

THE TARGET

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Treating Limited Metastatic Cancer with SAbR

Top Story

Systemic therapy has long been the standard of care for metastatic cancers, but recent evidence indicates that patients with only a few metastases may be treated effectively by local therapy to all sites of disease. **For such patients with limited metastatic or “oligometastatic” cancer, local therapy—such as surgery or radiation therapy—may help to avoid or delay systemic therapy, which would improve their quality of life.** Attacking major sites of metastatic disease aggressively may even extend patients’ survival.

By Jonathan Feinberg, Ph.D.

Puneeth Iyengar, M.D., Ph.D., Assistant Professor and Director of Clinical Research, believes this aggressive approach would benefit patients with non-small cell lung cancer (NSCLC) with limited metastases. The prognosis for metastatic NSCLC is poor—survival is typically around one to two years—so new approaches to improve patient outcomes are urgently needed. What’s more, studies of patterns of treatment failure have shown that, in metastatic NSCLC, sites of major disease are the first to progress when treated with systemic therapy, so local therapy to those sites could be especially beneficial for patients with this cancer. “Even in the modern era of immunotherapy, local therapies including radiation may offer a synergy with systemic therapies in fighting metastatic cancers,” Dr. Iyengar adds.

While surgery remains the definitive local therapy,

not all patients are good candidates because of their age, health condition, or personal preferences. Stereotactic ablative radiation therapy (SAbR)—a modern form of radiation therapy that uses innovative technology to deliver powerful, precise radiation doses in fewer sessions than conventional radiation—offers a non-invasive alternative. Patients treated with SAbR also benefit from a faster recovery than with surgery, so they can start or resume systemic therapy sooner after treatment.

The Department of Radiation Oncology’s renowned expertise in the study and clinical practice of SAbR makes UT Southwestern an ideal location to test SAbR for limited metastatic cancer in clinical trials. Robert Timmerman, M.D., FASTRO, FACR, Professor, Vice Chair, and Medical Director, who joined the Department in 2006, is a world-renowned expert and pioneer in the use of these SAbR techniques. His leadership and talent as



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*Using SAbR, a technology largely derived from UT Southwestern's Department of Radiation Oncology, in a majority of our clinical trials **will permit us to potentially offer the greatest impact on patient survival and quality of life across a multitude of cancers and stages.***

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-Puneeth Iyengar, M.D., Ph.D., Assistant Professor and Director of Clinical Research

SAbR of a metastatic NSCLC

a physician, researcher, and scientist has led to tremendous innovative advancements and outstanding quality in patient care within the field of radiation oncology.

Dr. Iyengar is leading an international phase III randomized clinical trial (NCT03137771) investigating whether SAbR, when added to maintenance systemic therapy after the initial rounds of systemic therapy, can extend survival for patients with limited metastatic NSCLC. In an earlier phase II trial, the results of which were published in *JAMA Oncology* in 2017, Dr. Iyengar's team found that patients who received SAbR to all major metastatic sites avoided disease progression almost three times longer than those who did not receive SAbR (9.7 vs. 3.5 months) and experienced no additional side effects. Just as importantly, SAbR altered patterns of failure, as patients treated with SAbR experienced progression

at new distant sites, not at the sites of major disease that received SAbR. This means that SAbR effectively controlled the disease where it was applied, in addition to delaying disease progression overall.

In a previous study published in the *Journal of Clinical Oncology* in 2014, Dr. Iyengar's team showed that using SAbR to treat limited metastases could also potentially benefit patients with NSCLC who had progressed through initial systemic therapies. “These early studies pioneered at UT Southwestern Medical Center have provided a foundation from which we can get closer to determining how well SAbR and systemic therapies eradicate metastatic disease and provide longer disease-free survival intervals,” Dr. Iyengar explains.

Whether delaying disease progression and shifting patterns of failure lead to longer

survival overall for patients treated with SAbR will be determined by the ongoing phase III trial, the results of which could transform the treatment paradigm for NSCLC with limited metastases. “Ultimately, with the international phase III study, we hope to show that adding local therapies such as SAbR will improve the overall survival of NSCLC patients with limited metastatic disease,” Dr. Iyengar says. “It is the largest study to date evaluating radiation and immunotherapy in stage 4 NSCLC patients, a patient population that historically would only receive radiation for palliation.”

Treating limited metastatic cancer with local therapies is still controversial, though, as it is not yet universally accepted that limited metastatic disease is distinct from, and can be treated

renal cell carcinoma. Asal Rahimi, M.D., M.S. Associate Professor, is leading a registry trial (NCT02170181) that prospectively follows patient outcomes and documents treatment characteristics for patients who receive SAbR for limited metastatic cancers. This registry will collect the data needed to determine trends in patterns of care and patient outcomes for a treatment regimen that is being increasingly incorporated into clinical practice.

By leveraging advanced technology and world-renowned expertise to perform groundbreaking clinical research, Dr. Iyengar and the Department of Radiation Oncology seek to shift the treatment paradigm to improve quality of life and extend survival for patients with limited metastatic cancer.

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*Ultimately, with the international phase III study, we hope to show that adding local therapies such as **SAbR will improve the overall survival of NSCLC patients with limited metastatic disease.** It is the largest study to date evaluating radiation and immunotherapy in stage 4 NSCLC patients, a patient population that historically would only receive radiation for palliation.*

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differently than, widely metastatic disease. It also remains unknown whether this emerging treatment paradigm applies to all cancers. Studies have shown survival benefits for patients with limited metastatic colorectal cancer and sarcomas treated with local therapies, but data are less plentiful for other cancers.

Investigators in the Department of Radiation Oncology are advancing the research in this area through innovative clinical trials—including Dr. Iyengar’s—that are studying SAbR for limited metastatic cancer. Raquibul Hannan, M.D., Ph.D., Associate Professor, is leading a phase II trial (NCT02956798) examining whether SAbR can prolong survival without disease progression and delay the start of systemic therapy for patients with limited metastatic



