

THE TARGET

DEPARTMENT OF RADIATION ONCOLOGY

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POTEN-C: A Trial Aimed at Preserving Sexual Function

Top Story

By Ryan Daugherty

Kevin Stanfield, 58, of Mount Vernon, Texas, remembers the chills running through his body when he got the phone call.

It was the Fourth of July holiday, and he had been on his way to pick up his son when he received the call from his doctor. Understandably, his first response was shock. He spent the next few hours on the road figuring out how to break the news to his family that he had just been diagnosed with prostate cancer.



Mr. Stanfield was living just outside of Denver when his local doctor referred him to a urologist after his blood samples revealed higher than normal PSA levels, leading to his biopsy and diagnosis. He had lost his grandfather to prostate cancer, so the initial thought was that it might be inherited. After talking with his wife, he started to research options.

Fortunately for Mr. Stanfield, a plan came into place. Career changes at the time led to him and his wife moving back to North Texas, where he was familiar with one of the leading medical centers in the world.

“I knew the reputation of the facility and physicians at UT Southwestern,” he says. “When I sat down with Dr. [Robert] Timmerman – there’s no guessing his professionalism, experience, and track record – he mentioned this clinical trial, to which I expressed interest. I knew I was with the best and I was as comfortable as possible.”

The clinical trial, named POTEN-C and led by Neil Desai, M.D., M.H.S., Assistant Professor of Radiation Oncology, is a multi-center randomized controlled trial that asks whether a new radiation planning technique can reduce erectile dysfunction in men getting stereotactic ablative radiation therapy, or SAbR, for prostate cancer. Mr. Stanfield is one of 120 patients who will be enrolled in the study, which will include patients across nine major medical center sites across the country.

SAbR is a highly potent treatment and, as such, can produce significant side effects. To address this, a UT Southwestern-led clinical trial featured placement of a spacer gel, called SpaceOAR, between the rectum and prostate, to greatly reduce the amount of radiation reaching the rectum. Helped by the success of this trial in minimizing bowel effects of radiation, SAbR has evolved into a standard treatment option. However, as with all surgical and radiation treatments for prostate cancer, the most frequent long-term quality-of-life metric change remains erectile dysfunction.

“It’s clear that sexual potency or sexual function after treatment, either with surgery or radiation, is absolutely on the top of the minds of not only men undergoing therapies, but also their spouses or partners,” says Dr. Desai.

The current POTEN-C trial aims to test a technique to diminish this toxicity and its impact on men’s quality of life. Specifically, the displacement of the prostate from the rectum using the spacer facilitates a radiation delivery that will de-escalate dose to nerves and blood vessels on the side of the prostate opposite the dominant disease.

“We’re just trying to give men more choices and trying to preserve their potency upfront,” says Dr. Desai.

“We know with the standard approach you’ll get around 50 to 60 percent rate of sexual function; we’re hoping with this technique that the rate of potency preservation will be raised to around 80 percent or higher.”

Erectile dysfunction is an issue that men keep to themselves too often. Mr. Stanfield believes men look at it as losing part of their manhood. Spreading overall awareness is a goal of his. He wants other men to have a complete understanding and know what options are available, and it is already taking effect, as some of his closest friends have started voluntarily getting their physical examinations. Knowing that taking part in the study could benefit his brothers, friends, or any man in general makes him proud.

It’s a topic that he wasn’t looking forward to talking about either, but he says it was the conversations he had with Dr. Desai and Dr. Timmerman that further solidified his decision to take part in the trial. They both have made him feel important throughout the process, and the excitement they have had to get the trial underway has been very apparent. He’s looking forward to starting the trial, too, and he can’t imagine any other place doing it better.

There is a possibility Mr. Stanfield won’t be treated with the nerve bundle-sparing technique, however. The trial is a patient-blinded randomized trial, so half of the patients will be randomly assigned to radiation that is shifted to one side. He doesn’t care though, as he feels he would be shorting himself if he passed on the opportunity.

“I might get the new treatment or I might not,” he says. “But why would I not take advantage to have the most renowned people working on my behalf? The worst that could happen is still the best that they could offer right now; that didn’t seem like a difficult decision to me.”

As for the trial itself, if successful, not only will a technique be produced to preserve sexual function, but UT Southwestern and its collaborating institutions on the trial will become training centers to help other institutions learn it as well, according to Dr. Desai. Already a main training center for those seeking to learn placement of the SpaceOAR gel, he and the UTSW group are eager to translate knowledge gained from this trial to the rest of the community.



For Mr. Stanfield, he continues to have an optimistic outlook toward the future. He and his wife are nearing a point in their lives where they can spend time alone with each other, and he wants intimacy to be a part of it. His kids, 15 and 21, are growing older and becoming more independent, and he and his wife have experiences they would like to share together, including a future trip to Europe.

“We enjoy our lives and we definitely don’t want to have to stop and slow down,” he says.

For more information, visit utswmed.org/poten-c-clinical-trial.

+ NEW FACULTY

Department News

CLINICAL



Aurelie Garant, M.D.
Assistant Professor

Dr. Garant received her medical degree from McGill University. She focuses on treating patients with genitourinary and gastrointestinal malignancies. She specializes in the treatment of complex pelvic tumors and hepatobiliary cancers. Her interests include treatment escalation in selected patient populations, integration of novel imaging tools into clinical practice, and patient-reported outcomes.



Wen Jiang, M.D., Ph.D.
Assistant Professor

Dr. Jiang is a physician-scientist who received his Ph.D. in bioengineering at the University of Toronto and his medical degree from Stanford School of Medicine, following a brief postdoctoral fellowship at Massachusetts General Hospital - Harvard Medical School. Dr. Jiang continued his residency training in radiation oncology at The University of Texas MD Anderson Cancer Center. Dr. Jiang's clinical interest focuses on the treatment of central nervous system tumors. His lab research aims to identify immune-suppressive processes within solid tumors and to develop new therapeutic strategies utilizing bioengineered nanomedicine and radiation to promote immune-mediated tumor eradication.



