported by a \$2 million First-Time Tenure Track Faculty Recruitment Award from the Cancer Prevention & Research Institute of Texas (CPRIT) and a \$250,000 Science and Technology Acquisition and Retention (STAR) Award from the University of Texas System, Dr. Jiang's lab is pursuing the biological and technological sides of the problem simultaneously. On the biology side, they are studying different inhibitory pathways in tumor cells that may suppress phagocytosis or other innate immune responses in the body. On the technology side, they are designing different constructs using either nanomaterials or engineered biological materials to target these inhibitory pathways. Their goal is to develop a therapeutic agent that can counter the tumor's immune suppressive mechanisms at the molecular level, thus leaving tumor cells vulnerable to phagocytosis and other innate immune responses.

Using nanomaterials allows great versatility in designing new therapeutics. Whereas engineering biological, protein-based molecules entails a lengthy, sequential process that has to be restarted from the beginning if changes are needed, engineering nanomaterials is more

of a "plug and play" process, where components can be swapped out on the fly. "It's like a Lego system," Dr. Jiang says. This means that these constructs can be developed and tested quickly and efficiently.

It also means that these constructs can be easily adapted to treat a variety of cancers. "The technology we develop is not targeted for one specific cancer type," Dr. Jiang explains. "A lot of the targets that we're interested in are universally expressed in almost all solid tumors." Under their current CPRIT grant, Dr. Jiang's lab is developing a nanomaterial-based construct that targets the HER2 protein to engage the immune system to fight metastatic breast cancer, but they are already working to adapt their constructs to treat glioblastoma, an aggressive brain cancer that expresses the EGFR protein, a "cousin" of HER2.

"Ultimately, our goal is to have a core substrate or infrastructure ready," Dr. Jiang says. "That would allow us to tailor or modify the design a little bit and then use it for different cancers."

Dr. Jiang's hybrid training as both bioengineer and clinical radiation oncologist facilitates a streamlined pipeline that can rapidly translate new therapeutics from the lab to the clinic. His group is currently engineering new synthetics using nanomaterials and testing them in mouse models as a proof of principle. Once they have shown that the new construct achieves the desired results, they will collaborate with industry partners to produce protein-based biological molecules that can be tested in humans in phase I clinical trials.

Dr. Jiang's dual expertise also facilitates translation in the other direction, as his clinical practice prompts him to engineer solutions to actual patient needs, rather than technical problems that have limited clinical relevance. "This difference in philosophy between nanoscientists and clinicians highlights their distinct approaches to tackling similar clinical scenarios: product-driven versus patient-centered," Dr. Jiang wrote in *Nature Nanotechnology* (August 2016). "Being trained as a scientist and as a physician has helped me bridge this divide."

In bridging the divide and combining the perspectives of clinician, biologist, and engineer, Dr. Jiang seeks to forge a new patient-centered nanotechnology that can advance the frontier of cancer treatment.

New Kidney Cancer Applications for Stereotactic Body Radiation Therapy

By Jonathan Feinberg, Ph.D.

The Department of Radiation Oncology at UT Southwestern has long been a pioneer in the research and clinical practice of stereotactic body radiation therapy, or SBRT. This modern form of radiation therapy uses innovative technology to deliver more powerful, more precise radiation doses in fewer sessions than conventional radiation therapy, thus minimizing the burden of treatment on patients and improving their quality of life.

Raquibul Hannan, M.D., Ph.D., Associate Professor of Radiation Oncology, is advancing the research and practice of SBRT for renal cell carcinoma (RCC), the most common type of kidney cancer. Historically, RCC has been considered resistant to conventional radiation therapy. However, increasing evidence suggests that delivering higher radiation doses in fewer sessions with SBRT may be effective against both localized and metastatic RCC. Building upon this research, Dr. Hannan and his group are extending SBRT's applications in RCC by investigating SBRT's potential to treat other conditions associated with this cancer.

RCC with inferior vena cava tumor thrombus

RCC is sometimes accompanied by an inferior vena cava tumor thrombus (IVC-TT), a rare but dangerous complication in which the tumor invades the venous system and extends toward the heart. A tumor thrombus is considered a source for metastasis because it is volatile and blood is constantly flowing through it. Currently, surgical removal is the only curative treatment for this condition, but many patients are poor candidates for surgery because of their age or other health conditions. Surgery can also bring additional risks and complications in cases where the tumor thrombus extends above the hepatic veins. For such patients, other treatment options are needed.

