UT Southwestern Harold C. Simmons Comprehensive Cancer Center

# ARGE!

DEPARTMENT OF RADIATION ONCOLOGY

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#### COVID-19 and our promise to our patients and families

Dear colleagues,

In light of the COVID-19 pandemic, our commitment to delivering exceptional patient care has not changed. However, how we go about delivering that care to ensure our patients and personnel are in the safest environment has.

Our clinics have precautionary measures in place to reduce the risk for COVID-19 transmission:

- · All patients, visitors, and personnel are screened daily and must wear a mask
- · We provide social distancing measures at all times
- Extra cleaning efforts are in place throughout the day

We are committed to offering the most advanced and innovative approaches to cancer care while meeting the needs of our patients.

Virtual medicine is one way to provide patients with access to our radiation oncologists from the comfort of home. When virtual medicine is a viable option, many of our patients find this to be an easy way to connect with their provider and a great alternative to an in-person appointment.

Virtual medicine is available for many of our appointments, including:

- · New patient visits
- · Managing cancer-related side effects
- Follow-up visits
- Second opinions

We want our patients to know that they have options in their care now and in the future. The way we approach patient care will always be the safest to protect our patients, staff, and the community.



Best cancer center in North Texas



- Professor & Department Chair

# Enhancing Radiotherapy with Superoxide Dismutase Mimetics

Featured Story By Jonathan Feinberg, Ph.D.

By using novel superoxide dismutase mimetics, UTSW Radiation Oncology and Galera Therapeutics seek to create a more desirable balance between the therapeutic effects of radiation and its unwanted side effects.

Radiation therapy kills tumor cells, in part, by generating an overabundance of reactive oxygen species in irradiated tissue. These reactive oxygen species include superoxide, which does not kill tumor cells but can damage normal, non-cancerous cells. All cells produce superoxide as a normal part of their metabolism but keep it in check by producing superoxide dismutase enzymes (SODs) that convert superoxide to hydrogen peroxide, which is then converted to water and oxygen. The burst of superoxide produced by radiation therapy, however, overwhelms natural levels of SODs and damages normal tissues irradiated during therapy, which can cause substantial treatment-related toxicity.

Researchers and clinicians in the Department of Radiation Oncology at UT Southwestern, in collaboration with industry partner Galera Therapeutics, are pursuing an innovative solution to minimize superoxide-related toxicity in normal tissues while enhancing radiation therapy's anti-cancer activity. By using novel superoxide dismutase mimetics, or synthetic compounds that mimic the effects of SODs, to manipulate superoxide dynamics, they seek to create a more desirable balance between the therapeutic effects of radiation and its unwanted side effects.

Galera originally developed the dismutase mimetic GC4419 to alleviate oral mucositis, a painful inflammation of the mucous membranes inside the mouth that commonly results from radiation therapy

for head and neck cancer. This often debilitating side effect occurs when the massive quantities of superoxide generated by irradiation attack the epithelial cells lining the mouth. GC4419 mitigates oral mucositis by converting the superoxide into hydrogen peroxide, which normal cells can detoxify more easily. This promising drug is currently being evaluated for this application in a phase III clinical trial, and it has received Breakthrough Therapy and Fast Track designations by the U.S. Food and Drug Administration.

We believe that GC4419 alters immune cell signaling and protects cells that would ordinarily be killed by superoxide.

When studying GC4419 in pre-clinical models alongside Galera scientists, however, Michael Story, Ph.D., Professor, Vice Chair and Chief of the Division of Molecular Radiation Biology, and his lab made a surprising discovery: the dismutase mimetics not only protect against toxicity from radiation therapy, but they can also increase radiation's anti-tumor efficacy,



Michael Story, Ph.D., Professor, Vice Chair & Chief of the Division of Molecular Radiation Biology

depending on the dose of radiation per treatment fraction. By removing superoxide, dismutase mimetics minimize toxicity to normal tissues when combined with radiation. With high dose per fraction radiation, such as stereotactic ablative radiotherapy (SAbR) protocols, however, their conversion of superoxide into immense quantities of hydrogen peroxide also yields a profound anti-tumor effect that amplifies the therapeutic effects of radiation.

"The anti-tumor mechanism of action, we believe, is through the massive generation of hydrogen peroxide when we irradiate cells at high dose per fraction," Dr. Story explains. "Tumor cells cannot detoxify the hydrogen peroxide quickly enough." Because hydrogen peroxide is toxic to tumor cells, but less toxic to normal cells, combining Galera's dismutase mimetics with SAbR may increase the anti-cancer effects of radiation without exposing normal tissues to additional toxicity.

What's more, Dr. Story and his lab discovered that combining GC4419 with high dose per fraction radiation enhances the immune system's anti-cancer response and synergizes with immunotherapy. They found that adding GC4419 to combination regimens of immune checkpoint and radiation therapies increases the anti-tumor immune response even in pre-clinical models where the checkpoint agent normally has no effect when added to radiation. The dismutase mimetic appears to overcome whatever mechanism allows tumors to evade the immune system in these models.

"We believe that GC4419 alters immune cell signaling and protects cells that would ordinarily be killed by superoxide," Dr. Story explains. Dr. Story's lab has now studied the anti-tumor effects of Galera's dismutase mimetic in pre-clinical models of several different cancers: not just head and neck, but also lung, pancreas, and breast. "The effect appears to be universal," Dr. Story says. "There is even a considerable single-agent effect in head and neck and pancreas."

These findings have prompted new laboratory studies and clinical trials investigating GC4419 as an anticancer agent across different disease sites. Notably, a multi-site pilot phase I/II randomized clinical trial tested the combination of GC4419 with SAbR for patients with locally advanced pancreatic cancer whose tumors could not be surgically removed. UT Southwestern participated in this trial, with Todd Aguilera, M.D., Ph.D., Assistant Professor of Radiation Oncology, leading as site principal investigator. Dr. Aguilera will continue in this role for future trials in collaboration with Galera.

Building upon the insights gained from these studies, Galera has developed GC4711, a second generation of their dismutase mimetics, to increase SAbR's effectiveness against cancer. In support of that, Dr. Story's lab has helped demonstrate that GC4711 performs at least as well as GC4419 in combination with SAbR. Puneeth lyengar, M.D., Ph.D., Assistant Professor and Associate Vice Chair for Clinical Research, will lead a phase I/II clinical trial testing GC4711 in combination with SAbR for patients with non-small cell lung cancer. This trial's rationale derives from pre-clinical findings from Dr. Story's lab that Galera's dismutase mimetics both enhance non-small cell lung cancer tumors' response to high dose per fraction radiation and mitigate lung fibrosis, a common side effect of radiation therapy for lung cancer.