Kiran Kumar, M.D.
Assistant Professor

Dr. Kumar focuses on the treatment of lymphomas and pediatric malignancies. He received his medical degree from the University of Chicago and completed his residency training at Stanford University Medical Center. In addition to his clinical research he has an interest in medical and patient education, health care policy, and quality improvement.



Nina Sanford, M.D.
Assistant Professor

Dr. Sanford received her medical degree from Harvard Medical School and completed her residency at the Harvard Radiation Oncology Program. Her clinical focus is on the treatment of gastrointestinal malignancies. Her research experience focuses on minimizing late effects of treatment and on racial disparities in access to care and cancer outcomes using large databases.

MOLECULAR RADIATION BIOLOGY



Laurentiu Pop, M.D.

Instructor

Dr. Pop received his medical degree from University of Medicine and Pharmacy of Craiova in Romania, where he also completed a combined residency and fellowship program in medical oncology. He completed his postdoctoral research training in the Cancer Immunobiology Center at UT Southwestern, where he was retained as a junior faculty member. His research interests focus on investigating tumor-escape mechanisms and developing cancer immunotherapy.



Nashir Udden, Ph.D.

Instructor

Dr. Udden received his bachelor's degree in biochemistry and master's degree in molecular biology from the University of Dhaka and his Ph.D. in medical sciences from Tohoku University. During his postdoctoral training, he investigated the role of pathogen recognition receptors, particularly NOD-like receptors (NLRs), in the pathogenesis of inflammatory bowel disease and inflammation-induced tumorigenesis, such as colorectal cancer and hepatocellular carcinoma. His research interests include intestinal immunity and microbiota, inflammation and tumorigenesis, radiation-mediated immunity and tumor regression, and the molecular mechanism of treatment resistance in cancers.

PHYSICS



Chenyang Shen, Ph.D.

Instructor

Dr. Shen received his bachelor's degree in mathematics from Yangzhou University. He continued his graduate studies in applied mathematics at Hong Kong Baptist University where he received both his master's degree in philosophy and Ph.D. Dr. Shen's research interests include medical image processing, machine-learning, and optimization techniques and algorithms.



Zhiguo Zhou, Ph.D.

Instructor

Dr. Zhou received both his bachelor's degree and Ph.D. in computer science from Xidian University in China. His research is focused on outcome modelling through artificial intelligence in cancer therapy.

+ PUBLICATIONS

Department News

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+ CLINICAL TRIALS

Department News

BREAST

THERAPEUTIC

062015-085: Phase I dose-escalation trial of single fraction adjuvant stereotactic body partial breast irradiation (SB-PBI) for early stage breast cancer.

052016-046/NRG-BR002: A phase IIR/III trial of standard of care therapy with or without SBRT and/or surgical ablation for newly oligometastatic breast cancer.

NON-THERAPEUTIC

052015-047: Intra-patient comparison of active breathing coordinator-based vs. vision RT-based deep inspiration breath-hold for left chest wall irradiation. A pilot study for breast cancer.

112014-004: The IDEA study (Individualized Decisions for Endocrine Therapy Alone).

022017-034: Population-based assessment of patient outcomes in older breast cancer survivors.

CENTRAL NERVOUS SYSTEM

THERAPEUTIC

022015-106: A phase I dose-escalation study of SRS for brain metastases without whole-brain radiation.

122016-064: Phase I/II trial to determine the neurocognitive decline in patients with multiple (>6) brain metastases treated with distributed SRS.

102014-014/NRG-BN001: Randomized phase II trial of hypofractionated dose-escalated photon IMRT or proton beam therapy vs. conventional photon irradiation with concomitant and adjuvant temozolomide in patients with newly diagnosed glioblastoma.

122017-011/NRG-BN003: Phase III trial of observation vs. irradiation for a gross totally resected grade II meningioma.

GASTROINTESTINAL

THERAPEUTIC

102014-018: A phase I therapeutic dose-

escalation study using percutaneous image-guided navigation for high-dose rate brachyablation of primary liver lesions.

102015-019: A randomized phase III study evaluating modified FOLFIRINOX (mFFX) with or without SBRT in the treatment of locally advanced pancreatic cancer.

trial of neo-adjuvant SABR for IVC tumor thrombus in newly diagnosed RCC.

102017-077/NRG-GU003: A randomized phase III trial of hypofractionated post-prostatectomy radiation therapy (hypof) vs. conventional post-prostatectomy radiation therapy (coport).



GENITOURINARY

THERAPEUTIC

102012-026: Phase II trial of sipuleucel-T and SABR for patients with metastatic castrate-resistant prostate cancer (mCRPC).

062014-027: Phase I clinical trial of SABR of pelvis and prostate targets for patients with high-risk prostate cancer.

122015-052: Phase II trial of nivolumab and SABR for metastatic clear cell renal cell carcinoma (mRCC).

022013-030: A phase II trial of SABR for patients with primary renal cancer (RCC).

022015-058: Safety lead-in phase II

102014-064/RTOG 924: Androgen-deprivation therapy and high-dose radiotherapy with or without whole-pelvic radiotherapy in unfavorable intermediate or favorable high-risk prostate cancer: a phase III randomized trial.

022017-032: Phase II/III trial of adjuvant radiotherapy and androgen deprivation following radical prostatectomy with or without adjuvant docetaxel.

122016-067: Phase II randomized placebo-controlled double-blind study of salvage radiation therapy (SRT) plus placebo vs. SRT plus enzalutamide in men with high-risk PSA-recurrent prostate cancer after radical prostatectomy (SALV-ENZA).