SBRT may provide a good alternative. Dr. Hannan's group recently published a paper in *Kidney Cancer* updating

their previously reported experience using SBRT to treat two patients with RCC IVC-TT, in one case substituting SBRT for surgery, and in the other case treating disease that had recurred after surgery. In both of these settings, Dr. Hannan's group found that SBRT to IVC-TT is safe and feasible, and it may be considered a viable treatment option for certain patients.

Dr. Hannan is also leading a phase II clinical trial (NCT02473536) that seeks to reduce systemic recurrence by killing off the tumor thrombus before surgery. "Surgery, which is the only curative treatment available for IVC-TT, can itself induce shedding of the thrombus due to its volatile nature. The idea is that SBRT prior to surgery will kill off these cells so they will no longer be able to metastasize at distant sites," explains Dr. Hannan.

Oligometastatic RCC

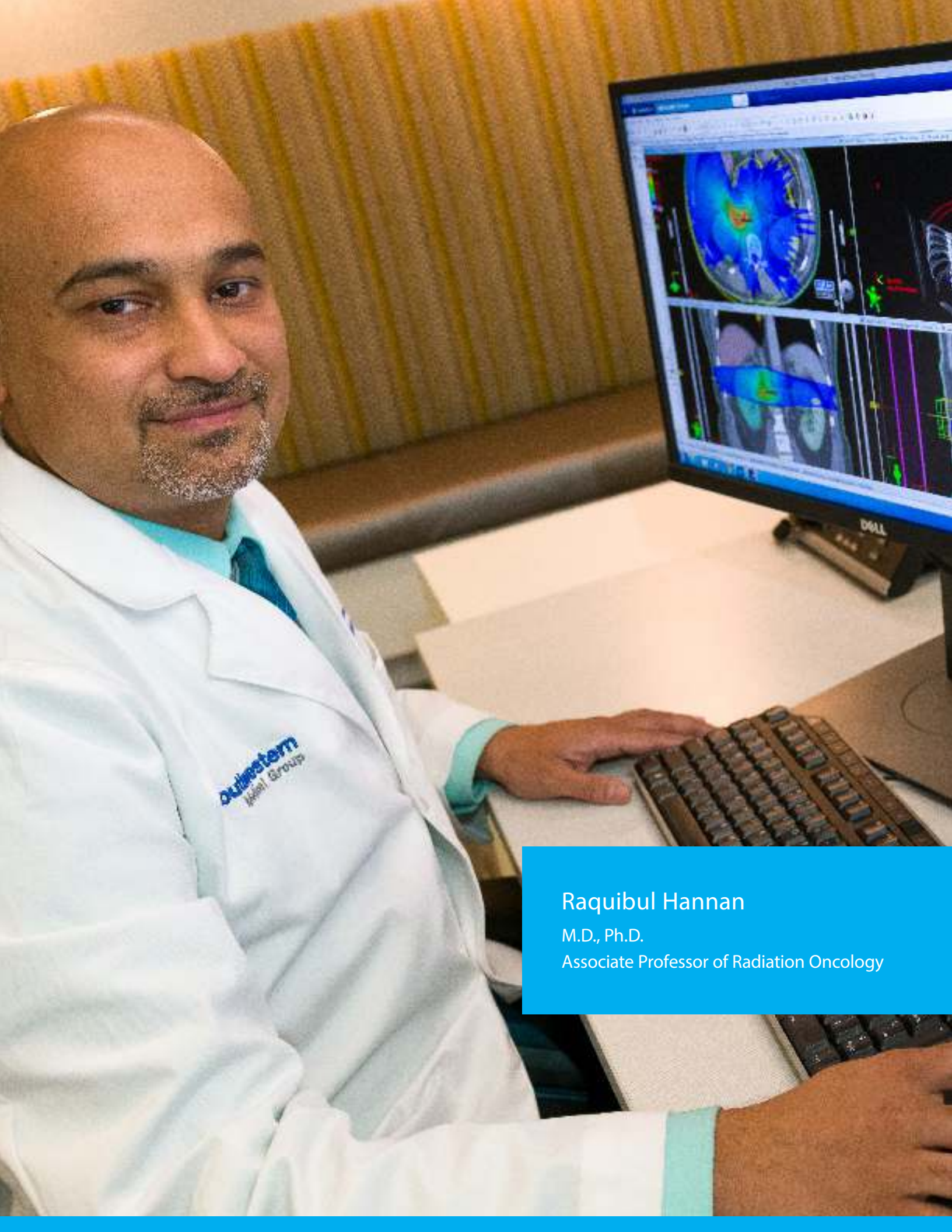
Dr. Hannan is also investigating SBRT's potential to treat oligometastatic RCC, or RCC with only a small number of metastatic tumors. Systemic therapy, such as targeted therapy or immunotherapy, has long been the standard of care for metastatic RCC, but recent evidence indicates that patients with only a few metastases may be treated effectively by local therapy, such as surgery or radiation therapy, to all sites of disease. While surgical removal of these metastases has shown promise, SBRT may offer a non-invasive option that would preserve patients' quality of life while treating their disease at multiple sites.