Like earlier versions of the drug, GC4711 is currently delivered intravenously; however, GC4711's unique chemistry is also conducive to formulation for oral delivery. Galera is evaluating several oral formulations of the drug in a phase I trial in healthy volunteers. Once the oral form has been determined, Dr. Story's lab will extend GC4711's application as a radioprotector in a NASA-funded study that investigates the drug as a countermeasure to protect astronauts from the harmful effects of space radiation. In its oral form, the drug



could be taken daily or before an impending radiation exposure, such as a solar storm.

Through groundbreaking collaborative research with industry partners, the Department of Radiation Oncology continues to advance the understanding and treatment of cancer.

\*Dr. Story receives research support from Galera.

Dr. Story holds the David A. Pistenmaa, M.D., Ph.D. Distinguished Chair in Radiation Oncology.



Michael Story, Ph.D. Molecular Radiation Biologist



Puneeth Iyengar, M.D., Ph.D. Radiation Oncologist



**Todd Aguilera**, M.D., Ph.D. Radiation Oncologist



HDR applicator during a brachytherapy procedure in the OR

## UT Southwestern's Brachytherapy Program: The Most Comprehensive of its Kind in North Texas

#### By Ryan Daugherty

UT Southwestern Medical Center has the most comprehensive brachytherapy program in North Texas with a team of radiation oncologists, medical oncologists, and cancer surgeons who work together to provide brachytherapy treatments for a wide range of cancers. Imaging is used during these procedures, which makes treatments safer and more effective – all while maintaining patients' quality of life.

Brachytherapy has been a factor in the curative management of cervical and prostate cancer patients for more than a century. External beam techniques such as intensity-modulated radiation therapy (IMRT), stereotactic ablative radiotherapy (SAbR), and proton therapy are unable to match the dose distribution and purposeful dose escalation achieved by brachytherapy. Led by Michael Folkert, M.D., Ph.D., Associate Professor of Radiation Oncology, UT Southwestern's brachytherapy program provides several ways of delivering treatment to patients.

One aspect of the brachytherapy program is the use of intraoperative radiation therapy (IORT). IORT is a

technique in which radiation treatment is applied to the area at highest risk for tumor relapse at the time of surgery. This allows the surgeon and radiation oncologist direct access without having to unnecessarily irradiate healthy normal tissue, sparing nearby organs. It enables the radiation oncologist to deliver less dosage to those tissues and to shorten the total course of radiation therapy by giving a large portion of the dose while the patient is still asleep in the operating room. This technique can be used to treat almost any tumor at the time of surgery and has an important role in the management of complex colorectal cancers.

With this shielded room, patients are treated in the hospital and don't have to be moved multiple times; it's safer, more convenient, and the treatment is more precise. Linda Farkas, M.D., Professor of Surgery, is the new head of colorectal surgery at UT Southwestern. She has put extensive effort into creating a dedicated tumor board and integrated multidisciplinary group that is focused solely on colorectal cancer, a huge benefit to the brachytherapy program.

"This is really going to help us integrate our management for recurrent or very advanced rectal tumors to be able to offer intraoperative radiation therapy in a very seamless and well-coordinated manner," says Dr. Folkert. "This [IORT] is a powerful tool in the treatment of the most aggressive diseases, and one that very few hospitals have the capability of performing."

UT Southwestern has a well-developed high-dose-rate brachytherapy program for prostate cancer patients. In 2015, prostate cancer brachytherapy patients at UT Southwestern were treated with permanent seed implants, in which radioactive iodine or cesium seeds would be permanently placed inside the patient. In 2018, high-dose-rate brachytherapy was commissioned at UT Southwestern, where a powerful radiation source could be temporarily placed in the prostate via brachytherapy needles and then removed at the end of the treatment.

There are many benefits to high-dose-rate brachytherapy. It can be used for all stages of prostate cancer and, specifically, has been shown to have a significant cancer control benefit in therapy for highrisk prostate cancer. Additionally, after treatment is completed, no radioactive material or radiation are left inside the patient.

Imaging quality has improved across modalities such as CT, ultrasound, and MRI, allowing visual optimization of tumor and normal anatomy for preplanning, intraoperative guidance, and image-guided brachytherapy. Imageguided, high-dose-rate brachytherapy is a new technology at the intersection of imaging and the delivery of radiation offered at UT Southwestern.

"This method allows physicians to see more precisely where radiation is going," says Kevin Albuquerque, M.D., Professor of Radiation Oncology, who leads the gynecological brachytherapy team for UT Southwestern. "With this technique, our team can use a variety of imaging tools to match the location of tumors at the time of treatment with the planning location."



Post-implant dosimetry plan for a low-dose-rate prostate seed implant

Cervical cancer patients receiving brachytherapy at UT Southwestern are treated in a special "shielded" operating room. Previously, patients would have the treatment applicator implanted inside them in the hospital operating room, and then be transported in an ambulance to the radiation oncology center to receive the radiation treatment.

"That process was inconvenient and uncomfortable for patients; they experienced a lot of transfers from stretchers to beds with the treatment applicator in place, which had the potential for the needles to migrate to a different position from where they were implanted," says Dr. Albuquerque. "With this shielded room, patients are treated in the hospital and don't have to be moved multiple times; it's safer, more convenient, and the treatment is more precise."



Linda Farkas, M.D. Surgeon



Michael Folkert, M.D., Ph.D. Radiation Oncologist



Kevin Albuquerque, M.D., FACR Radiation Oncologist

## Patient Story: Brachytherapy

By Ryan Daugherty

In 2017, Deanna Ireland, 54, was working as a café manager for a local school district in Frisco, Texas. A big part of her job involved lifting heavy items and storing them in the kitchen freezers, a routine task she never had any problems with. However, there came a point where lifting became an issue and her co-workers would have to jump in and help.

"I just remember having pain," she says. "My joints and muscles hurt, but it was mostly in my upper body; I really didn't think much of it. I just thought 'something's going on' and that it wasn't a big deal."

It became a big deal once she started to notice spotting. She had been seeing her gynecologist regularly and just six months earlier they had found an abnormality. However, after testing, results came back inconclusive.

She planned to see a different gynecologist for a second opinion, but as the spotting worsened, she went back to her usual gynecologist because she could be seen sooner.

What she was told came as a shock.

"I told her that something was wrong," says Mrs. Ireland. "She ran another test and, soon after, called me at home and said, 'You have cancer."

Mrs. Ireland was set up with an oncologist and a radiation oncologist in Dallas who told her she had stage 3B vaginal cancer. The plan included three different forms of treatment – chemotherapy, radiation, and brachytherapy.

Mrs. Ireland's plan involved five rounds of chemotherapy, 31 rounds of radiation, and a referral to UT Southwestern for brachytherapy.

Brachytherapy is a special type of radiation therapy that can be very effective for targeting cancerous tumors. It involves the use of small radioactive sources such as capsules, seeds, pellets, or wires that are implanted into the body either temporarily or permanently. This treatment method can deliver a high dose of radiation to a small area, thereby maximizing cancer killing while minimizing damage to nearby healthy tissues.