042016-046: Phase II trial of SABR for

GRANTS & PARTNERSHIPS

Todd Aguilera, M.D., Ph.D. received President's Research Council's Distinguished Researcher Award for \$75,000.

Kevin Albuquerque, M.D. received \$517,057.25 for Pfizer clinical trial, a phase II trial of concurrent anti-PD-L1 and SAbR for patients with persistent or recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer.

Neil Desai, M.D. received \$896,148.50 for Augmenix clinical trial, a phase II randomized controlled trial of stereotactic ablative body radiotherapy (SAbR) with or without neurovascular sparing for erectile function preservation in localized prostate cancer, and \$170,665 for a SCC-funded clinical trial, a phase I/II trial of pembrolizumab and total skin electron beam radiotherapy in advanced stage refractory/relapsed mycosis fungoides and Sézary syndrome.

Xun Jia, Ph.D. received two RO1 grants from the NIH: \$2,781,649 for next generation small animal radiation research platform and \$1,978,983 for precise image guidance for liver cancer stereotactic body radiotherapy using material-resolved cone-beam CT.

Wen Jiang, M.D., Ph.D. received CPRIT Recruitment Award for a CPRIT First-Time, Tenure-Track Faculty Member Award for \$2,000,000.

Jennifer Shah, M.D. was recipient of Eugene P. Frenkel, M.D. Program for Endowed Clinical Scholars in Cancer Medicine Award for \$1,000,000.

Yiping Shao, Ph.D. received an RO1 grant from the NIH for \$2,175,017 for novel online intra-beam range verification and delivery optimization for improved particle radiation therapy.

Robert Timmerman, M.D. received SCC: Funds for SPORE preliminary data for \$100,000.

patients with oligometastatic renal cell carcinoma.* (*Replaces former title of phase II randomized trial of pazopanib vs. SAbR for renal cell carcinoma patients with limited metastases.)

092017-018: Prostate oncologic therapy while ensuring neurovascular conservation (POTEN-C): a phase II randomized controlled trial of SAbR with or without neurovascular sparing for erectile function preservation in localized prostate cancer.

062017-067: Post-market registry to evaluate toxicity and clinical outcomes following the use of temporary hydrogel rectal spacer in the treatment of localized prostate cancer with radiation therapy.

NON-THERAPEUTIC

022016-012: Registry study to evaluate the clinical outcome of patients with hematologic malignancies treated with radiotherapy and patterns of relapse when radiotherapy is omitted.

GYNECOLOGICAL

THERAPEUTIC

032017-078: Phase II trial of concurrent anti-PD-L1 and SAbR for patients with persistent or recurrent epithelial ovarian, primary peritoneal, or fallopian tube cancer (with safety lead-in).

NON-THERAPEUTIC

092017-034: Concurrent chemoradiotherapy with etoposide and cisplatin as the treatment regimen of choice for locally advanced small cell carcinoma of the cervix: a multicenter retrospective study.

HEAD & NECK

THERAPEUTIC

122017-043: A phase II trial of glottic larynx SAbR for early stage glottic larynx cancer.

072014-041/NRG-HN001: Randomized phase II and phase III studies or individualized treatment for nasopharyngeal carcinoma based on biomarker Epstein-Barr virus DNA.

022011-213/RTOG-1008: A randomized phase II/phase III study of adjuvant concurrent radiation and chemotherapy vs. radiation alone in resected high-risk malignant salivary gland tumors.

052016-044/INFIELD: A prospective phase II study of involved field elective volume deintensification for oropharyngeal and laryngeal squamous cell carcinoma treated with IMRT.

NON-THERAPEUTIC

102016-059: Open-label feasibility study of a wearable sensor for acquisition of biometric data in head and neck cancer patients during locoregional therapy.

LUNG

THERAPEUTIC

052011-093: Hypofractionated IGRT in patients with stage II-III non-small cell lung cancer.

042017-024: Maintenance chemotherapy with or without SBRT in treating patients with stage IV non-small cell lung cancer.

072010-049: Phase III comparison of thoracic radiotherapy regimens in patients with limited small cell lung cancer also receiving cisplatin and etoposide.

022015-069: JoLT-Ca sublobar resection vs. SAbR for lung cancer (STABLEMATES).

042017-024/NRG-LU002: Maintenance systemic therapy vs. consolidative SBRT plus maintenance systemic therapy for limited metastatic non-small cell cancer (NSCLC). A randomized phase I/III trial.

072010-049/CALGB 30610/RTOG 0538: Phase III comparison of thoracic radiotherapy regimens in patients with limited small cell lung cancer also receiving cisplatin and etoposide.

NON-THERAPEUTIC

082014-030: 4-D cone-beam CT reconstruction for radiotherapy via motion vector optimization.

062016-073: Investigating radiation-induced injury to airways and pulmonary vasculature in lung SAbR.

092013-001: PET avidity in cachexia-inducing lung and gastrointestinal tumors.

122014-052: Multiparametric image analysis and correlation with outcomes in lung cancer screening and early stage lung cancer.

INTERVIEW

Elizabeth Polsdofer

By Damiana Chiavolini, Ph.D.

Elizabeth Polsdofer is a graduate student in Biomedical Engineering, Medical Physics track, currently working in the lab of Michael Story, Ph.D. in the Division of Molecular Radiation Biology. She earned her Bachelor of Science degree in physics in 2013 at Iowa State University, and her Master of Science in medical physics in 2016 at Oregon State and Oregon Health and Science Universities. As a graduate student in Dr. Story's lab, she has focused on using artificial intelligence tools to predict radiation therapy outcomes in head and neck cancer. Elizabeth recently agreed to discuss her experience as a woman in research.

Q: What and who inspired you to start a career in physics?