Robert Timmerman, M.D., FASTRO, FACR



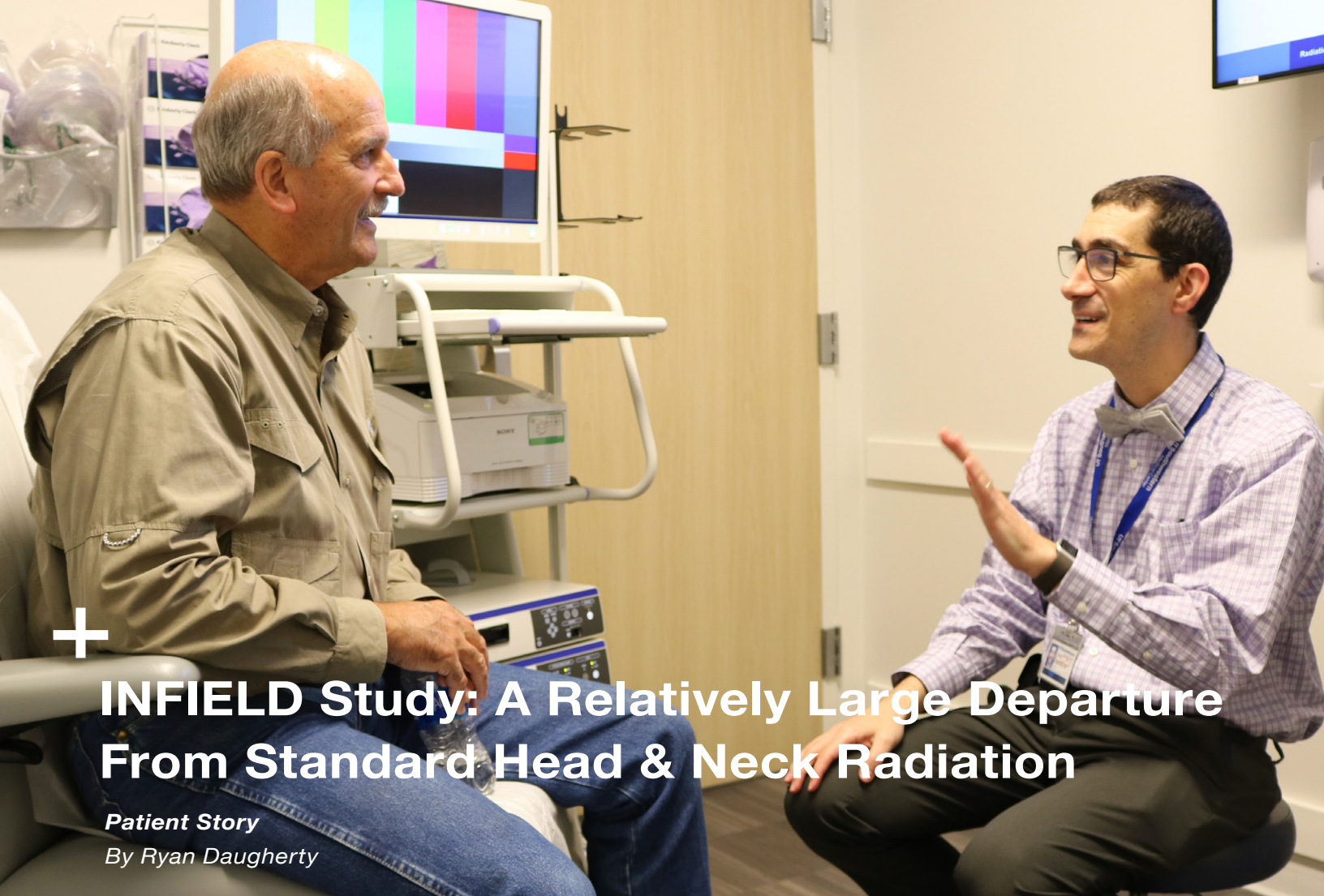
Puneeth Iyengar, M.D., Ph.D.



Raquibul Hannan, M.D., Ph.D.



Asal Rahimi, M.D., M.S.



INFIELD Study: A Relatively Large Departure From Standard Head & Neck Radiation

Patient Story

By Ryan Daugherty

A few years ago, Clyde Ledgerwood and his wife, Donna, moved to a community in Oklahoma with one goal in mind—to demonstrate a different and better method of agriculture to produce high-quality food through the use of aquaponics.

Four years earlier, Mr. Ledgerwood had retired as operations manager of air traffic at Dallas/Fort Worth International Airport. Shortly after, he and his wife moved to Europe where he taught air traffic control procedures. It was after this four-year stint in Europe that they decided to move back to the United States to a farm in Oklahoma.

Before undergoing construction of a 10,500-square-foot greenhouse for their aquaponics farm, Mr. Ledgerwood decided it would be smart for him and his wife to get physicals prior to jumping into so much labor. Both their primary physician and cardiologist said there were no issues and that they were completely healthy.

However, Mr. Ledgerwood did have a question about a small bump in his neck. It didn't bother him and he didn't feel any pain or have a cough, but he was curious as to what it was; he figured perhaps a lymph node had gotten stuck in an odd place. A month earlier, he had visited a local doctor who performed an esophagogastroduodenoscopy, but nothing was found.

"We were pretty confident that whatever that



Mr. Ledgerwood's scans before and after treatment.

On the left photo the tumor mass can be seen.

little bump was that it was nothing," said Mr. Ledgerwood. "Because I had no problems with it there really wasn't any cause for alarm on our part."

Their primary physician had the same feeling as he checked it out but wanted to do a CAT scan just to be sure. The next day the scan was performed, and by the time the Ledgerwoods were home, they received a call from their doctor about taking additional tests. One week later, a biopsy was performed and revealed a tumor on the base of Mr. Ledgerwood's tongue.

The first place he was referred to was UT Southwestern Medical Center. Initially, Mr. Ledgerwood was leaning toward robotic surgery because he wanted nothing to do with chemoradiation. They met with Baran Sumer, M.D., Associate Professor and Chief of the Division of Head and Neck Oncology. Dr. Sumer went over the surgical plan with Mr. Ledgerwood, but not wanting to rush into anything and still on the fence about the desired treatment path, they decided to take a couple of months to figure things out.

Over those two months, Mr. Ledgerwood went on a ketogenic diet and even took enzymes to get in the best health possible to prepare

for his upcoming battle. He went from 220 pounds to a healthy 185 pounds; he felt great. His wife, daughter, and daughter-in-law, all registered nurses, each had ideas for his best treatment option, but the decision was his to make. Ultimately, they decided to take one final weekend in the Ozarks to clear their minds.

"It was a very tough weekend," says Mr. Ledgerwood. "We just prayed about it and thanked God for everything he had done for us. We finally had peace about it so we went back to UT Southwestern to try another outlet."

David Sher, M.D., M.P.H., Associate Professor and Associate Director of Clinical Operations, specializes in the treatment of head and neck cancers. He's also the lead investigator of a clinical trial, INFIELD (Involved Field Elective Volume De-Intensification Radiation Therapy for Head and Neck Cancer), which aims to reduce total amount of radiation to certain parts of the neck.

The study is a relatively large departure from standard head and neck radiation. Similar to standard procedures, treatment in the study is being administered over seven weeks; however,

much of the radiation is delivered in a relatively significant dose to the lymph nodes in the left and right neck, above the jaw, and down to the collarbone. Much of that dose is an insurance policy, treating an area of the neck that may, or may not, have cancer. The dose that is delivered to the concerning parts of the neck get about a third less dose and some parts get no radiation—a dramatic change from current practice. After four weeks, the insurance dose is stopped and the patient continues receiving only the dose to infected areas.

The Ledgerwoods admired Dr. Sher as soon as he walked in the door. Mr. Ledgerwood recalls his warmth and manner as being exceptional: His introduction as “David” rather than “Dr. Sher” was a comforting feeling. Before he could even explain the details of the study, they knew he was the right physician for them.

“When we met Dr. Sher, I just trusted him,” says Mr. Ledgerwood. “He instilled a sense of confidence and there was just something about his demeanor—it was about you, not him. I wanted to go with somebody I knew had my back, and I knew I was in the room with the man that I wanted to go to battle with.”