"He [the primary oncologist] told me he was going to send me to the best, and that was Dr. Albuquerque at UT Southwestern," she says.

Kevin Albuquerque, M.D., FACR, Professor and Holder of the Ken Sharma Professorship in Radiation Oncology, is one of the few radiation oncologists in North Texas who offers specialized brachytherapy – specifically, image-guided, high-dose rate brachytherapy to treat tumors in the gynecological tract.

Mrs. Ireland's treatment entailed complex interstitial brachytherapy, a treatment combining templatebased interstitial brachytherapy with intracavitary brachytherapy and involving the placement of radioactive sources in a cavity close to the tumor.

"Her cervical cancer type was very extensive, which is why she needed this procedure," says Dr. Albuquerque. "The alternative, had she not opted for this, would have been taking out all of her surrounding organs, so we spared that for her."

From the minute Mrs. Ireland met Dr. Albuquerque, she felt she was in the best hands. She recalls going into the

waiting room "nervous and scared to death." However, Dr. Albuquerque turned that fear into confidence.

"He told me 'We're going to cure you'," she says. "Not all doctors have good bedside manner, but he does. He had my scans and sat right down with me and showed us where, what, and how everything was going to happen. And, if we didn't do something, what would happen next."

Mrs. Ireland's pre-brachytherapy MRI scan showed good response. However, there was thickening of the vaginal wall that indicated residual cancer. She successfully underwent the brachytherapy procedure, which involved placing needles into the tumor in a special "shielded" brachytherapy operating room at William P. Clements Jr. University Hospital (CUH).

This operating room has a brachytherapy machine that allows patients to receive treatments easily, as inpatients at CUH. This was very convenient for Mrs. Ireland as she received five total treatments over a three-day stay in the hospital. In the past, patients would have required ambulance transfer to the Radiation Department, a highly painful process.

Mrs. Ireland took extremely well to the procedure and experienced no noticeable pain during the actual treatments. Two important factors in getting through daily treatments were maintaining a positive attitude and eliminating the negativity around her. She would drive herself to radiation treatments every day with her husband, which helped her feel as if she was still strong and in control of something. After good appointments, she would reward herself by going to Starbucks. During the entire treatment process, she was able to take time off work and a few additional months after treatment as well. Her husband could work from home, which was a key factor in her recovery.

About two weeks after treatment, Mrs. Ireland says she was ready to go back to work but was told to stay home a while longer to fully recuperate. She mentions that she started to feel better not long after the treatment needles were taken out in the operating room. Three years out, the only side effects



Deanna Ireland with her husband

are occasional fatigue and joint soreness, but she is currently managing those.

Today, Mrs. Ireland is retired and lives in Maryland with her husband. Her daughter is married and attending college, and she recently welcomed a new grandchild. She is living life to the fullest and can't be more thankful for the care she received at UT Southwestern.

"Ever since I had this treatment, I've been telling people to go to UT Southwestern," she says. "They are a cutting-edge hospital with the best people who really want to help patients. I would tell anyone to go there."



Kevin Albuquerque, M.D., FACR Radiation Oncologist

## + FEATURED CLINICAL TRIAL

**Department News** 

STU 2019-1506: A Phase II Trial of Stereotactic Ablative Radiation (SAbR) for Urothelial Cancer Patients with Progression While on Anti-PD-1/PD-L1 Immunotherapy

- Condition: Stage IV urothelial cancer that has responded to immune checkpoint inhibitor (anti–PD-1/PD-L1) therapy but has progressed at 1-6 metastatic sites
- Treatment: Stereotactic ablative radiation to 1-6 metastatic lesions that progressed on immune checkpoint therapy
- Benefit: Patients remain on maintenance immune checkpoint therapy for longer and avoid or delay second-line chemotherapy, which is less effective and more toxic

Immune checkpoint therapy is a standard firstline therapy for metastatic urothelial cancer, or cancer of the bladder or upper urinary tract. When one to six sites of metastasis resist therapy while others respond or decrease in size, the current practice is to abandon the first-line therapy that was otherwise working and tolerated in favor of chemotherapy, which is typically much more toxic than immune therapy and less biologically effective as a second-line therapy.

Aurelie Garant, M.D., Assistant Professor of Radiation Oncology, is proposing a new

strategy: continue the immune checkpoint therapy that is working and treat the few resistant metastatic sites with stereotactic ablative radiation therapy (SAbR).

Currently, radiation is used only for palliation at nonablative doses for metastatic urothelial cancer, so using ablative radiation as a cancer controlling therapy in this setting is unorthodox. However, Dr. Garant has reason to think that this innovative approach will be effective.

"Radiation is used for bladder preservation in patients who have nonmetastatic urothelial cancer. Therefore, we know that bladder cancer, or urothelial cancer if we extrapolate, is radiosensitive," Dr. Garant explains. "So now, we're trying to use that knowledge base to go beyond the current standard of care."

If successful, this approach would benefit patients by allowing them to stay on the more effective, less toxic immune checkpoint therapy for longer, while delaying or even avoiding the need for chemotherapy.



Aurelie Garant, M.D. Radiation Oncologist



## Research Highlights

Research

MOLECULAR RADIATION BIOLOGY

Exploiting KRAS Mutations to Identify Targeted Therapies for Patients with Cancer



By Damiana Chiavolini, Ph.D.

RAS is a family of proteins expressed throughout the body and involved in transmitting signals that control the survival and growth of cells. Mutations in these proteins commonly lead to the development of different cancer types. Within the RAS family, mutated KRAS is a major driver of pancreatic, colorectal, and lung cancers and has been studied to identify targeted therapies for cancers that carry this type of mutation.

Kenneth Westover, M.D., Ph.D., Associate Professor of Radiation Oncology, is a radiation oncologist with expertise in biochemistry and structural biology who researches RAS mutations to design pharmacological approaches that might inhibit certain cancers by curtailing RAS activity.

Dr. Westover started researching RAS proteins as a summer undergraduate research fellowship student at UT Southwestern in 1997, where he worked with Nobel Laureate scientists Michael Brown, M.D., and Joseph Goldstein, M.D. He later started a program that focused on designing RAS inhibitors as a trainee in Nathanael Gray's lab at Harvard University. In 2012, he was recruited to UT Southwestern through a recruitment award from the Cancer Prevention and Research Institute of Texas to work on inhibitors of KRAS G12C, the most common RAS mutation found in lung cancer.

"RAS had the potential to be a major drug target but was felt to be undruggable for many decades. We saw a foothold with KRAS G12C to use irreversible inhibitors that can only bind to the cancer-causing cysteine mutation," Dr. Westover says. "We believed that if the KRAS G12C strategy worked, it would have a major impact on lung cancer treatment and reinvigorate efforts to target other mutant versions of RAS. Anticipating this, we devoted considerable effort to characterizing the unique properties of specific RAS mutants by various methods, including X-ray crystallography," he explains.