EP: I loved calculus in high school and once I figured out how it worked, it became natural for me to be good at it. Over time, I realized how I could use it to solve problems. Pursuing a degree in physics wasn't always easy, though. I often wondered if I had "impostor syndrome" because I felt like I didn't belong in such a competitive field. Then, one of my professors encouraged me to apply for an astronomy internship at the Space Telescope Institute in Baltimore. Being accepted in this program as an intern was a true turning point. I studied the infrared variability of objects using data from the Spitzer Space Telescope and published my results as first author in the *Astronomical Journal* in 2015.

Q: How did you decide to enter the field of medical physics?

EP: My dad was diagnosed with stage IIIB bladder cancer, which he later recovered from. Right before his surgery, I remember looking at a group of doctors having a casual conversation during breakfast in the hospital cafeteria. This was a normal day of hard work for them, and right then, I realized that my dad would be in good hands. This made me wonder if I could use my skills to help people in a similar way and led to the decision to pursue a higher degree in medical physics. It has been a great journey so far, and I am honored to be working in a radiation biology lab as part of my graduate studies. I like how biology focuses on understanding the mechanisms behind processes, which explains why certain radiation treatments work better than others.

Q: What do you feel are your most exciting achievements and discoveries in the field?

EP: I have worked on a project in which we are testing GC4419, an experimental drug that reduces severe adverse effects of radiation therapy, in clinical trials. We studied its role in protecting against lung fibrosis caused by irradiation, with the goal of providing dose-escalation to patients whose tumors are near critical normal tissues. These patients might not receive as high irradiation doses

because of sensitivity of the surrounding normal tissues. However, if the drug can protect against this damage, then we may get better local control with higher doses. Since the start of the project, a clinical trial has been completed, and GC4419 has been designated by the FDA as a Breakthrough Therapy.

Q: What are you most proud of so far?

EP: I was invited by two former professors to speak at the Conference for Undergraduate Women in Physics (CUWiP) in January 2018 at Iowa State University, the institution where I earned my undergraduate degree in physics. I was part of a session panel titled "Thriving in Physics" along with six other women physicists. We discussed topics such as succeeding in classes, keeping a good work-life balance, and starting a career in research or industry. It was inspiring to share my experience with other undergraduate women in physics and I felt truly honored to be part of this important initiative.



Q: Only a few women begin a career path in physics. Did you experience any difficulties in a scientific environment that is mostly male-dominated?

EP: As a minority in this field, I have sometimes felt uncomfortable with male classmates because they didn't always relate to me in the same way they did to other men. The reasons are several. I have received unwanted attention and felt like I had to tweak my behavior to be less feminine because of it. Also, I have had to fight the perception by some of being the helpful one only because I am a woman. And as a single woman, I have experienced pressure to be in a relationship by both men and women. In terms of gender equality in the field of physics, we still have much work to do.

Q: What advice do you have for young women wishing to pursue a career in physics?

EP: If you are strongly motivated to pursue this career path, don't give up because it's highly rewarding and always exciting. Find good

mentors. Dr. Story has been very encouraging, supporting me along the way with his calm demeanor and ability to provide straightforward, easy solutions to different problems. And bond with other women scientists so you can help one another during difficult times.

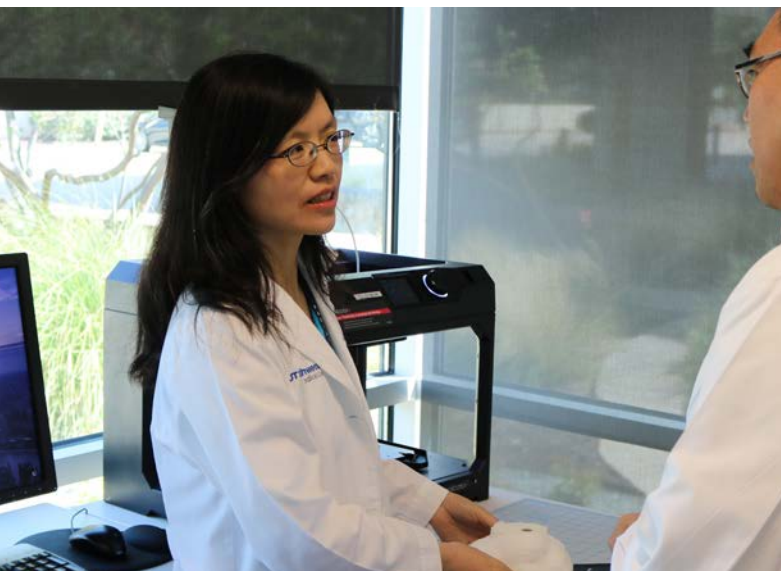
INTERVIEW

Xuejun Gu, Ph.D.

By *Ryan Daugherty*

Xuejun Gu, Ph.D., is an Associate Professor in the Department of Radiation Oncology. She earned her Bachelor of Science degree in biomedical engineering from Tianjin University and her Ph.D. in biomedical engineering from Columbia University. Her research interests revolve around online adaptive radiotherapy, brain radiosurgery, and non-sedated pediatric radiation treatment. Dr. Gu recently agreed to discuss her experience as a woman in research.

Q: What inspired you to start a career in radiation oncology, science, and research?



XG: I have been interested in physics ever since I was in middle school and it was something I was very good at. I wanted to major in science and engineering, while my parents strongly recommended medicine, so I chose a career in biomedical engineering where I could cover both the engineering and the medicine. After I came to the U.S., I got my Ph.D. in biomedical engineering and after graduation I started looking for a job. I found this medical physicist career path in radiation oncology that fit my career goal well. As a medical physicist, not only do I closely work with physicians to directly help with patient treatment on a daily basis, but I also conduct research in science and engineering topics to address general radiation physics problems in the field.

Q: What do you feel are your most exciting achievements and discoveries in the field?