Mr. Ledgerwood underwent radiation treatments every week for seven weeks, Monday through Friday, with one day a week of chemotherapy. For most of the treatments, he did fine as the only side effects were issues with saliva and tasting ability and, oddly enough, hiccups from the chemotherapy. The final few weeks were rougher—he had to use a feeding tube during the last week—but a number of resources were available to help with discomfort.

After finishing treatment, the Ledgerwoods returned to UT Southwestern every few months to find out how he was improving. In the very first follow-up visit with Dr. Sher, the results showed good signs; his tumor was decreasing in size. Each visit the tumor continued to show improvement. Monthly checkups were no longer dreaded, they were desired.

“We lived for Tuesday appointments,” says Mrs.

Ledgerwood. One day, Mr. Ledgerwood returned for another routine checkup. Dr. Sher sat down with him and his wife and pulled up the scans. His tumor was all gone. Today, they still look forward to returning to UT Southwestern, not just to see the scans, but to talk with Dr. Sher about their aquaponics farm, something he has grown very fond of hearing about.

“We won the minute we walked into Dr. Sher’s office. There’s nothing I wouldn’t do for that man,” says Mr. Ledgerwood. “And I just can’t emphasize enough, when you find yourself in a situation where you’re facing this kind of thing, what it means to have the type of personnel that UT Southwestern has. We couldn’t ask for more.”

The overall results for the INFIELD trial have thus far been superb. Of the 72 enrolled patients, not one has developed an extra recurrence due to the de-intensified treatment. Swallowing outcomes have been impressive and less than half have needed a stomach tube. In addition, the promising results from INFIELD has led to the development and activation of another clinical trial, INRT-AIR (Involved Nodal Radiation Therapy using AI-based Radiomics), developed by Jing Wang, Ph.D., Associate Professor, which uses artificial intelligence to personalize treatment even more by eliminating radiation to normal-appearing areas of the neck.

“We want to have confidence that we’re not going to miss anything,” says Dr. Sher. “PET and CT scans are good but probably not sufficient so we needed to take the next degree of analysis using artificial intelligence, because it can analyze information that CT and PET scans simply cannot see.”



David Sher, M.D., M.P.H.



Jing Wang, Ph.D.

+ NEW FACULTY

Department News

CLINICAL



Vladimir Avkshtol, M.D.

Assistant Professor

Dr. Avkshtol received his bachelor's degree from Boston College and his medical degree from the University of Toledo College of Medicine. He completed his radiation oncology training at Fox Chase Cancer Center in Philadelphia, where he also served as Chief Resident. He joins the head and neck disease-oriented team where his practice focuses on treating head and neck cancer as well as skin malignancies. His research interests include optimizing current radiation treatment practices in order to improve disease and toxicity outcomes.



Dominic Moon, M.D.

Assistant Professor

Dr. Moon received his bachelor's degree in biology and economics from the University of Virginia and his medical degree from the University of Michigan Medical School. During medical school he also spent a year conducting clinical and translational research at the National Cancer Institute through the Medical Research Scholars Program. Dr. Moon completed his residency training in radiation oncology at the University of North Carolina Hospitals. He joins the head and neck disease-oriented team. His research interests include application of biomarkers to personalize care and investigation of patient-reported outcomes and toxicities related to cancer therapy.



Chika Nwachukwu, M.D., Ph.D.

Assistant Professor

Dr. Nwachukwu received her bachelor's degree from Grinnell College, her Ph.D. from the University of Chicago, and her medical degree from Mayo Medical School. She completed her radiation oncology training at Stanford University, where she also served as Chief Resident. Dr. Nwachukwu joins the gynecologic and breast teams. Her research interests are in gynecologic malignancies, women's health, and global initiatives with the goal of expanding the role of radiation oncologists in achieving more equitable health care for all through humanitarian outreach, education, and research.



Dat Vo, M.D., Ph.D.

Assistant Professor

Dr. Vo received his bachelor's degree in biochemistry from the University of Texas at Austin. He then received his M.D. and Ph.D. from the University of Texas Health Science Center at San Antonio, where he studied post-transcriptional gene regulation in malignant brain cancers. He completed his transitional internship at John Peter Smith Hospital in Fort Worth and his residency in radiation oncology at UT Southwestern. Dr. Vo joins the head and neck disease-oriented team. His research interests include post-transcriptional gene regulation, nucleic acid-based diagnostics and therapeutics, and clinical trial design.

PHYSICS



Tsuicheng David Chiu, Ph.D.

Assistant Professor

Dr. Chiu joined the Department back in 2013 as a postdoc researcher and pursued his medical physics training from our CAMPEP-accredited

Medical Physics Residency Program. He graduated in 2019 and joined our medical physics faculty. Dr. Chiu earned his B.S. in mechanical engineering from National Chung Hsing University in Taiwan and his Ph.D. in biomedical engineering from the University of Connecticut. Combining his strong engineering background and medical physics knowledge, he focuses on clinical innovation implementation, including development and fabrication of quality assurance apparatuses, motion phantoms, patient immobilization devices, and patient-specific treatment accessories.



Andrew Godley, Ph.D.

Associate Professor and Director of Clinical Physics

Dr. Godley joins the Department where he will help to implement upcoming technologies and protocols to continue providing the best treatment for patients. He earned his Ph.D. in the field of high-energy physics from the University of Sydney in 2001, basing his research on experiments at CERN in Geneva, Switzerland. He continued in high-energy physics at the University of South Carolina and Fermilab (Chicago, IL) until 2007 when he switched to the medical physics field, training at the Medical College of Wisconsin in Milwaukee. He then spent seven years as a staff physicist at the Cleveland Clinic where he gained broad experience in radiation therapy. In 2018, he moved to the Miami Cancer Institute to help develop its MR-linac and SAbR programs.



FACULTY PROMOTIONS



Bo Zhao, Ph.D.

Associate Professor

Dr. Zhao was promoted to Associate Professor in September. She joined the Department in 2012 and has worked as a certified medical physicist and lead physicist for the Department's head and neck disease-oriented team where she provides both routine and special clinical physics services. Since joining the Department she has worked as a machine physicist to maintain the quality of linear accelerators by performing monthly and annual QA checks and working with engineers to address machine problems.



AWARDS & RECOGNITION



Robert Timmerman

M.D., FASTRO, FACR

Dr. Timmerman, Professor and Vice Chair of Radiation Oncology and Professor of Neurosurgery, focuses on central nervous system cancers. Dr. Timmerman was awarded the Patricia and William L. Watson Jr., M.D. Award for Excellence in Clinical Medicine - UT Southwestern's highest honor in clinical care. This award recognizes a UTSW clinician who "exemplifies excellence in patient care and is a leader in advancing clinical innovations."



Nina Sanford

M.D.

Dr. Sanford, Assistant Professor, is part of our gastrointestinal team. Dr. Sanford was named Dedman Family Scholar in Clinical Care. The Dedman Foundation established the Dedman Family Endowed Program for Scholars in Clinical Care in 2009 to help recruit the most promising early career physicians to UTSW. Additionally, Dr. Sanford was recognized as an AAAS IF/THEN Ambassador. IF/THEN is a national initiative that aims to further advance women in science, technology, engineering, and math (STEM) by empowering current innovators and inspiring future generations.