In 2013, Dr. Westover published his inhibitor concept



Renderings of an X-ray crystal structure solved by the Westover Lab of KRAS G12C protein bound to GDP and a covalent inhibitor

and, later that year, he reported the first comprehensive biochemical analysis of KRAS mutations. Over the years, his work has focused on understanding the characteristics of KRAS A146T, V14I, and G13D mutations that cause colorectal cancer; KRAS P34R, a rare mutation found in leukemia; and KRAS Q61H, a mutation found in lung cancer, and at the same time, on developing small-molecule inhibitors for KRAS G12C, in collaboration with the Gray lab. Dr. Westover's lab played a major role in defining the biochemical and structural properties of KRAS G12C, which led to the discovery of several molecules, including covalent guanosine mimetic inhibitors and covalent quinazoline inhibitors specific to this mutation.

The KRAS G12C concept has been enthusiastically adopted with multiple companies sponsoring clinical trials (NCT04006301, NCT04165031, NCT03785249, NCT04185883) that investigate whether newly developed KRAS G12C inhibitors can prolong the survival of patients with cancers harboring the G12C mutation. "Recently, Mirati and Amgen reported promising safety and efficacy for their compounds in early phase trials," Dr. Westover says. "For us this was exciting because their inhibitors share structural features with the quinazoline inhibitors we reported earlier. To play any part in research that leads to improvements in cancer outcomes is a privilege," he adds.

Dr. Westover earned both his medical degree and Ph.D. at Stanford University. As a graduate student in biophysics, he worked under the mentorship of Nobel Laureate Roger Kornberg, Ph.D., and his work was mentioned in the 2006 Nobel Prize for Chemistry awarded to Dr. Kornberg.



Kenneth Westover, M.D., Ph.D. Radiation Oncologist



CLINICAL

## **Preoperative Partial Breast Irradiation** for Early-Stage Breast Cancer

By Jonathan Feinberg, Ph.D.

The current standard of care for early-stage breast cancer is to first surgically remove the tumor, then deliver postoperative radiation therapy. This protocol entails irradiating the entire surgical cavity, plus a margin around the cavity, which is a much larger area than just the tumor. Inevitably, this unnecessarily exposes surrounding organs and tissues to high doses of radiation.

Asal Rahimi, M.D., Associate Professor of Radiation Oncology, thinks that reversing the standard order of therapies and delivering radiation before surgery could lessen the amount of unnecessary tissue exposure to radiation. Dr. Rahimi is investigating this strategy in a new phase I clinical trial (NCT04040569) that tests preoperative partial breast irradiation for early-stage breast cancer. The idea is that treating with radiation before surgery would allow radiation oncologists to irradiate only the tumor, not the entire surgical cavity.

"If we were able to deliver the radiation up front, we could treat the tumor, with some margin around it, and we would irradiate magnitudes of volume less than if we treated in the postoperative setting," Dr. Rahimi explains.

Treating less tissue would mean dramatically reducing the radiation dose to surrounding organs, and treating a smaller volume would mean that radiation could potentially be delivered in fewer fractions. Both could alleviate the toxicity associated with radiation therapy.

What's more, performing surgery after treating with radiation would remove most of the irradiated tissue from the body, which could further minimize adverse effects after treatment.

One of the greatest advantages of delivering radiation before surgery is that more patients could be offered partial-breast, rather than whole-breast, irradiation. During surgical resection, surgeons perform a variety of oncoplastic techniques that rearrange the tissue to ensure a good cosmetic outcome after surgery. Unfortunately, rearranging the tissue can make partialbreast irradiation very difficult. Instead, those patients are usually offered whole-breast irradiation, which exposes more tissue to radiation. Delivering radiation preoperatively, before oncoplastic rearrangement, would eliminate this problem.

"If we were to treat with radiation first, before surgery, then the surgeons could still do all the oncoplastic rearrangements they want to do to ensure the best cosmetic outcome, and the patient would still be able to receive the partial-breast irradiation," Dr. Rahimi says.

The clinical trial might also benefit research into the biological mechanisms and effects of radiation therapy for breast cancer. Because tumor tissue will be removed after irradiation, this tissue will be available for researchers to study the pathological response to radiation. This biological research might yield insights that could lead to future advances in treatment for breast cancer.

The current phase I dose escalation study will determine the radiation dose required to elicit a high pathologic response rate and ablate the tumor without causing excessive toxicity. If the trial is successful, the next step would be a phase II clinical trial to evaluate the efficacy of the preoperative protocol.

If implemented into clinical practice, this innovative treatment approach could ultimately reduce the toxicity associated with radiation therapy and improve the overall quality of life for patients with early-stage breast cancer.

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Plan of pre-operative single fraction of radiation to primary breast tumor



Asal Rahimi, M.D., M.S. Radiation Oncologist

#### PHYSICS

## Predicting Lymph Node Metastasis in Head and Neck Cancer

By Jonathan Feinberg, Ph.D.

Cervical lymph node metastasis is an important prognostic marker in head and neck cancer that predicts further metastasis to distant sites and can shorten patient survival.

Because of this, the standard of care for patients with oropharyngeal and laryngeal squamous cell carcinoma is to irradiate a large region of the neck to cover both the tumor and the cervical lymph nodes. However, this approach inevitably delivers radiation to noncancerous tissue, resulting in significant side effects that detract from patients' quality of life. Physicians and physicists in the Department of Radiation Oncology are collaborating on a new approach to minimize these unwanted side effects without sacrificing the effectiveness of treatment.

David Sher, M.D., M.P.H., Professor of Radiation Oncology, is investigating strategies to tailor the treatment plan to irradiate only the cervical lymph nodes that are at high risk for metastasis. In the recently completed Involved Field Elective De-Intensification Radiation Therapy for Head and Neck Cancer (INFIELD) phase II clinical trial (NCT03067610), Dr. Sher studied whether scaling back the radiation dose and targeting only high-risk lymph nodes to reduce treatment side effects would increase disease recurrence.

But selectively irradiating cervical lymph nodes according to their risk of metastasis requires accurately assessing that risk in the first place. Conventionally, physicians classify the malignant risk of patients' cervical lymph nodes by evaluating PET and CT images, but such classification relies on physicians' judgment and experience, which can vary substantially between treatment centers. What's more, small lymph nodes are difficult to classify, which adds to the uncertainty in planning radiation therapy.

Jing Wang, Ph.D., Associate Professor of Radiation Oncology, has developed an artificial intelligencebased solution: a machine learning algorithm that predicts the cervical lymph nodes' malignant probability based on PET and CT images. If broadly implemented, this tool could help standardize lymph node metastasis prediction and clinical care across treatment centers. If properly optimized, the algorithm could even improve upon physicians' judgment in accurately classifying small lymph nodes.