XG: I started as a clinical physicist at UTSW in 2011. The most exciting things are also the most difficult things I need to overcome. For example, if we're looking back, the most exciting achievement is that we are able to treat bone marrow transplant patients with our newly developed total body irradiation (TBI) technology. This new TBI technology allows those very sick patients to be accurately treated on their comfortable flat-back position rather than the conventional standing position. That was really challenging at the time because no one did that before. Not only did we need to design and fabricate a body frame to assist treatment, but we also needed to educate and train clinical staff to implement a brand new treatment workflow. It took several iterations to construct the body frame and a year to make the entire treatment workflow smooth. Now, three years later, the majority of the therapists and physicians in our department accept this clinical workflow. This new TBI technique not only benefits patients, but clinical staff who won't need to worry about patients falling down. To me it is a really big achievement.

Q: What are you most proud of and what has been the biggest challenge in your career?

XG: There are a lot of challenges for me coming into the field. Coming from a bioengineering background I'm not originally trained into medical physics. I started my career kind of training on the job; I took this clinical physicist job and I have to deal with all these daily workflows I haven't seen before. Another challenge I face is balancing the clinical and research aspects, because I have to allocate my time for both with clinical duties and research projects. I am proud with the excellent job I have done in balancing the clinic and research and making the two time-conflicting tasks help each other. My clinical work inspires my research ideas and the research helps to solve problems in clinical duties.

Q: Fewer women than men begin a career path in science. Did you experience any difficulties in scientific environments that are historically male-dominated?

XG: I don't think that women cannot be in research and science; if they are good at it, then they should be. Of course, compared to men, naturally women are bounded more toward family and have to devote more time to their kids. Balancing the family and the career is quite challenging.

Q: What do you think can be done to increase recruitment and retention of women in science?

XG: If we want more women working in this research and science field, then we should start them early in middle and high school by encouraging them to be interested in science, technology, engineering, and math (STEM). If they are interested in STEM, then naturally they will go into this career rather than just getting tracked into it after graduation.

Q: What advice do you have for women trying to get in this career?

XG: I think radiation oncology and science and research is a very good career for a young woman because there are a lot of things men can do that women still can do, so they should not be afraid of that. Regarding advice, to me the first thing is that you have to love your job. If you don't love your job, I don't think you can do it well.

In radiation oncology when you help patients you feel like your job is meaningful, and that encourages you to work hard every day to help the patients in the best way possible. If you are such a person, I would definitely advise you to come into radiation oncology.

RESEARCH AWARD

Jennifer Shah, M.D.

Jennifer Shah, M.D., Assistant Professor in the Department of Radiation Oncology, was recently awarded a Eugene P. Frenkel, M.D. Scholar in Clinical Medicine award. Funded by an anonymous private endowment, the program was established to attract and support young clinicians who have the potential to become leaders in cancer care at UT Southwestern. Dr. Shah's clinical mission is to establish a multidisciplinary approach to the use of immunotherapy in head and neck cancer.



Dr. Shah was an undergraduate at the Massachusetts Institute of Technology. She attended the University of Michigan Medical School, followed by an internship at St. Joseph Mercy Hospital and a residency in radiation oncology at Stanford University Medical Center. - MW

CLINICAL / RESEARCH HIGHLIGHTS

Advancements in Breast Cancer Care at UTSW

By Ryan Daugherty

UT Southwestern offers the most advanced technologies and techniques available for breast cancer diagnosis, screening, and personalized treatments, such as medications and other therapies that are not available at every hospital. Each patient is offered personalized strategies to improve their overall health and well-being, with the goal of enhancing quality of life both today and in the future as a cancer survivor. Patients benefit from the knowledge and experience of an entire team of breast care specialists who have dedicated their entire clinical activities to treating breast cancer.

UT Southwestern's Department of Radiation Oncology will become just the second center in the world to offer the GammaPod, the world's first stereotactic radiotherapy system optimized for treating breast cancer. Standard therapy for breast cancer often involves surgery to remove tumors along with weeks of radiation therapy. The



GammaPod could eventually eliminate this need for invasive surgery and reduce treatment time from 4 to 6 weeks to just a handful of treatments over 1 to 5 days. The treatments are given with a high accuracy, all while minimizing damage to surrounding healthy tissue, as well as to the heart, lungs, and skin. By using stereotactic radiotherapy to deliver high doses in one or several large fractions, the GammaPod differentiates itself from conventional techniques.

Understanding & Overcoming Immunosuppression

By Jonathan Feinberg, Ph.D.

Immunotherapy, which harnesses the immune system to attack tumor cells in the same way that it attacks foreign pathogens, holds great promise for advancing cancer treatment, especially when combined with other therapies, such as radiation or chemotherapy. However, not all tumors respond to immunotherapy the same way, which suggests that specific factors within the tumor microenvironment affect how the immune system and particular tumors interact. Understanding these factors is essential to developing new therapies or therapeutic combinations that can improve outcomes for patients with cancer.



Todd Aguilera, M.D., Ph.D., Assistant Professor of Radiation Oncology, and his lab study the genetic factors that influence whether immune responses are suppressed or activated in the tumor microenvironment in response to cancer therapies. Specifically, they seek to identify factors that allow the tumor to withstand or even hijack the immune response stimulated by radiation therapy.

Dr. Aguilera initially investigated these factors in mouse models of breast cancer as a postdoctoral fellow at Stanford University. The Department of Radiation Oncology at UT Southwestern brought him to Texas in June 2017, aided by a First-Time Tenure Track Faculty Recruitment Award from the Cancer Prevention & Research Institute of Texas (CPRIT), which seeks to attract promising new cancer researchers to Texas institutions. This CPRIT award provided substantial funding to establish Dr. Aguilera's lab at UT Southwestern, where he continues to study breast cancer, but is transitioning to study pancreatic cancer as well. This shift in focus more closely aligns Dr. Aguilera's lab research with his clinical expertise as a gastrointestinal radiation oncologist who specializes in treating patients with pancreatic cancer, but it also serves a strategic purpose. "Part of the attraction of pancreatic cancer is

that there are very poor outcomes, and it's known to be incredibly immunosuppressive," Dr. Aguilera explains, "so the tumor is very good at turning off the immune system, or actually utilizing the immune system for its own benefit." This makes pancreatic cancer an ideal test-case for studying mechanisms of immune resistance in the tumor microenvironment, many of which are common across cancer types.