Prasanna Alluri

M.D., Ph.D.

Dr. Alluri, Assistant Professor, part of our breast team, also runs his own lab, which is focused on understanding the molecular mechanisms of treatment resistance in breast cancer. Dr. Alluri was awarded ASCO's Young Investigator Award, which provides funding to promising investigators to encourage and promote quality research in clinical oncology.

CLINICAL TRIALS

Department News

Breast

THERAPEUTIC

STU 042018-083: GammaPod 5 fxn - Phase II Multi-Center Trial Evaluating 5 Fraction S-PBI (Stereotactic Partial Breast Irradiation) for Early Stage Breast Cancer Using the GammaPod

STU 052018-052: GammaPod Boost - Tumor Bed Boost Using a Breast-Specific Radiosurgery Device, the GammaPod: Registry Study and Evaluation of Quality of Life with Development of Sizing Nomogram

STU 062015-085: SF CK Breast - Phase I Dose Escalation Trial of Single Fraction Adjuvant Stereotactic Body Partial Breast Irradiation (SB-PBI) for Early Stage Breast Cancer

STU 2018-0236: Tailor RT - A Randomized Trial of Regional Radiotherapy in Biomarker Low-Risk Node-Positive Breast Cancer

CNS

THERAPEUTIC

STU 122016-064: Neurocog. Decline - Phase I/II Trial to Determine the Neurocognitive Decline in Patients with Multiple (>6) Brain Metastases Treated with Distributed Stereotactic Radiosurgery

STU 42011-075: Pituitary - Interstitial Radioactive Iodine Implants for the Treatment of Pan-Invasive Pituitary Macroadenomas

STU 022015-106: SRS-Dose Escalation - A Phase I Dose-Escalation Study of Stereotactic Radiosurgery for Brain Metastasis without Whole Brain Radiation

NON-THERAPEUTIC

STU 042018-100: AVM - Validation Study of Treating Arteriovenous Malformation with Stereotactic Radiosurgery Using CT Angiography for Treatment Planning

Gastrointestinal

THERAPEUTIC

STU 102014-018: Liver Mets Brachy - A Phase I Therapeutic Dose-Escalation Study Using Percutaneous Image-Guided Navigation for High-Dose Rate Brachyablation of Primary Liver Lesions

STU 022016-002: CIPHER - A Prospective, Multi-Center Randomized Phase 3 Trial of Carbon Ion Versus Conventional Photon Radiation Therapy for Locally Advanced, Unresectable Pancreatic Cancer

Genitourinary

THERAPEUTIC

STU 022017-032: NRG-GU002 - Phase II-III Trial of Adjuvant Radiotherapy and Androgen Deprivation Following Radical Prostatectomy with or without Adjuvant Docetaxel

STU 042016-046: Oligo Metastatic Renal Cell - Phase II Trial of SAbR for Patients with Oligometastatic Renal Cell Carcinoma

STU 122016-067: Salvenza - Phase II Randomized Placebo-Controlled Double-Blinded Study of Salvage Radiation Therapy (SRT) Plus Placebo Versus SRT Plus Enzalutamide in Men with High-Risk PSA-Recurrent Prostate Cancer after Radical Prostatectomy (SALV-ENZA)

STU 062014-027: High-Risk Spacer - Phase I Clinical Trial of Stereotactic Ablative Radiotherapy (SABR) of Pelvis and Prostate Targets for Patients with High-Risk Prostate Cancer

STU 022015-058: IVC Thrombus - Safety Lead-In Phase II Trial of Neo-Adjuvant SABR for IVC Tumor Thrombus in Newly Diagnosed RCC

STU 052018-001: Oligo-Progressive - A Phase II Trial of Stereotactic Ablative Radiation Therapy (SABR) for Patients with Oligo-Progressive Renal Cancer (RCC)

STU 092017-018: POTEN-C - Prostate Oncologic Therapy While Ensuring Neurovascular Conservation (POTEN-C): 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

STU 2018-0269: NRG-GU006 - A Phase II, Double-Blinded, Placebo-Controlled Randomized Trial of Salvage Radiotherapy with or without Enhanced Anti-Androgen Therapy with Apalutamide in Recurrent Prostate Cancer

STU 2019-1065: RTOG-3506 - STEEL: A Randomized Phase II Trial of Salvage Radiotherapy with Standard vs Enhanced Androgen Deprivation Therapy (with

Enzalutamide) in Patients with Post-Prostatectomy PSA Recurrences with Aggressive Disease Features

Gynecology

THERAPEUTIC

STU 2018-0151: AZ Durva/Treme SABR - Phase I Multi-Center Study of Stereotactic Ablative Radiotherapy (SABR) in Combination with Durvalumab and Tremelimumab in Patients with Recurrent/Metastatic Advanced Cervical, Vaginal, or Vulvar Cancer

Head & Neck

THERAPEUTIC

STU 072014-041: NRG-HN001 - Randomized Phase II and Phase III Studies of Individualized Treatment for Nasopharyngeal Carcinoma Based on Biomarker Epstein Barr Virus (EBV) Deoxyribonucleic Acid (DNA)

STU 122017-043: LT-SABR - A Phase II Trial of Glottic Larynx Stereotactic Ablative Radiotherapy (LT-SABR) for Early Stage Glottic Larynx Cancer

STU 022011-213: RTOG-1008 - A Randomized Phase II/Phase III Study of Adjuvant Concurrent Radiation and Chemotherapy Versus Radiation Alone in Resected High-Risk Malignant Salivary Gland Tumors

STU 2019-0711: INRT- AIR - A Prospective Phase II Study of Involved Nodal Radiation Therapy using Artificial Intelligence-Based Radiomics for Head and Neck Squamous Cell Carcinoma

NON-THERAPEUTIC

STU 2019-0748: IPET - Pilot Study of Interim PET/CT in Patients Treated with Definitive Chemoradiotherapy for Head and Neck Cancer

Lung

THERAPEUTIC

STU 042017-024: NRG-LU002 - Maintenance Systemic Therapy Versus Consolidative Stereotactic Ablative Radiation Therapy (SABR) plus Maintenance Systemic Therapy for Limited Metastatic Non-Small Cell Cancer

Department News

(NSCLC): A Randomized Phase II/III Trial

STU 022015-069: JoLT-Ca A Randomized Phase III Study of Sublobar Resection (SR) versus Stereotactic Ablative Radiotherapy (SAbR) in High-Risk Patients with Stage I Non-Small Cell Lung Cancer (NSCLC), the STABLE-MATES Trial

STU 2018-0261: ADRIATIC - A Phase III, Randomized, Double-Blind, Placebo-Controlled, Multi-Center, International Study of Durvalumab or Durvalumab and Tremelimumab as Consolidation Treatment for Patients with Limited Stage Small-Cell Lung Cancer Who Have Not Progressed Following Concurrent Chemoradiation Therapy (ADRIATIC)