Dr. Wang's team initially developed and trained the algorithm using patient images from the INFIELD trial, but this dataset had limitations. "The problem is that we didn't have a gold standard," Dr. Wang explains. "In that trial, classification was based on the physician's judgment." Consequently, an algorithm trained on such images could only replicate that judgment at best.

Dr. Wang's team fine-tuned the algorithm on PET and CT images from patients who had undergone surgical resection at UT Southwestern. Since these images could be compared against postoperative pathological reports of the nodes' malignant status, the dataset provided the desired "gold standard," a ground truth on which to base the algorithm's predictions.

"We hope that this artificial intelligence (AI) can



From left to right: malignant, suspicious and normal lymph nodes

differentiate malignant from benign in small nodes that are hard to classify," Dr. Wang says. "If the predictive model can accurately match pathological reports, then it has the potential to outperform clinical judgment in classifying such nodes."

Dr. Wang's predictive algorithm is currently being deployed in Dr. Sher's recently launched Involved Nodal Radiation Therapy Using Artificial Intelligence-Based Radiomics for Head and Neck Squamous Cell Carcinoma (INRT-AIR) clinical trial (NCT03953976), in which radiation is delivered only to the cervical lymph nodes that the algorithm identifies as at risk for metastasis.

"To my knowledge, this is the first AI-based radiation oncology study that incorporates AI-based classification or diagnosis in a radiation treatment," says Dr. Sher. "This technology is the backbone for our confidence that we can significantly reduce the dose even further."

If the trial finds that patients treated with this method

have fewer side effects with no added risk of disease recurrence, then that would validate both the algorithm and the treatment approach, ultimately providing a new strategy to effectively treat head and neck cancer while maintaining patients' quality of life.

Innovative collaborations between clinicians and researchers in the Department of Radiation Oncology continue to drive advances in clinical care for patients with cancer.



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



Jing Wang, Ph.D. Physicist

#### WOMEN IN RESEARCH

INTERVIEWS By Damiana Chiavolini, Ph.D.

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

Chika Nwachukwu, M.D., Ph.D., Assistant Professor, is an attending radiation oncologist and clinical researcher. She received her Ph.D. in cancer biology from the University of Chicago, her medical degree from the Mayo Medical School, and completed a clinical residency in radiation oncology at Stanford University. Dr. Nwachukwu treats patients with gynecologic and breast cancers and pursues global initiatives and humanitarian outreach activities in underprivileged countries to promote education, research, and technology in radiation oncology.

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

CN: I wanted to become a doctor for as long as I can remember, but initially I didn't know why. I liked biology and anatomy, and I enjoyed learning about how the human body functions and responds to disease. In college, I especially valued the mini-research projects in all our science classes. I was fortunate to be hired as a summer intern in a cancer research lab at the University of Chicago; the principal investigator was a female breast oncologist who played a major role in my choice to enter this field. I ended up working in her lab for the next four years studying the genetic and epigenetic basis of breast cancers. Although oncology was a natural choice for me after my Ph.D., in medical school I found great mentors in radiation oncology who invested in nurturing my interests and passions. Radiation oncology practices are largely driven by scientific evidence coupled with evolving technological



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

advances, which largely affect the management of patients. This field nicely couples my interest in research and my passion for taking care of patients with cancer.

## Q. How did you become interested in global oncology initiatives?

CN: I am originally from Nigeria, and I was brought up in a family who believes in always giving back to others, both personally and professionally. Having had the opportunity and privilege to study, train, and work in the United States, I've always wanted to share my knowledge and experience to help improve the health of underprivileged patients worldwide. Therefore, I decided to focus on studying cervical cancer in low-income countries. One aspect of my research involves training health care providers from hospitals in these disadvantaged areas on advanced radiation techniques in the hope that these technologies may be implemented in the future. Another future goal is to collect tumor samples from women with cervical cancer and analyze them for genetic variability.

#### Q. What do you like most about your job?

CN: My patients are my favorite part of the job and the reason I work hard. I strive to develop personal relationships with all of them and, thus, I take the time to listen to questions and concerns. As a radiation oncologist who treats women with gynecologic and breast malignancies, I am always trying to use my knowledge to make a difference in their lives and their social communities. I also really enjoy that my job is multidisciplinary; designing the best treatment plan for the patient's health and quality of life requires the input of physicists, dosimetrists, nurses, therapists, and office assistants. I feel privileged to work with so many different people focused on providing patients with the best care and experience possible.

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

CN: I think it's challenging for women to thrive and succeed in science and medicine mostly because of a general lack of suitable mentoring. I have been especially lucky to have women mentors who understood the issues I faced as a woman scientist, so I was always motivated to move forward throughout my studies and professional career. I know this isn't the case for everyone, though. As women, we often need to use additional time, resources, and energy to obtain the mentorship we need to succeed in academic environments – from getting job interviews to balancing work and personal lives. More efforts should be dedicated to improving gender equity in radiation oncology.

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

CN: Radiation oncology isn't always appealing to women because it is highly technical and mostly male dominated. However, women who wish to pursue this career path should know that working in this field is highly rewarding from professional and human standpoints. Therefore, my advice is to pursue your interests with passion and vigor. Do not pigeonhole yourself, but always find a way to speak up and express what your needs are. And never forget to bring other women along with you through mentoring and education.

### Yuanyuan "Faith" Zhang, M.D., Ph.D.



Yuanyuan "Faith" Zhang, M.D., Ph.D.

Yuanyuan "Faith" Zhang is Chief Resident in Radiation Oncology and a clinical fellow in the laboratory of Ralph DeBerardinis, M.D., Ph.D., Professor and Chief of Pediatric Genetics and Metabolism at the Children's Research Institute at UT Southwestern. She is currently studying the role of tumor microenvironment metabolism in radiation sensitivity and is using CRISPR, a novel technology for screening radiation responses to identify new drug targets. Dr. Zhang is a recipient of the Holman Pathway, designed for trainees who show outstanding clinical and research abilities, and she was recently awarded a \$25,000 seed grant from our department to continue her work in this field.

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

FZ: What inspired me to become a physician is rather timely, considering the current coronavirus pandemic. My mom was one of the doctors who took care of the first severe acute respiratory syndrome (SARS) patient in China. I was a high school senior at the time, and while she was gone, I remember being worried but also proud of her dedication to patients. She didn't become a doctor for the awards and recognitions, but to make a difference in other peoples' lives. I knew then what my path would be. By following my mother's example, I wanted to practice medicine but also overcome its current limitations by working in research. I decided to specialize in radiation oncology because it's a technologyfueled, evidence-based practice that provides many opportunities for collaboration and for conducting basic and clinical research to offer patients the best care.