The pancreas undergoes extensive inflammatory changes as pancreatic cancer develops, which leaves this cancer well-adapted to an inflammatory environment and less susceptible to current cancer therapies, including radiation. "In a number of cancers that are adapted to an inflammatory environment, the immune response is quite subdued after radiation, and it can trigger a wound-healing response that supports tumor cell recovery within the tumor and the tumor microenvironment," says Dr. Aguilera. "We actually need to add novel agents that help generate productive antitumor responses to combat immune responses that help the tumor recover."

For patients with locally advanced pancreatic cancer, adding an immune agent after treatment with stereotactic radiation or ablative radiation – which delivers a focused, powerful dose of radiation – could generate a systemic immune response to complement the superior local tumor control that ablative radiation provides. As the UT Southwestern site principal investigator for the multi-institution PanCRS phase III clinical trial, Dr. Aguilera is investigating whether ablative radiation improves longer-term outcomes for patients with locally advanced pancreatic cancer when added to the standard-of-care chemotherapy regimen, FOLFIRINOX. Many of these patients still progress with metastasis, which Dr. Aguilera thinks is attributable to insufficient systemic therapies to treat disease that has already left the pancreas but cannot be detected. Adding an immune active agent that uniquely couples with ablative radiation to generate antitumor immune responses could eradicate this micro-metastatic disease – or the microscopic, undetectable beginnings of metastasis – before it progresses. This could offer a compelling approach that uses ablative radiation to improve outcomes in patients with localized pancreatic cancer.

Dr. Aguilera's lab also seeks to develop new immune active agents with funding support from a Distinguished Researcher Award given by UT Southwestern's President's Research Council, a group of community friends of UT Southwestern who help support researchers at an early stage in their careers. With this award, Dr. Aguilera's lab will screen a library of millions of single-domain antibodies to identify molecules that can target factors that influence the immune response within the tumor microenvironment. The Distinguished Researcher Award will also help translate the lab's research from mouse models to human tissue by funding the procurement and Next Generation Sequencing of patient tumor tissue to better understand the tumor microenvironment before and after radiation therapy. Their findings will guide the development of their antibody targets.

Identifying novel immune active agents could substantially advance the treatment of pancreatic and other cancers by enabling new therapeutic combinations that could maximize the effects of immunotherapy to direct the power of the immune system against tumor cells.

Artificial Intelligence in Radiation Treatment of Head & Neck Cancer

By *Damiana Chiavolini, Ph.D.*

Artificial intelligence (AI) is a process through which machines mimic human functions, such as learning and problem-solving, by analyzing large amounts of data that humans cannot process.

Recent breakthroughs in AI using novel mathematical algorithms and high-performance computing technologies have advanced the fields of computer vision, speech, and decision-making. In health care, human-created algorithms have allowed clinicians to review electronic medical records, databases, and journals to determine the best steps to diagnose, treat, and manage diseases, prevent hospital readmissions, and develop personalized treatments for patients.

In radiation oncology, AI shows great potential to improve tumor detection, classification, and delineation to better treat patients with cancer. “AI allows us to learn from human experience and perform human-like tasks,” says Steve Jiang, Ph.D., Professor and Vice Chair in the Department of Radiation Oncology and Division Chief of Medical Physics and Engineering. With the support of Professor and Chairman Hak Choy, M.D., and Vice Chair and Medical Director Robert Timmerman, M.D., Dr. Jiang has formed the Medical Artificial Intelligence and Automation (MAIA) Lab and the Program of Excellence in Intelligence Medicine (PEIM) to develop, implement, and translate novel AI technologies to the clinical practice of cancer radiation therapy. The MAIA Lab is an internal program focused on research, while the PEIM promotes interdisciplinary collaborations with other departments and centers. “Our AI-based segmentation and radiation toxicity prediction algorithms are showing advantages over traditional methods,” says Dr. Jiang.

Clinicians and physicists in the Department of Radiation Oncology are using AI to advance and standardize treatment planning for patients with head and neck cancer. Although technological advances in radiation therapy have improved survival of patients with this cancer type, many challenges remain. The delicate structures in this area of the body require clinicians to plan treatment very carefully to avoid damaging critical tissues and organs with the high doses of radiation needed to kill tumors. Also, oncologists need improved sensitivity in detecting malignant lymph nodes to determine the proper dose for different regions of the neck; both over-treatment and under-treatment can have potentially dramatic oncologic and functional implications. AI may also play a groundbreaking role in translating highly specialized cancer treatment techniques into routinely delivered, community-based therapy. David Sher, M.D., leader of the radiation oncology team that specializes in treating patients with head and neck cancer at UT Southwestern, published a study reporting a relative difference in five-year survival rates of 16% between high- and low-volume clinical centers treating oropharyngeal cancer. These findings, consistent with analyses from cooperative group studies, indicate the critical need to transfer knowledge, experience, and expertise from large academic institutions to small community centers with fewer resources, standardizing the level of care for all patients. “We are studying the use of AI in radiation therapy planning to emulate highly specialized clinicians, physicists, and dosimetrists, so we can free up their time to focus on other aspects of patient care,” explains Dr. Sher. “The genius of AI is applying the knowledge generated from large amounts of data to a patient’s unique anatomy and needs, raising the standard of care and cure rates.”