STU 2019-0858: PACIFIC 4/RTOG-3515 - A Phase III, Randomized, Placebo-Controlled, Double-Blind, Multi-Center, International Study of Durvalumab Following Stereotactic Ablative Radiation Therapy (SAbR) for the Treatment of Patients with Stage I/II Non-Small Cell Lung Cancer (PACIFIC-4/RTOG-3515)

NON-THERAPEUTIC

STU 062016-073: Lung SAbR - Investigating Radiation-Induced Injury to Airways and Pulmonary Vasculature in Lung Stereotactic Ablative Body Radiotherapy (SAbR)

STU 102016-005: Optical Imaging - Optical Surface Monitoring for Deriving Real-Time Volumetric Imaging

STU 022017-075: Vision RT - VisionRT-Based Deep Inspiration Breath-Hold (DIBH) Respiratory Motion Management Strategy, a Pilot Study for Thoracic and Abdominal Tumors Stereotactic Body Radiotherapy

All/Other

NON-THERAPEUTIC

STU 072010-098: Tissue Procurement - Tissue Procurement and Outcome Collection for Radiotherapy-Treated Patients

Albuquerque K, Hrycushko BA, et al. Compendium of fractionation choices for gynecologic HDR brachytherapy--an American Brachytherapy Society task group report. *Brachytherapy*. 2019;18(4):429-36. PMID: 30979631.

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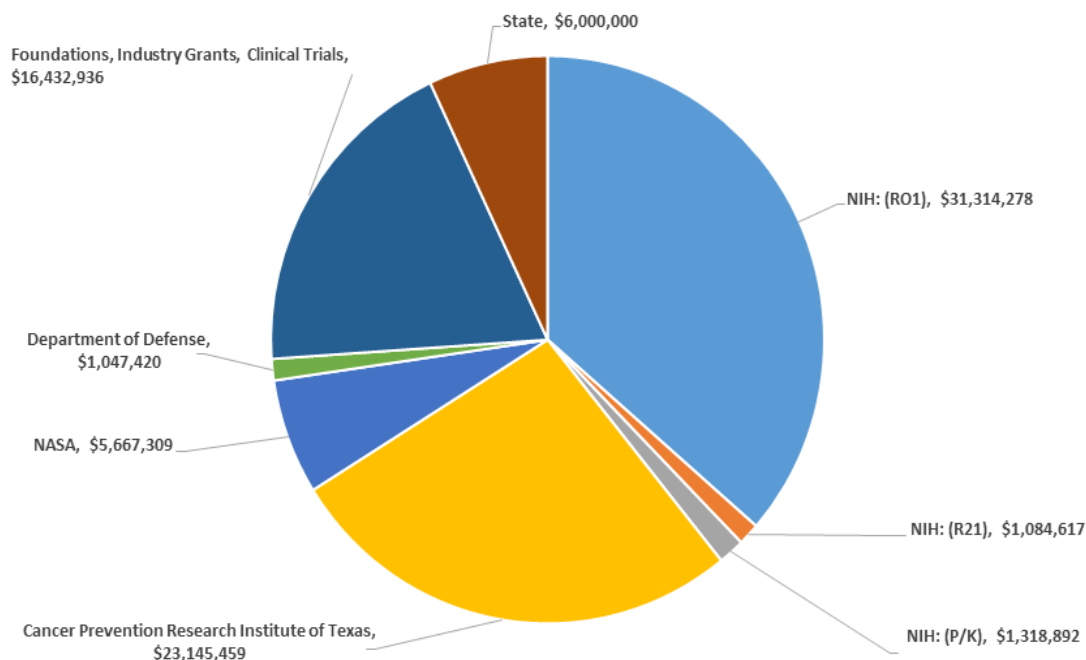
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GRANTS, SPONSORED RESEARCH & PARTNERSHIPS

Awarded Research Funding FY15 - FY19



Our team of dedicated researchers and scientists innovate to accelerate breakthrough advancements in the field of radiation oncology. In 2019, UT Southwestern ranked eighth overall in NIH funding nationwide among all radiation oncology departments.

FY 2019 AWARDED RESEARCH BY FACULTY

Todd Aguilera, M.D., Ph.D., awarded \$100,000 from Shelby Foundation Pancreatic Cancer Research Grant for his work on developing novel antibodies to target pancreatic cancer, and \$17,820 from iTeos for work evaluating immunologic effects of A2AR inhibition in combination with radiation therapy in immunologically unresponsive cancers.

Prasanna Alluri, M.D., Ph.D., received \$50,000 DocStars Award from Cary Council, which supports young UT Southwestern investigators working on promising early stage research and a \$150,000 grant from the Office of the President of UT Southwestern to work in collaboration with Dr. Salomon Stemmer at Rabin Medical Center in Israel to study treatment resistance in breast cancer.

Asaithamby Aroumougame, Ph.D., and **Hesham Sadek, M.D., Ph.D.**, Department of Internal Medicine, awarded a \$900,000 CPRIT entitled "Modulating Cardiomyocyte DNA Damage in Response to Genotoxic Stress."

Benjamin Chen, Ph.D., awarded \$75,000 by NCI and \$1,852,875 by NIH/NCI for DNA-PKcs and PIDD interaction in DNA damage response.

Hak Choy, M.D., FASTRO, awarded \$1,000,000 from the State of Texas for Heavy Ion Center for Advanced Radiation Therapy.

Neil Desai, M.D., M.H.S., accepted \$250,000 on behalf of GU team from Once Upon A Time: Once Upon A Time Advanced Bladder Cancer Research. Funding originally obtained by Dr. Yull Arriaga.

Aurelie Garant, M.D., received a Kidney Cancer SPORE Career Enhancement Program award for \$20,000 to fund a companion study on patients affected with kidney tumors invading the inferior vena cava.

Raquibul Hannan, M.D., Ph.D., awarded the Prostate SPORE Development SEED grant for \$50,000. In addition, alongside Xiankai Sun, Ph.D., Department of Radiology, he was awarded \$486,000 by the Department of Defense for immune checkpoint-targeted immuno-PET to identify therapy-induced adaptive resistance.

Steve Jiang, Ph.D., Xuejun Gu, Ph.D., and **Raquibul Hannan, M.D., Ph.D.**, awarded \$322,642 by Varian for artificial-intelligence-based clinical target volume segmentation for postoperative

radiotherapy of Prostate Cancer.

Steve Jiang, Ph.D., and **Jing Wang, Ph.D.**, awarded \$285,000 by Varian for CT image synthesis from CBCT images with artifacts and truncations for adaptive re-planning via deep learning.

Wen Jiang, M.D., Ph.D., awarded \$449,982 by Susan G. Komen for engaging the immune system to improve metastatic breast cancer treatment, \$760,131 by NIH/NCI K08 for a phagocytosis-modulating nanomedicine for targeted breast cancer immunotherapy, and \$50,000 by ABTA for bridging innate and adaptive GBM immunity via phagocytosis checkpoint blockade.