## Q. What do you like most about your job, and what are you most proud of?

FZ: I greatly enjoy collaborating with other scientists. As a radiation oncologist, I work closely with medical oncologists, surgical oncologists, physicists, and therapists to best treat our patients. In the lab, I am inspired by my brilliant colleagues who often take on risky projects and constantly push boundaries to expand the limits of the unknown. I enjoy the constant search for innovative treatments for our patients using a bench-to-bedside approach. Therapeutic innovation is the "element of hope" I can bring to my patients as I continue studying tumor metabolism. My area of research is relatively unexplored, so I hope to successfully lay the groundwork to pursue important discoveries that will solve radiation resistance problems.

## Q. As a woman, have you experienced any difficulties in entering a scientific/medical environment?

FZ: Although I haven't personally experienced discrimination in my field because of my gender, I

know that women are often underrepresented because of their struggle to balance family duties, financial decisions, and career choices. As a woman, I try to encourage and inspire the younger generation of physician-scientists to not tolerate gender bias and discrimination in academia. We should always speak up without being afraid to do so. We should stick together and find the support of mentors, both men and women. I am grateful for the advice I have received from Dr. DeBerardinis, as well as Dr. Story in the Division of Molecular Radiation Biology. I am also grateful for my clinical mentor, Dr. Choy, and his guidance on clinical practices and clinical trials.

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

FZ: Don't feel discouraged to pursue a specialty that relies so much on technology, and follow a career path you are truly passionate about. Be curious, fearless, and vigorous, and work on important research questions that are dear to your heart.

### Janice Ortega Rodriguez, Ph.D.

An instructor in Radiation Oncology, Janice Ortega Rodriguez, Ph.D., earned a B.S. in chemistry at the University of Puerto Rico in Rio Piedras and a Ph.D. in toxicology at the University of Kentucky. She currently works in the lab of Guo-Min Li, Ph.D., Professor of Radiation Oncology, where she researches mechanisms of DNA mismatch repair and how they can help identify new cancer therapeutics. In addition, Dr. Ortega is highly committed to educating the next generation of scientists.

#### Q. How did you become interested in research?

JO: I grew up in Puerto Rico with the idea of becoming a doctor and, thus, decided to pursue a



Janice Ortega Rodriguez, Ph.D.

degree in chemistry before entering medical school. Biology wasn't appealing to me at the time because it didn't seem especially useful or practical; however, learning chemistry made me appreciate how it could be applied to solve problems. In my third year of undergraduate school, I joined a cancer research lab and worked on drug screening assays until I graduated. The principal investigator encouraged me to consider coming to the mainland U.S. to pursue a Ph.D. So, after completing an internship at the University of Kentucky in Lexington, I pursued a graduate degree in toxicology there.

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

JO: I came to UT Southwestern with the title of instructor in Dr. Guo-Min Li's lab, where I had already been working as a postdoctoral fellow back at the University of Kentucky. As a naturally inquisitive person, I enjoy applying innovative concepts and techniques to discover and understand new mechanisms, a feeling that is similar to that of solving puzzles. What I have grown to love about biology is how it continuously sparks my curiosity while advancing science and medicine.

## Q. What do you feel are your most exciting achievements, and what are you most proud of?

JO: I was proud to see my first paper published in PNAS in 2015. I had been studying the role of proliferating cell nuclear antigen in DNA replication and DNA mismatch repair for much of my academic career, so it felt rewarding to see my hard work come together and get published in such a prestigious journal. The other aspect of my job that makes me happy is coaching and guiding younger scientists in the lab. I am also involved in other outreach activities such as the All Things Made New nonprofit program, where I mentor high school students from lowerincome communities to succeed in their work, apply for college, and grow as leaders. I am dedicated to influencing and helping the new generation succeed, especially those who may not have as many opportunities to pursue scientific careers.

Q. Have you experienced, as a woman, any difficulties in entering a scientific/medical environment, and do you have any advice for young women who would like to pursue your same career?

JO: While I haven't experienced any problems during my graduate studies, I know that, as women, we face daily challenges when balancing our career and personal life. For this reason, we may be underrepresented in many areas of science. This should not discourage us, though. I advise young women interested in this field to enroll for summer internships and programs to gain enough experience and find mentors. Overall, I'd like to see more incentives and mentoring programs to recruit and, especially, to retain more women in science.

## Education Highlights

**New Medical Residents** 

Medical Physics Residents – First Clinical Year



Michael Christensen, M.D. Undergraduate Education: Brigham Young University Medical School: University of Utah School of Medicine



Liyuan Chen, Ph.D. Undergraduate Education: Beijing Normal University Ph.D.: Hong Kong Baptist University



Ambrosia Simmons, M.D., Ph.D. Undergraduate Education: University of Michigan Medical School: Temple University School of Medicine



Samaneh Kazemifar, Ph.D. Undergraduate Education: Shiraz Azad University Ph.D.: University of Western Ontario



Allen Yen, M.D. Undergraduate Education: University of Oklahoma Medical School: UT Southwestern Medical Center



Heui (Hugh) Lee, Ph.D. Undergraduate Education: Hanyang University Ph.D.: Purdue University



Xinran Zhong, Ph.D. Undergraduate Education: Tsinghua University Ph.D.: UCLA



#### 2020 Medical Physics Resident Graduates



Andrew Leiker, M.D. Medical School: Medical College of Wisconsin Practicing: Ellis Fischel Cancer Center, University of Missouri



Nima Hassan-Rezaeian, Ph.D. Ph.D.: University of North Texas Practicing: Memorial Sloan Kettering Cancer Center / Cornell University



Travis Mendel, M.D. Medical School: Paul L. Foster School of Medicine at Texas Tech University Health Science Center Practicing: Rio Grande Urology



Zohaib Iqbal, Ph.D. Ph.D.: University of California, Los Angeles Practicing: University of Alabama-Birmingham



Samuel Schroeder, M.D. Medical School: University of Iowa Carver College of Medicine Practicing: John Stoddard Cancer Center



David Parsons, Ph.D. Ph.D.: Dalhousie University Practicing: UT Southwestern Medical Center



Jun Tan, Ph.D. Ph.D.: Oakland University Practicing: UT Southwestern Medical Center

## NEW FACULTY

**Department News** 



beneficial way.