In a report just submitted to the *International Journal of Radiation Oncology, Biology, Physics*, Dr. Hannan's group retrospectively reviewed 49 patients treated with SBRT for oligometastatic RCC at UT Southwestern from 2007 to 2017, and they found that SBRT effectively controlled the disease without introducing serious side effects. SBRT was curative for many of the patients and, for others, it successfully delayed the start of systemic therapy by over a year, thus preserving the patients' quality of life during this time. These findings provided the rationale to study SBRT for oligometastatic RCC prospectively in a clinical trial currently underway at UT Southwestern (NCT02956798).

"To evaluate this application of SBRT for oligometastatic RCC, we designed a phase II trial to assess whether we can safely delay the start of systemic therapy for metastatic RCC patients," adds Dr. Hannan, principal investigator of the trial.

Oligo-progressive metastatic RCC

Sometimes during systemic therapy for metastatic RCC, one to three sites of metastasis resist therapy while others respond or decrease in size. The current practice



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is to abandon the systemic therapy that was otherwise working and tolerated in favor of a different systemic therapy, which may be less effective and may introduce unwanted side effects.

Investigators at UT Southwestern are proposing a new strategy: continue the systemic therapy that is working, and treat the few resistant metastatic sites with SBRT. This benefits patients by preserving subsequent lines of systemic therapy for the future. Dr. Hannan's team recently reviewed their experience of treating 44 such patients and showed that, on average, this strategy can increase the duration of the systemic therapy by over eight months. Dr. Hannan is currently leading a phase II clinical trial (NCT03696277) to study this strategy prospectively.

"We have designed a phase II clinical trial to evaluate if we can extend the ongoing systemic therapy by over six months by eliminating the resistant metastatic sites using SBRT in patients where only a few sites are progressing on systemic therapy," says Dr. Hannan, principal investigator of eight such innovative investigator initiated clinical trials in the Department of Radiation Oncology.

Dr. Hannan's studies show a commitment to patient-centered innovation that makes UT Southwestern an attractive choice for patients seeking treatment for cancer.

PHYSICS

Novel PET/CT Imaging Technologies in Radiation Therapy

By Damiana Chiavolini, Ph.D.

Historically used to diagnose disease and to evaluate treatment, positron emission tomography-computed tomography (PET/CT) is becoming an essential tool in imaging various types of cancers to facilitate different phases of radiation therapy. PET/CT reveals biological and functional information of tumors as well as anatomical information provided by more standard imaging techniques like CT alone and magnetic resonance. Therefore, through PET/CT-guided imaging, radiation beams will be planned and delivered more precisely, and healthy organs will be spared more effectively, contributing to advancing personalized care for patients with cancer.