Michael Story, Ph.D., received \$371,650 from Galera: examination of the radioprotection and anti-tumor effects of galera therapeutics GC4419 and GC4401, and \$250,000 by AACR/Novocure for exploiting the conditional vulnerabilities caused by TTFIELDS exposure.

Jing Wang, Ph.D., and **Raquibul Hannan, M.D., Ph.D.**, awarded an NIH/NIBIB RO1 grant for \$1,427,514 for real-time prostate lesion tracking during SAbR.

Kenneth Westover, M.D., Ph.D., awarded \$25,000 by the University of Texas lung SPORE and \$195,000 by Welch to cover various aspects of SRC inhibitor development.



Research Highlights

RESEARCH

MOLECULAR RADIATION BIOLOGY

New breakthrough role for enzyme in the DNA damage response

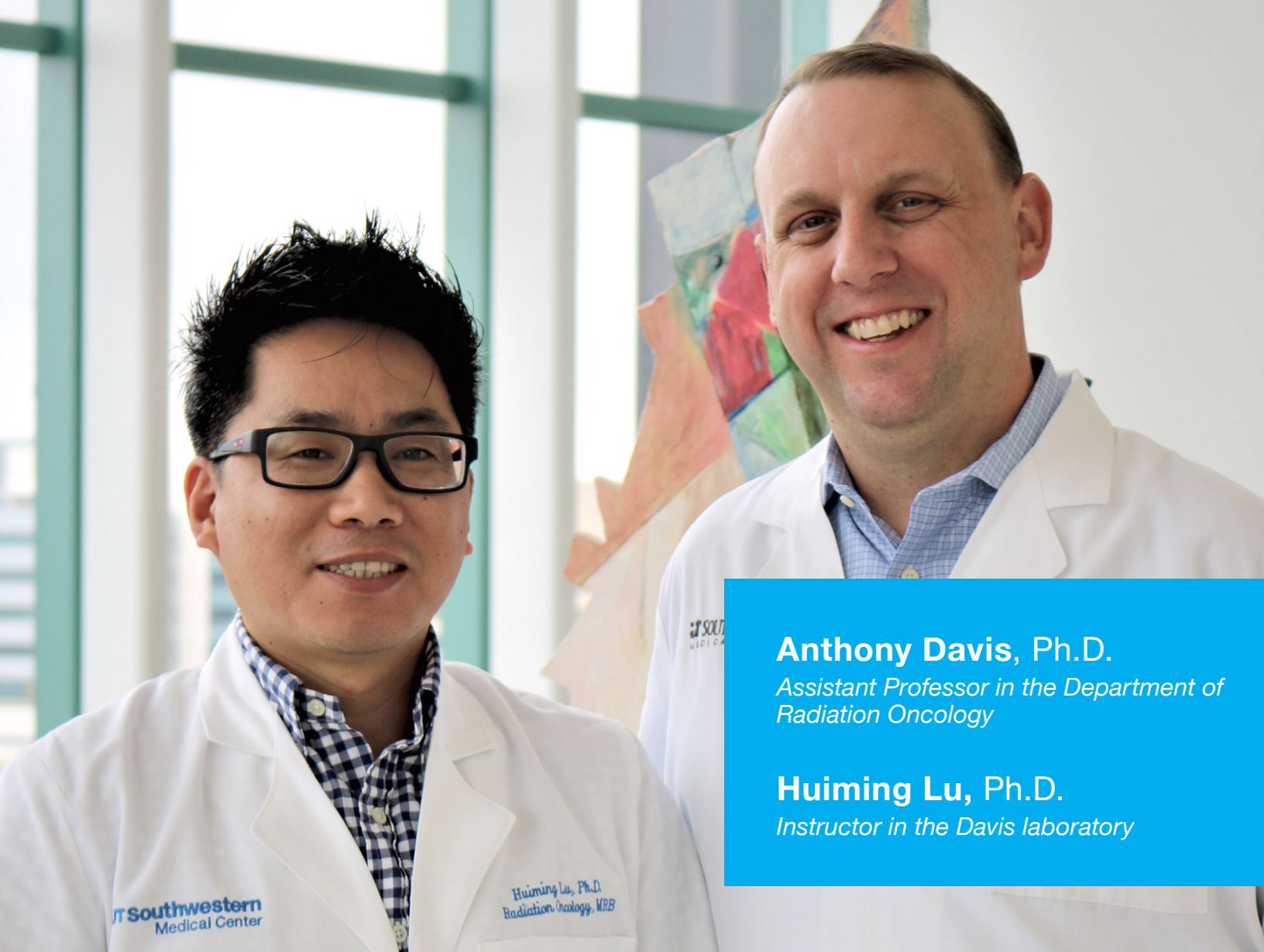
By Damiana Chiavolini, Ph.D.

Researchers in the Department's Division of Molecular Radiation Biology have found a new key role for an enzyme named DNA-dependent protein kinase catalytic subunit (DNA-PKcs) in initiating the DNA damage response (DDR), a complex network of processes that is responsible for the cellular response to and repair of DNA double strand breaks (DSB). Defects in the DDR can lead to cancer, premature aging, and other diseases of the nervous, immune, and reproductive systems; therefore, it is important to understand the factors and mechanisms that modulate its proper functioning in order to design future medical therapies.

The study, recently published in the high-impact

factor journal *Nucleic Acids Research (NAR)*, was led by UT Southwestern alumnus Anthony Davis, Ph.D., Assistant Professor, and his team. Using novel human cell lines generated by the Davis Lab and its collaborators at the University of Minnesota, the investigators found that DNA-PKcs is required for the initial cellular response to DNA breaks. Specifically, DNA-PKcs' enzymatic activity initiates phosphorylation, a transfer process that forms energy-rich molecules, of two chromatin factors after exposure to ionizing radiation, leading to chromatin relaxation, which, in turn, recruits the rest of the DDR machinery to begin repairing the DNA breaks generated by the radiation.

Selected by the journal's editors upon the recommendation of NAR's reviewers and editorial board members, this paper received



Anthony Davis, Ph.D.

Assistant Professor in the Department of Radiation Oncology

Huiming Lu, Ph.D.

Instructor in the Davis laboratory

“Breakthrough” status, which is bestowed upon high-impact studies that solve long-standing problems and provide exceptional innovation in the field of nucleic acids research. “Breakthrough” articles represent the best 1 to 2% of papers published in NAR.

“Our study challenges the current dogma that the ataxia telangiectasia mutated (ATM) enzyme is the main factor responsible for initiating the DDR,” says Dr. Davis. “Previously, we had identified that DNA-PKcs is quickly recruited to DSBs, but it was unknown what DNA-PKcs’ enzymatic activity did once it was recruited. Our study shows that DNA-PKcs is not a back-up player in the DDR as initially believed, but plays an active role in this process and is upstream of ATM.”

“We believe that DNA-PKcs’ activity initiates the DDR and that ATM amplifies the signal that DNA-PKcs started,” notes lead author Huiming Lu, Ph.D., Instructor in the Davis laboratory, who was involved with most of the experiments and with drafting the paper. “We are pleased that we could identify an initial role for DNA-PKcs’ enzymatic activity and have now started to identify other proteins that DNA-PKcs regulates immediately after inducing DSBs,” adds Dr. Davis.