In the Department of Radiation Oncology, research teams led by Dr. Jiang and Dr. Sher have focused on using AI tools to overcome these and other difficulties in the radiation treatment of patients with head and neck cancer. Their research could lead to benefits, such as:

- Reducing the large variation in pathologic characterization of head and neck tumors to improve diagnosis and classification, using digital pathology.
- Differentiating between malignant and benign lymph nodes more accurately to improve treatment efficacy, predict metastasis development, and reduce toxicity, using imaging techniques.
- Ensuring safer and more precise radiation treatment for better clinical outcomes in patients by improving delineation of tumors and critical organs.
- Reducing the time taken to design radiation treatment plans to improve the overall quality of treatment, using a novel guidance tool.
- Predicting tumor persistence and recurrence more effectively, using imaging techniques.



Also, with the Department’s support, Dr. Jiang has established a seminar series called AI in Medicine (AIM), co-sponsored by PEIM, the Department of Bioinformatics, and the Quantitative Biomedical Research Center at UT Southwestern. Through this series, world-renowned experts share their latest advances in the AI field every two weeks, promoting collaborations between UT Southwestern and other centers and institutions.

Through the Department’s research initiatives, AI has great potential to help clinicians treat head and neck cancer more effectively and efficiently, which should significantly improve and standardize outcomes for patients diagnosed with these malignancies.

+ DISEASE-ORIENTED TEAM FACULTY

Our Team

BREAST



Asal Rahimi, M.D. *

Assistant Professor and Director of Clinical Research

Trained: University of Virginia



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

Assistant Professor

Trained: University of Minnesota



Nathan Kim, M.D., Ph.D.

Associate Professor

Trained: Vanderbilt University Medical Center



Ann Spangler, M.D.

Associate Professor

Trained: Shands Hospital at the University of Florida



Xuejun Gu, Ph.D.

Associate Professor

Trained: Columbia University



Anthony Davis, Ph.D.

Assistant Professor

Trained: UT Southwestern Medical Center



Shohreh Bahrini, APRN, FNP-BC

Nurse Practitioner

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Holder of the Effie Marie Cain Distinguished Chair in Cancer Therapy Research

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Tu Dan, M.D.

Clinical Instructor

Trained: Sidney Kimmel Medical College at Thomas Jefferson University



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Trained: UT MD Anderson Cancer Center



Lucien Nedzi, M.D.

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Trained: Harvard Medical School



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Trained: UC San Diego School of Medicine



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Trained: Harvard Radiation Oncology
Program



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Trained: Harvard Radiation Oncology
Program



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Trained: Ohio State University



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Awarded the Dedman Family Scholar
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Trained: Peking University

HEAD & NECK



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Trained: Stanford University



Bo Zhao, Ph.D.

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Benjamin Chen, Ph.D.

Associate Professor

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Gina Chorley, MSN, APRN-BC

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LUNG



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Chairman, Professor

Holder of the Nancy B. & Jake L. Hamon
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Trained: University of Western Ontario



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Vice Chairman, Professor

Director, Division of Molecular Radiation Biology
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Awarded the Dedman Family Scholar in Clinical Care

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Kiran Kumar, M.D.

Assistant Professor

Trained: Stanford University



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Assistant Professor and Associate Director of Medical Residency Program

Trained: Stanford University



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Trained: Georgia Institute of Technology



Matthew Strunk, PA-C

Physician Assistant

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Holder of the Effie Marie Cain Distinguished
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Trained: Johns Hopkins Hospital



Tu Dan, M.D.

Clinical Instructor

Trained: Sidney Kimmel Medical College at
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Michael Folkert, M.D., Ph.D.

Assistant Professor and Residency Program Director

Trained: Memorial Sloan Kettering Cancer Center



Kiran Kumar, M.D.

Assistant Professor

Trained: Stanford University



Zabi Wardak, M.D.

Assistant Professor

Trained: UT Southwestern Medical Center



Ming Yang, Ph.D.

Assistant Professor

Trained: University of Texas Health Science
Center at Houston

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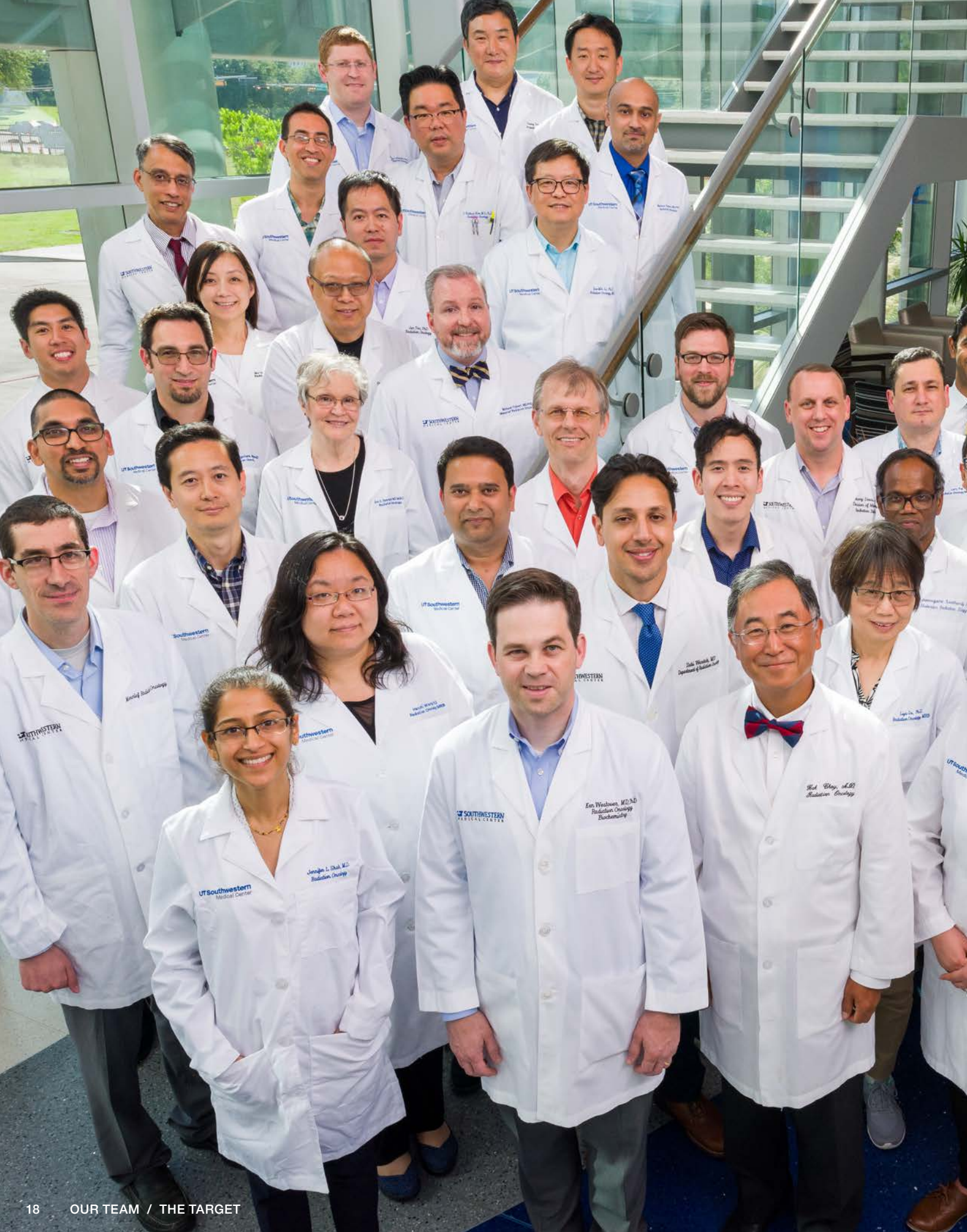