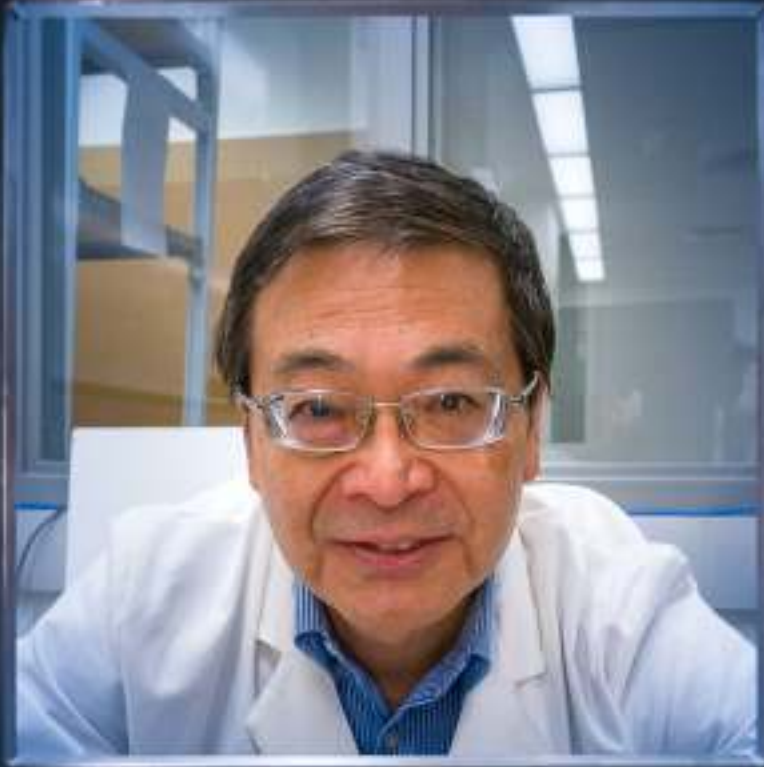
Yiping Shao, Ph.D., Professor of Radiation Oncology, and

his team research how to apply new PET/CT imaging strategies to successfully guide many aspects of radiation therapy. "It is essential to deliver radiation to a tumor with the correct dose level and distribution," says Dr. Shao. "PET/CT provides biological, functional, and molecular information on tumors that standard imaging cannot, and could be included in the multi-step treatment planning process to ensure that radiation is delivered more precisely and effectively," he adds.

Dr. Shao is interested in studying PET/CT imaging applications both pre-clinically and clinically. His lab is currently developing a small animal PET system that will be integrated into an existing CT image-guided small animal radiation therapy system to allow pre-clinical radiation oncology studies and to improve translational research in the field overall. "We're the first group to propose such an advanced animal PET system for radiation therapy research. We have to overcome technical and logistic hurdles, but we're excited to improve PET imaging performance through an innovative design that will enable us and other research groups to study combined functional and anatomical image-guided radiation therapy at a translational research level," says Dr. Shao. Overall, this new system will lead to clinical applications of a new image-guided radiation treatment system that is based on tumor biological and molecular function and status.

In February 2018, Dr. Shao and Weiguo Lu, Ph.D., Associate Professor of Radiation Oncology, were awarded \$2 million in NIH funds to develop a new, clinically practical "on-line" PET imaging system that will better verify particle beam range and optimize radiation delivery. This system is being specifically designed to improve particle therapy, a form of radiation that uses protons, neutrons, or positive ions to treat cancer. Although this modality presents advantages over traditional photon therapies, such as higher precision and lower toxicity, its intrinsic uncertainty, or margin of error, in beam range may lead to severe damage to healthy organs near the tumor that needs to be treated with high-dose radiation. Therefore, verifying the beam range for targeting a tumor precisely is essential to successfully deliver particle therapy. The best way to attain this is to develop an "on-line" imaging system that can measure the particle beams while the patient is on the treatment couch waiting to receive radiation, as opposed to "off-line" imaging, which measures the beams only after treatment is completed. "Our system will allow clinicians to either confirm or modify the therapeutic dose to be delivered to an individual patient before and during treatment, improving treatment accuracy and enhancing clinical outcomes for patients with cancer," says Dr. Shao.

Through these pre-clinical and clinical research studies, advanced PET/CT may become fully integrated in everyday clinical practice, improving radiation treatment planning and delivery procedures.



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INTERVIEWS

By Damiana Chiavolini, Ph.D.

Aurelie Garant, M.D.

Aurelie Garant, M.D., Assistant Professor of Radiation Oncology, completed her medical degree at the Université Laval in Quebec City, Canada in 2012 after attending the Health Sciences program at the Jean-de-Brébeuf Jesuit College in Montreal. She earned her specialized residency in Radiation Oncology at McGill University in Montreal in 2017 and completed a fellowship in gastrointestinal and hepatobiliary radiation oncology at the Mayo Clinic in Rochester, Minnesota in 2018. She currently treats patients with genitourinary cancer and researches ways to use stereotactic ablative radiotherapy (SABR) in patients with pelvic, prostate, and renal cancers. In January 2019, Dr. Garant talked about her work in the clinic, her research interests, and her views on succeeding as a woman in radiation oncology.