Dr. Davis earned a Ph.D. in cell regulation under the mentorship of Marc Mumby, Ph.D., retired Professor in the Department of Pharmacology. He trained as a postdoctoral fellow with David Chen, Ph.D., also a retired Professor in the Department of Radiation Oncology, and is currently on the tenure track.

WOMEN IN RESEARCH

INTERVIEW

Mu-Han Lin, Ph.D.

By Damiana Chiavolini, Ph.D.

Mu-Han Lin, Ph.D., Assistant Professor, works as a medical physicist in our clinic. She earned a master's degree in 2005 and a Ph.D. in 2010, both in medical physics, at the National Tsing Hua University in Taiwan. Dr. Lin completed her residency in 2013 at the Fox Chase Cancer Center in Philadelphia. We talked about her interest in new treatment technologies, her most important accomplishments, and her experience as a woman in the field of medical physics.

Q. What inspired you to start a career in medical physics?

M-H L: I always wanted to work in the medical field. I was fascinated by how people worked together to help patients and even by the smell of hospitals. I studied medicine for two years and then I realized I couldn't bear the sight of blood and dealing with so many emotions. Therefore, I decided to switch to a career that would allow me to be behind the scenes while still working in a clinical setting. I soon discovered that medical physics, a professional area that would allow me to be a "scientist in a hospital," might be a perfect fit for me, so I decided to pursue my graduate studies and residency in the field.

Q. What do you enjoy the most about your job?

M-H L: I appreciate that much of the research in medical physics can be translated to clinical use more quickly than in other scientific areas. I

enjoy learning new things in a dynamic and ever-growing field and clinically implementing new tools that will help improve clinical workflows. I am grateful to work at UTSW. We receive support from both clinical and programming teams to develop tools that will improve clinical quality and efficiency, making a difference in patients' lives on a daily basis.

Q. What are your research interests?

M-H L: I am especially interested in translational science projects and clinical implementation of new technologies. I am currently working on translating research products developed by our Medical and Artificial Intelligence and Automation (MAIA) lab and applying them to the clinic. We recently worked on a 3D dose prediction tool that will allow physicians to examine and review radiation doses before the planning phase to design the best treatment for patients with cancer.

Q. What are you most proud of so far?

M-H L: I was especially proud of receiving the "Educator of the Year" award in 2015 from the American Society for Radiation Oncology for teaching medical residents at the University of Maryland School of Medicine, where I worked as a medical physicist. I supervised trainees from different divisions to implement post-treatment dose reconstruction and validation for patients receiving radioembolization for liver cancer, and also to implement breath-hold treatments for patients with left-sided breast cancer using real-time surface image technology. I coached medical residents to present their work at national meetings and to publish their work in peer-reviewed journals. The work and recognition were highly rewarding!



Mu-Han Lin, Ph.D.
Assistant Professor of Radiation Oncology

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?

M-H L: My experience as a woman in medical physics has primarily been positive. As a mom of two young children, I have to balance a busy job schedule and my family life, which isn't easy. I work out three times a week to keep physically and mentally strong, and try to stay positive like a proton!

Q. What advice do you have for young women wishing to pursue a career in physics or biomedical engineering?

M-H L: If you want to pursue a career in medical physics, just go for it and don't let anything stop you. I would recommend women physicists look for events and trainings held by the American Association of Physicists in Medicine and learn more about medical physics. Always stay healthy and strong because this kind of job can be intense and require some heavy lifting and other activities. And always keep a positive attitude.

INTERVIEW

Katy Swancutt, D.V.M., Ph.D.

By Damiana Chiavolini, Ph.D.

Katy Swancutt, D.V.M., Ph.D., a postdoctoral fellow in the laboratory of Todd Aguilera, M.D., Ph.D., brings to our Department her unique expertise blending small animal veterinary medicine and radiation cancer biology research. Dr. Swancutt completed her B.S. degree in biology at California State University Long Beach and her D.V.M. and Ph.D. at the College of Veterinary Medicine and Biomedical Sciences at Colorado State University, where she studied stereotactic radiation therapy in dogs with soft tissue sarcomas. She is currently developing orthotopic mouse models to study pancreatic cancer progression and response to radiotherapy and immunotherapy.

Q. How did you decide to become a veterinarian?

KS: As a life-long animal lover, my earliest memory is of playing with my first dog at 3 years old. He suffered from atopic dermatitis, and I have vivid memories of going to the vet's office for his treatments. By the time I turned 5, I had already decided I wanted to become a vet. I pursued the small animal medicine track but also spent much time working with horses, cattle, small ruminants, birds, reptiles, small mammals (both exotic pets and laboratory animals), and even some residents of the Colorado Wild Animal Sanctuary and Cheyenne Mountain Zoo.

Q. How did you become interested in research?

KS: My first experience in research was in college when I worked as a research assistant in a radiation chemistry laboratory. My early efforts landed me an Arnold and Mabel Beckman scholarship that allowed me to study the kinetics of free radical molecules and to work on linear and Van de Graff particle accelerators at the Notre

Dame Radiation Laboratory and Brookhaven National Labs. I enjoyed the competitive nature of scientific research and the challenge of being part of high-profile scientific projects.

Q. What brought you to UT Southwestern, and what do you like most about your job?

My reasons for coming here are related to funding. Veterinary medical schools only bring in a tiny fraction of the research funds that human medical institutions do. It was frustrating to plan my projects toward a certain direction but to fail after running out of funds or not having access to cutting-edge technology and expertise. We had advantages in terms of accessing animal patients for clinical trials (UTSW may consider these "preclinical" trials), but I wanted to work in an environment better equipped for basic scientific research. In that regard, UTSW has delivered beyond my expectations. Here, I have the freedom to balance different projects without financial constraint, and I can use the skills I learned in veterinary school (e.g. surgical techniques, abdominal ultrasound, necropsy, and histopathology). The best part of my job, however, is interacting with the brilliant members of my lab, learning new techniques, and doing research that asks fundamental questions about biology but that still connects me with the animals.

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

KS: Having mostly been surrounded by women students in veterinary school, I was a little surprised to see that only a few women occupy faculty positions in radiation oncology and to see that none of these positions are leading a lab. More incentives and mentoring opportunities should be offered to women interested in entering this field. I am currently looking for opportunities to start conversations with more experienced women researchers who could provide mentorship and guidance to facilitate my path toward becoming an independent investigator.



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

KS: My career path is unusual, but there are plenty of veterinarians with research training who would be interested in careers in research but cannot pursue them for financial reasons. We all have the medical training to succeed in translational research, but as D.V.M., Ph.D. graduates, we could dedicate more time to research without serving the clinical hours that ultimately consume the time and energy of our M.D., Ph.D. counterparts. For cancer research in particular, spontaneously occurring tumors in dogs remain the best “preclinical” model of human disease so far; radiation oncologists in particular have gained tremendous knowledge from approaching veterinary radiation oncologists with research projects to be conducted in purpose-bred or pet animals and translated to humans. Vets are well-poised to advance biomedical research, and I would encourage any woman to consider it as an alternative career path. Never stop looking for opportunities to connect, collaborate, brainstorm, and improve your scientific, leadership, and soft skills. Always look for mentoring opportunities, especially those provided by other women. And don’t be afraid to make that jump out of your comfort zone; take an alternative or unusual career path, and pursue scary but rewarding opportunities.