#### CLINICAL

Heidi McKellar, M.D. Assistant Professor



#### **MEDICAL PHYSICS & ENGINEERING**

Justin Chunjoo Park, Ph.D. Assistant Professor & Director of Adaptive Therapy

Dr. McKellar received her bachelor's degree in philosophy from Smith College, Northampton, Massachusetts, and her medical degree from UT Health Science Center in Houston. She completed her training in radiation oncology at MD Anderson Cancer Center and has worked in both academic and community-based cancer centers. Her interests include stereotactic radiation using both CyberKnife and TrueBeam technology. Dr. McKellar became board certified in palliative care after many years of research in the psychosocial and spiritual aspects of cancer. Her areas of interest include symptom management and optimization of quality of life for patients with serious diagnoses, along with understanding how patients make decisions regarding care in the setting of advanced cancer, what they prioritize, and what is most meaningful. She believes this knowledge allows the treatment team to provide technologically advanced treatment coupled with U15041111231311 personalized care in the most

Dr. Park received his Ph.D. from the University of California San Diego and completed his postdoctoral training at the University of Florida. Following completion of his residency, he joined the Department of Radiation Oncology at Washington University as assistant professor and adjunct faculty in the Department of Biomedical Engineering, where he was actively involved in developing an MRI-guided adaptive radiotherapy program. His research interests include CT/CBCT imaging and reconstruction, dose calculation and optimization, and developing machine learning technologies to adaptive radiotherapy applications.

## FACULTY PROMOTIONS

Department News

#### CLINICAL



#### Michael Folkert, M.D., Ph.D.

Associate Professor & Associate Vice Chair for Education

Dr. Folkert was promoted to Associate Professor and Associate Vice Chair for Education. He leads our gastrointestinal disease-oriented team and oversees our Medical Residency Program.



#### Puneeth lyengar, Ph.D.

Associate Vice Chair for Clinical Research

Dr. Iyengar was promoted to Associate Vice Chair for Clinical Research. He leads our lung disease-oriented team and runs his own lab, which is focused on metabolic and immune regulation of cancer cachexia, lung cancer tumor metabolism, and inflammationdriven radiation resistance of lung cancer.



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

Professor & Associate Vice Chair for Clinical Operations

Dr. Sher was promoted to Professor and Associate Vice Chair for Clinical Operations. He leads our head and neck disease-oriented team.

#### MOLECULAR RADIATON BIOLOGY



Asaithamby Aroumougame, Ph.D. Associate Professor

Dr. Aroumougame was promoted to Associate Professor. His lab focuses on DNA damage response signaling in development and tumor suppression.



## Jinzhen Guo, Ph.D.

Dr. Guo was promoted to Instructor. He works in Dr. Guo-Min Li's lab where his research focuses on understanding the molecular mechanisms of trinucleotide repeat expansion.



#### Narasimha Kumar Karanam, Ph.D. Instructor

Dr. Karanam was promoted to Instructor. He works in Dr. Michael Story's lab where he is currently working on a novel physical modality of cancer therapy called Tumor Treating Fields (TTFields).

#### **MEDICAL PHYSICS & ENGINEERING**



Brian Hrycushko, Ph.D. Associate Professor

Dr. Hrycushko was promoted to Associate Professor. He is lead physicist for brachytherapy and for our melanoma/sarcoma disease-oriented team.



#### Xun Jia, Ph.D.

Professor & Associate Vice Chair of Physics and Engineering Research

Dr. Jia was promoted to Professor and Associate Vice Chair of Physics and Engineering Research. He is lead physicist for our gynecological disease-oriented team and principal investigator of the iTORCH lab, which focuses on the development and implementation of novel techniques to advance radiotherapy.



Mu-Han Lin, Ph.D. Associate Professor

Dr. Lin was promoted to Associate Professor. She also serves as Director of Treatment Planning overseeing a team of dosimetrists and is lead dosimetrist for our head and neck disease-oriented team.

## **DISEASE-ORIENTED TEAM FACULTY**

Our Team

#### BREAST



#### Asal Rahimi, M.D., M.S. \* **Radiation Oncologist** Associate Professor Chief of Breast Radiation **Oncology Service** Trained: University of Virginia



Prasanna Alluri, M.D., Ph.D. **Radiation Oncologist** Assistant Professor Trained: University of Minnesota



Nathan Kim, M.D., Ph.D. **Radiation Oncologist** Associate Professor Trained: Vanderbilt University Medical Center



Chika Nwachukwu, M.D., Ph.D. Radiation Oncologist Assistant Professor Trained: Stanford University



Anthony Davis, Ph.D. Molecular Radiation Biologist Assistant Professor Trained: UT Southwestern Medical Center



Xuejun Gu, Ph.D. Physicist Associate Professor Trained: Columbia University



Shohreh Bahrami, APRN, FNP-BC **Nurse Practitioner** Trained: Texas Woman's University

#### **CENTRAL NERVOUS SYSTEM**

#### Zabi Wardak, M.D. \*



**Radiation Oncologist Assistant Professor** Chief of CNS Radiation Oncology Service Trained: UT Southwestern Medical Center





#### Tu Dan, M.D. **Radiation Oncologist**

**Assistant Professor** Trained: Sidney Kimmel Medical College at Thomas Jefferson University

#### Wen Jiang, M.D., Ph.D.

**Radiation Oncologist** Assistant Professor Trained: UT MD Anderson Cancer Center

#### Kiran Kumar, M.D., MBA



Assistant Professor & Associate Director of the Medical Residency Program Chief of Lymphoma and Pediatrics Radiation **Oncology Services** Trained: Stanford University

#### Robert Timmerman, M.D., FASTRO, FACR

**Radiation Oncologist** Professor, Vice Chair & Medical Director Holder of the Effie Marie Cain Distinguished Chair in Cancer Therapy Research Trained: The Johns Hopkins Hospital

Trained: Harvard Radiation Oncology Program



#### Terri Kelley-Griffis, APRN, FNP-C

Yang Park, Ph.D. Physicist

**Assistant Professor** 

**Nurse Practitioner** Trained: Texas Woman's University

#### GENITOURINARY



#### Raquibul Hannan, M.D., Ph.D. \*

Radiation Oncologist Associate Professor Chief of GU Radiation Oncology Service Trained: Albert Einstein College of Medicine



#### Neil Desai, M.D., M.H.S.

Radiation Oncologist Assistant Professor Dedman Family Scholar in Clinical Care Trained: Memorial Sloan Kettering Cancer Center



#### Aurelie Garant, M.D. Radiation Oncologist

Assistant Professor Trained: McGill University



Debabrata Saha, Ph.D. Molecular Radiation Biologist Associate Professor Trained: University of Calcutta – India



Jing Wang, Ph.D. Physicist Associate Professor & Director of Data Analytics and Informatics Trained: University of Science & Technology of China



#### Tamara Dickinson, APRN, AGPCNP-BC Nurse Practitioner

Trained: University of South Alabama

#### GYNECOLOGICAL



Kevin Albuquerque, M.D., FACR \* Radiation Oncologist Professor, Director of Quality Improvement/ Quality Assurance Chief of Gynecological Radiation Oncology Service Holder of the Ken Sharma Professorship in Radiation Oncology Trained: University Hospital of Brooklyn



Kanchandip Koshy, M.S.N., APRN, FNP-C Nurse Practitioner Trained: University of Texas at Arlington