Q. How did you get inspired to start a career in medicine and radiation oncology?

AG: Medicine and science have interested me since an early age. My mother is a radiation oncologist and my father was an electrical engineer by training; their example drove me closer and closer to pursue a career in science. While I was in medical school, I became interested in diagnostic radiology and, later, interventional radiology. However, these specialties did not involve as much contact and follow-up with patients as I had hoped. In contrast, radiation oncology seemed to blend meaningful patient interaction with evidence-based practice, so it was quite natural for me to enter the field. My mother's career and several family members receiving cancer treatment further influenced my decision. One of my relatives beat cancer three times, and he was also of great inspiration for me to become a radiation oncologist.

Q. What do you enjoy most about your current activities?

AG: I am excited to be part of the Department's mission to provide the best patient care through highly advanced radiation therapy technology. I like the efficiency of the clinic and referral system, and I appreciate the inspired building design that promotes a great experience for patients. Also, our Department and the Simmons Cancer Center offer excellent resources, such as equipment to perform SABR, brachytherapy, intraoperative radiotherapy,

and much untapped potential for research growth. I am very excited to collaborate with translational scientists and clinicians in a number of projects.

Q. What are your primary research interests?

AG: From a research standpoint, I am interested in patient-reported outcomes for different radiation treatment modalities. We need to pay special attention to patient opinion and feedback so that we can truly improve cancer care, life quality, and safety. I believe these will be more meaningful than the traditionally defined toxicity terminology, especially in an era where we are offering abbreviated courses of high-dose radiotherapy, which is in major contrast with classical teachings in our specialty. I became passionate about patient-reported outcomes during my fellowship in gastrointestinal and hepatobiliary radiation oncology at the Mayo Clinic. I gave an oral presentation of my results that specifically addressed patients with esophageal cancer at the 2018 ASTRO conference. Additionally, I am interested in various concepts such as stage migration as well as radiotherapy escalation and de-escalation. I believe we will see major shifts in staging classifications for various illnesses in the years to come, and the role of radiation will evolve tremendously as dynamic imaging flourishes. In the Department, I currently work with Dr. Raquibul Hannan and Dr. Neil Desai on combining radiation and immunotherapy checkpoint inhibitors to treat genitourinary malignancies. We are also testing dose-painted SABR for selected patients with prostate cancer.

Q. What are you most proud of?

AG: I was recently selected to participate in UT Southwestern's 2019 Leadership Emerging in Academic Departments (LEAD) Program for junior faculty physicians and scientists. This is a unique opportunity for me to advance my team-building, communication, and diversity-embracing skills, and also to develop relationships with various mentors. I am also excited to share my results on organ preservation in rectal cancer by giving a talk at the 2019 ESTRO conference in Milan, Italy.

Q. Have you experienced, as a woman, any difficulties in your current field?

AG: During medical school in Canada, I never saw gender inequality as an issue. In fact, 77 percent of the students in my class were women! Things were certainly different when I transitioned to radiation oncology, a typically male-dominated field. Even here at UT Southwestern, the genitourinary disease-oriented team I am currently part of only includes me and another woman. It's been a great experience so far, but I would still like to see more women enter and work in radiation oncology.



UT Southwestern
Medical Group

Aurelie Garant

M.D.

Assistant Professor of Radiation Oncology

Q. What advice do you have for young women wishing to pursue your same career?

AG: I believe women shouldn't be afraid to pursue radiation oncology and to bring new ideas to advance the field, clinically, scientifically, and technologically. This is a specialty with much unexplored territory and endless possibilities to make a difference. Radiation oncology offers a lot of latitude in terms of combining noninvasive and invasive techniques into clinical practice. Also, the opportunities for interdisciplinary collaborations with other specialties, such as surgery, medical oncology, and radiology, are numerous, exciting, and rewarding. Young women should see this as a chance to pave the way for themselves but also for other women in the future.

Nina Niu Sanford, M.D.

Nina Niu Sanford, M.D., Assistant Professor of Radiation Oncology, earned her medical degree from Harvard Medical School in 2013 and completed her residency at the Harvard Radiation Oncology Program in 2018. In our Department, she treats patients with gastrointestinal malignancies and she studies racial disparities in health care access and pancreatic cancer outcomes using large databases. In this interview from January 2019, Dr. Sanford talks about her motivation to start a clinical career in radiation oncology and also about her inspiration to study health disparities in cancer care.