Daniella Hall, MPAS, PA-C

Physician Assistant

Trained: UT Southwestern Medical Center

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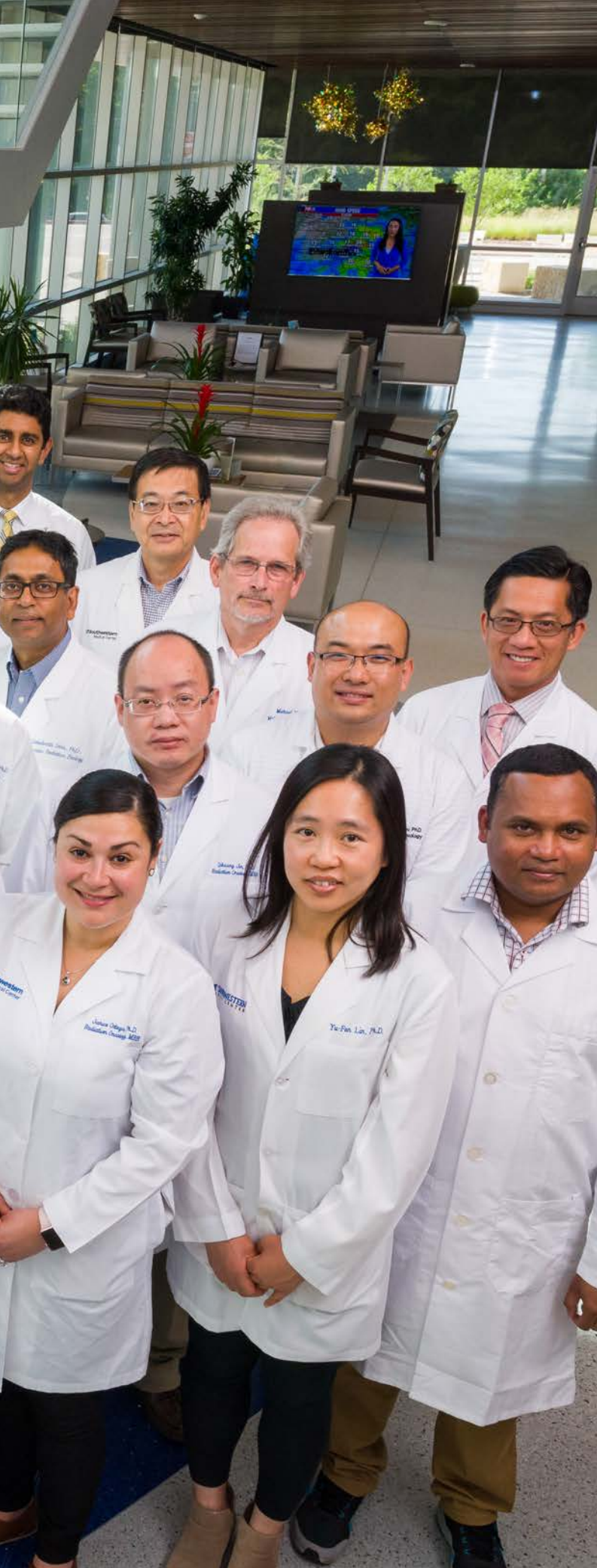
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In Memoriam

Larry Kun, M.D., a Professor in the UT Southwestern Radiation Oncology and Pediatrics departments and Director of Radiation Oncology Education Programs, passed away in May. Dr. Kun was instrumental in the development of the Radiation Oncology Department's strategic plan and the seed-funding initiative to support innovative projects. He was also an active participant in pediatric tumor boards and was a valued senior colleague and advisor to our residents and junior faculty.

Before joining the UT Southwestern faculty in 2016, Dr. Kun spent 32 years at St. Jude Children's Research Hospital, establishing a department to study and optimize radiation therapy for children and initiating the hospital's multidisciplinary brain tumor program, now the nation's largest clinical and translational research program in pediatric brain tumors. Dr. Kun and his kind, gentlemanly manner will be missed.

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