Katy Swancutt, D.V.M., Ph.D.

Postdoctoral fellow in the laboratory of Todd Aguilera, M.D., Ph.D.



Education Highlights

The Department of Radiation Oncology is committed to providing comprehensive and advanced educational programs to train the next generation of medical professionals, as well as those already established in their career.

Our programs include multi-year, accredited training programs, including both a radiation oncology clinical and medical physics residency program, several graduate programs, and an SAbR/SBRT fellowship. We also offer several specialized training programs, including SAbR/SBRT, Gamma Knife, and CyberKnife that are offered multiple times each year.

Our programs are widely attended by health care professionals around the world. To learn about our programs, visit us at utsouthwestern.edu/education/medical-school/departments/radiation-oncology/education-training/.

Jan Wilkens, Ph.D., Professor and Head of Medical Radiation Physics, Klinikum rechts der Isar, Technical University of Munich, who recently attended the Gamma Knife Training Program:



*I think the quality of medical treatment here at UT Southwestern is so high, so it made sense to attend this course. I like the mixture of hands-on training and lectures; **having a mixed group of physicists and faculty is extremely helpful** and, as a physicist, I was shown exactly what I needed to know.*

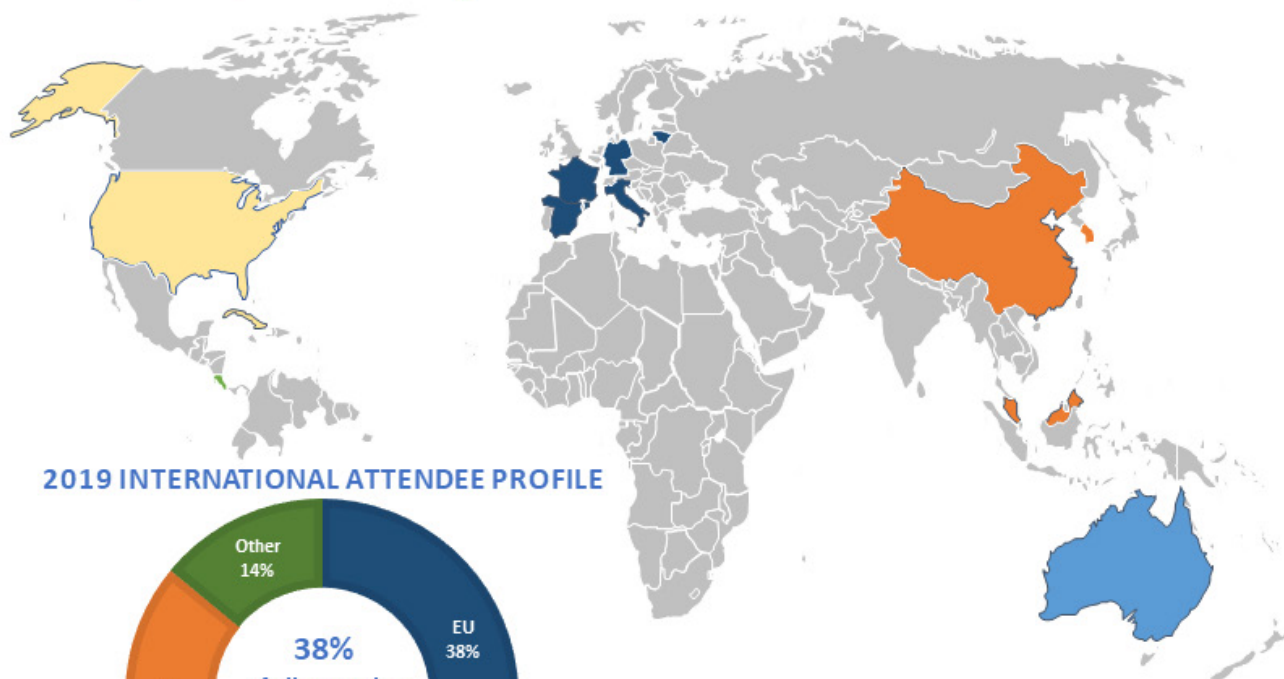


One-Year SAbR/SBRT Fellowship

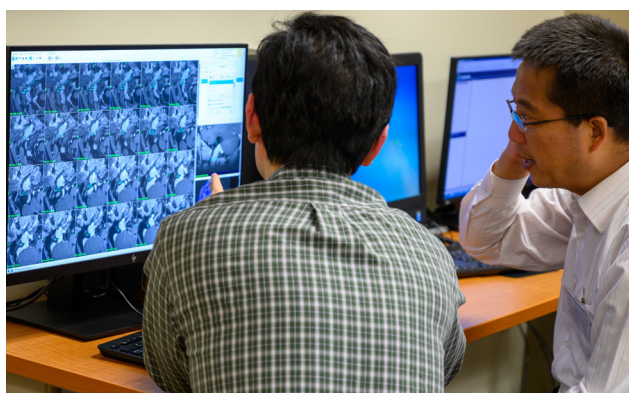
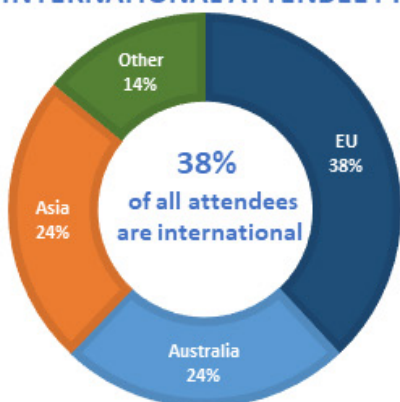
- Accepting applicants for 2020 (course runs from July 1 through June 30).
- Fellowship is led by Program Director Michael Folkert, M.D., Ph.D., Assistant Professor, and Program Advisor Robert Timmerman, M.D., FASTRO, FACR, Vice Chair, Professor, and Medical Director.
- Clinical training focuses on application of SAbR/SBRT to treat malignant and benign tumors of the brain, base of skull, head and neck, lung, spine, pancreas, and pelvis with an evidence-based approach.
- For more info about the program, visit: utsouthwestern.edu/education/medical-school/departments/radiation-oncology/education-training/sbrrt-fellowship/.

+ TRAINING PROGRAMS

SABR/SBRT | CYBERKNIFE | GAMMAKNIFE ICON



2019 INTERNATIONAL ATTENDEE PROFILE





DISEASE-ORIENTED TEAM FACULTY

Our Team

BREAST



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Assistant Professor
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Shohreh Bahrami, APRN, FNP-BC

*Nurse Practitioner
Trained: Texas Woman's University*

CENTRAL NERVOUS SYSTEM



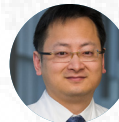
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