Q. How did you get inspired to start a career in medicine and radiation oncology?

NS: I really looked up to my mom, who became a primary care physician while I was in middle school here in the U.S. We emigrated from Beijing, China when I was 3, and she worked hard to retrain as a physician in the U.S, which ultimately helped her integrate into the American society as a health care professional. My mom's example and also my interest in science and math inspired me to pursue a medical degree. Later on, one of my mentors from medical school, a radiation oncologist, encouraged me to consider this specialty. I quickly realized this would be a good fit for me, in part because I liked the idea of practicing evidence-based medicine. Also, my dad, a professionally trained artist and currently an elementary and middle school art teacher, taught me how to think creatively and three-dimensionally, which also applies to our field.

Q. How did you become interested in health disparities?

NS: As an immigrant who grew up in a modest two-

family home in a wealthy suburb outside of Boston, I have been naturally exposed to and, therefore, interested in understanding the factors that contribute to inequalities, both social and health-related. Also, having pursued a BA in Spanish and pre-medical studies, I had the opportunity to study abroad in Spain and Nicaragua, and to learn more about the differences in access to health care in other countries. During my residency, I started to think that studying disparities in the context of race and ethnicity would be especially relevant in cancer care.

Q. What do you like most about your job?

NS: I enjoy the combination of seeing patients in the clinic and pursuing research. I focus on treating gastrointestinal cancers because they are especially diverse and require a team approach that brings together radiation oncologists, medical oncologists, and surgeons. I like how this collaborative spirit leads us to provide the best care to a highly diverse patient population here at UT Southwestern. I feel extremely fortunate to be working alongside an amazing talented gastrointestinal oncology team within the Department, including Dr. Michael Folkert, Dr. Todd Aguilera, and Cindy Tonkovich, RN, who have all offered me a tremendous amount of guidance, wisdom, and support as I embark on my career as a new attending. Also, disparities in gastrointestinal cancer are less well-studied than those in breast and prostate cancer, for example, so there seems to be a real need and opportunity to advance this area of study. In one of my projects, I have studied the socioeconomic disparities in adjuvant chemotherapy for resected pancreatic cancer through an observational large database study. In the near future, I hope to have the opportunity to study these issues prospectively.

Q. Have you experienced, as a woman, any difficulties in entering a scientific/medical environment?

NS: Although I've mostly had positive experiences so far in my career, I have noticed that outspoken women are often labeled as aggressive and emotional. In contrast, this trait appears to be accepted in men, who are instead perceived as natural leaders.

Q. What advice do you have for young women wishing to pursue your same career?

I strongly encourage young women to pursue this career path if they are passionate about it. There is much women can do to help patients with cancer and also to advance research in radiation oncology. The one piece of advice I would give would be to find mentors whose lives you aspire to, both professionally and personally. Ideally, this would be a female mentor, but I've had several outstanding male mentors as well!



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Nina Niu Sanford

M.D.

Assistant Professor of Radiation Oncology



DISEASE-ORIENTED TEAM FACULTY

Our Team

BREAST



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Associate Professor and Director of Clinical
Research
Trained: University of Virginia



Prasanna Alluri, M.D., Ph.D.

Radiation Oncologist
Assistant Professor
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Nathan Kim, M.D., Ph.D.

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Associate Professor
Trained: Vanderbilt University Medical Center



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Trained: Shands Hospital at the University
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Molecular Radiation Biologist
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Molecular Radiation Biologist
Associate Professor
Trained: Columbia University



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Nurse Practitioner
Trained: Texas Woman's University

CENTRAL NERVOUS SYSTEM



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Nurse Practitioner
Trained: Texas Woman's University

GASTROINTESTINAL



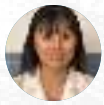
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Todd Aguilera, M.D., Ph.D.

Radiation Oncologist
Assistant Professor
Trained: UC San Diego School of Medicine



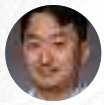
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Trained: Interservice Physician Assistant
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Trained: Albert Einstein College of Medicine



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Radiation Oncologist
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Awarded the Dedman Family Scholar in Clinical Care
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Assistant Professor
Trained: McGill University



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Molecular Radiation Biologist
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Assistant Professor
Trained: SUNY at Stony Brook



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Assistant Professor
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LYMPHOMA

LUNG



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Chairman, Professor
Holder of the Nancy B. & Jake L. Hamon
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Trained: Stanford University



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Matthew Strunk, PA-C

Physician Assistant

Trained: Interservice Physician Assistant Program (IPAP)



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Trained: Memorial Sloan Kettering Cancer Center



Zabi Wardak, M.D.

Radiation Oncologist

Assistant Professor

Trained: UT Southwestern Medical Center



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Physicist

Assistant Professor

Trained: University of Texas Health Science Center at Houston



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Physicist

Assistant Professor

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PEDIATRICS



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Radiation Oncologist

Assistant Professor and Associate Director of Medical Residency Program

Trained: Stanford University

* Denotes team lead

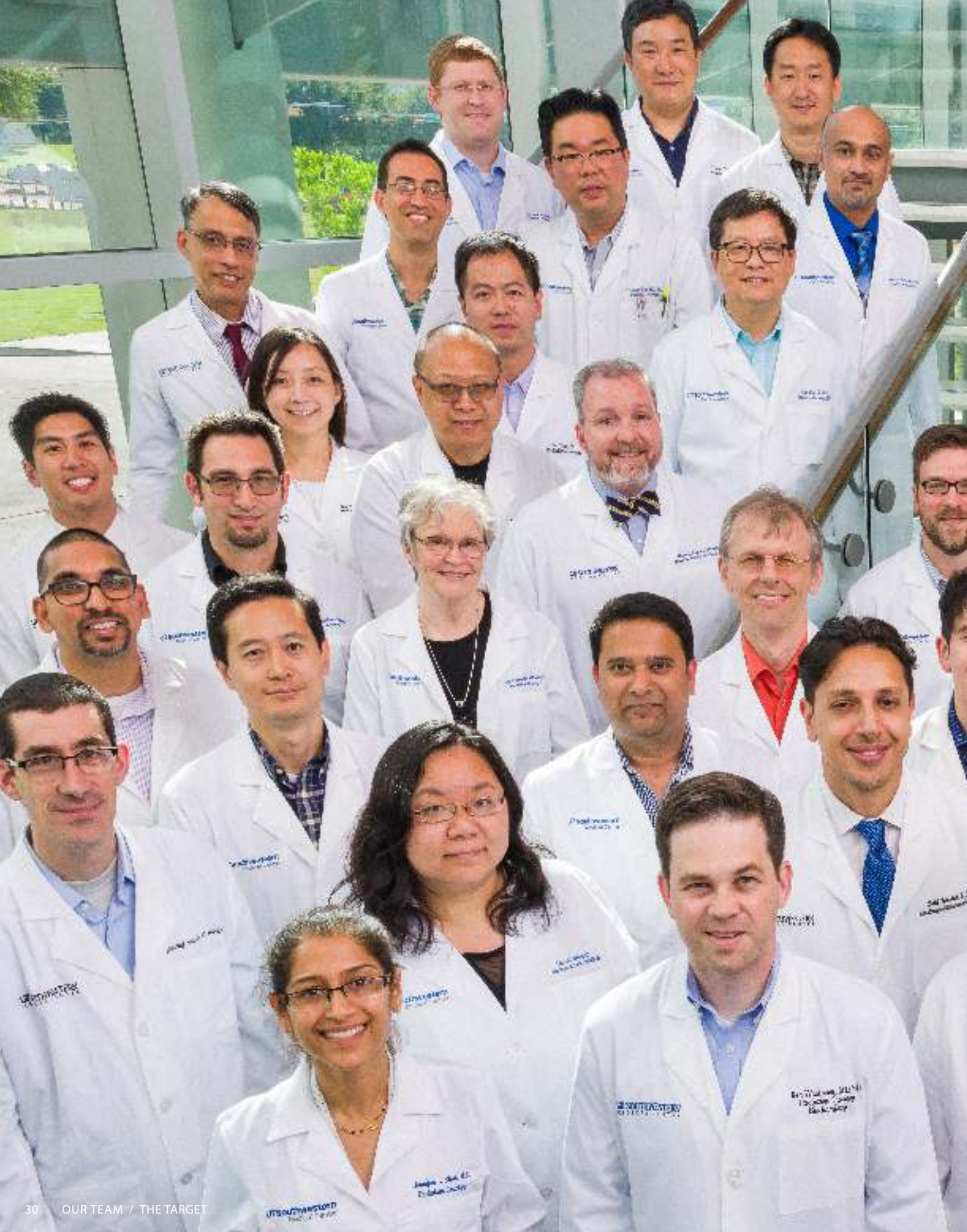


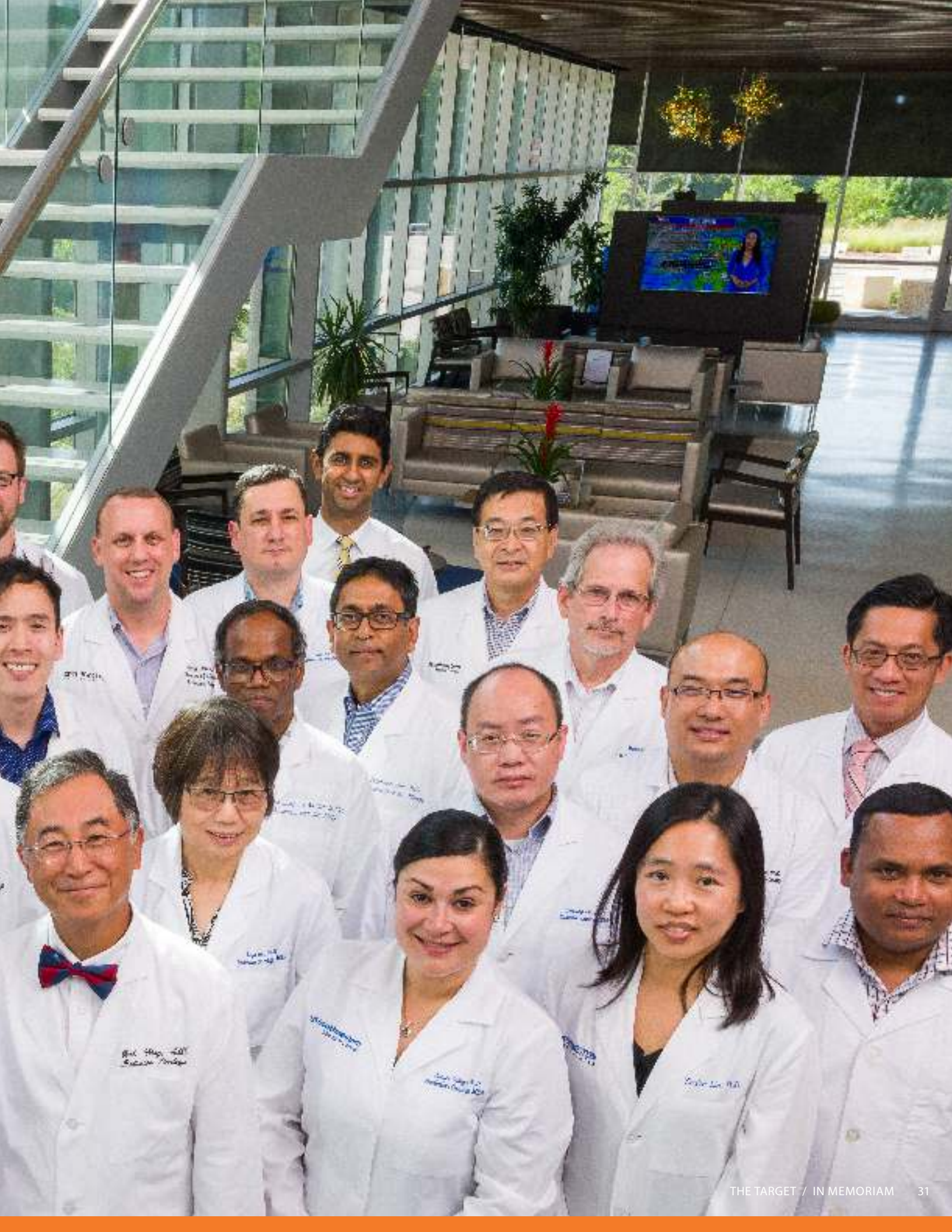
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Radiation Oncologist

Assistant Professor

Trained: Sidney Kimmel Medical College at Thomas Jefferson University





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