#### GASTROINTESTINAL



Michael Folkert, M.D., Ph.D. \* Radiation Oncologist Associate Professor & Associate Vice Chair for Education Chief of GI Radiation Oncology Service Trained: Memorial Sloan Kettering Cancer Center



Todd Aguilera, M.D., Ph.D. Radiation Oncologist Assistant Professor Trained: Stanford University Medical School



Nina Sanford, M.D. Radiation Oncologist Assistant Professor Dedman Family Scholar in Clinical Care Trained: Harvard Radiation Oncology Program



Benjamin Chen, Ph.D. Molecular Radiation Biologist Associate Professor Trained: Ohio State University



Justin Chunjoo Park, Ph.D. Physicist Assistant Professor and Director of Adaptive Therapy Trained: University of Florida



Amy Sessions, PA-C Physician Assistant Trained: Texas Tech University Health Sciences Center



#### Chika Nwachukwu, M.D., Ph.D. Radiation Oncologist Assistant Professor Trained: Stanford University



Xun Jia, Ph.D. Physicist Professor & Associate Vice Chair of Physics and Engineering Research Trained: Peking University



#### Astrid Medrano, APRN Nurse Practitioner Trained: University of Texas at Arlington

#### HEAD & NECK



#### David Sher, M.D., M.P.H. \*

Radiation Oncologist Professor & Associate Vice Chair for Clinical Operations Chief of Head and Neck Radiation Oncology Service Trained: Harvard Radiation Oncology Program



Vladimir Avkshtol, M.D. Radiation Oncologist Assistant Professor Trained: Fox Chase Cancer Center



Dominic Moon, M.D. Radiation Oncologist Assistant Professor Trained: UNC School of Medicine



Dat Vo, M.D., Ph.D. Radiation Oncologist Assistant Professor Trained: UT Southwestern Medical Center



Benjamin Chen, Ph.D. Molecular Radiation Biologist Associate Professor Trained: Ohio State University



Mu-Han Lin, Ph.D. Physicist Associate Professor & Director of Treatment Planning Trained: SUNY at Stony Brook



#### Gina Chorley, M.S.N., APRN-BC Nurse Practitioner

Trained: Northern Illinois University

#### LUNG



#### Puneeth Iyengar, M.D., Ph.D. \*

Radiation Oncologist Assistant Professor & Associate Vice Chair for Clinical Research Chief of Lung Radiation Oncology Service Trained: UT MD Anderson Cancer Center



#### Hak Choy, M.D., FASTRO

Radiation Oncologist Professor & Department Chair Holder of the Nancy B. & Jake L. Hamon Distinguished Chair in Therapeutic Oncology Research Trained: Ohio State University Hospital; UT Health Science Center at San Antonio



#### Kenneth Westover, M.D., Ph.D.

Radiation Oncologist Associate Professor & Director of Clinical Innovation and Information Systems Trained: Harvard Radiation Oncology Program

#### Michael Story, Ph.D. Molecular Radiation Professor Vice Chair





#### Asaithamby Aroumougame, Ph.D.

Molecular Radiation Biologist Associate Professor Trained: Banaras Hindu University



Amir Owrangi, Ph.D. Physicist Assistant Professor Trained: University of Western Ontario

#### LYMPHOMA & PEDIATRICS



#### Kiran Kumar, M.D., MBA \*

Radiation Oncologist Assistant Professor & Associate Director of the Medical Residency Program Chief of Lymphoma and Pediatrics Radiation Oncology Services Trained: Stanford University



#### Tu Dan, M.D.

Radiation Oncologist Assistant Professor Trained: Sidney Kimmel Medical College at Thomas Jefferson University



#### Neil Desai, M.D., M.H.S. Radiation Oncologist Assistant Professor

Assistant Professor Dedman Family Scholar in Clinical Care Trained: Memorial Sloan Kettering Cancer Center



### Michael Folkert, M.D., Ph.D.

Radiation Oncologist Associate Professor & Associate Vice Chair for Education Chief of GI Radiation Oncology Service Trained: Memorial Sloan Kettering Cancer Center



#### Robert Timmerman, M.D., FASTRO, FACR Radiation Oncologist Professor, Vice Chair & Medical Director Holder of the Effie Marie Cain Distinguished Chair in Cancer Therapy Research Trained: The Johns Hopkins Hospital



#### Zabi Wardak, M.D. Radiation Oncologist Assistant Professor Chief of CNS Radiation Oncology Service Trained: UT Southwestern Medical Center



Tsuicheng David Chiu, Ph.D. Physicist Assistant Professor Trained: University of Connecticut



#### Matthew Strunk, M.P.A.S., PA-C

Physician Assistant Trained: Interservice Physician Assistant Program (IPAP)

#### MELANOMA & SARCOMA



#### Kevin Albuquerque, M.D., FACR \* (Melanoma)

#### Radiation Oncologist Professor, Director of Quality Improvement/ Quality Assurance Chief of Gynecological Radiation Oncology Service Holder of the Ken Sharma Professorship in Radiation Oncology Trained: University Hospital of Brooklyn



#### Michael Folkert, M.D., Ph.D. \* (Sarcoma)

Radiation Oncologist Associate Professor & Associate Vice Chair for Education Chief of GI Radiation Oncology Service Trained: Memorial Sloan Kettering Cancer Center



#### Brian Hrycushko, Ph.D.

Physicist Associate Professor Trained: UT Health Science Center at San Antonio

#### PALLIATIVE CARE



#### Heidi McKellar, M.D. Palliative Care Physician

Assistant Professor Trained: UT MD Anderson Cancer Center

#### INPATIENT SERVICES



Daniella Hall, M.P.A.S., PA-C Physician Assistant Trained: UT Southwestern Medical Center

\* Denotes team lead

## GRANTS & PARTNERSHIPS

#### FY 2020 Awarded Research by Faculty

Todd Aguilera, M.D., Ph.D., was awarded \$600,000 by the Damon Runyon Cancer Research Foundation to investigate immunologic responses to short-course radiotherapy in rectal adenocarcinoma and the impact of CD40 agonist immunotherapy.

Prasanna Alluri, M.D., Ph.D., was awarded \$50,000 by METAvivor to identify therapeutic vulnerabilities in RB1-negative, ER-positive breast cancers.

Yesenia Gonzalez was awarded \$34,644 to investigate automated treatment planning for high-dose-rate brachytherapy for cervical cancer as her NCI predoctoral fellowship under mentor Xun Jia, Ph.D.

Xun Jia, Ph.D. (PI) and Anke Henning Ph.D., (AIRC, co-PI) were awarded \$250,000 by CPRIT to study low-cost compact retrofit MR scanner for the next-generation MR-guided radiation therapy.

Wen Jiang, M.D., Ph.D., was awarded \$50,000 by UT Southwestern's Circle of Friends to investigate CD24 as a novel therapeutic target for glioblastoma immunotherapy.

Narasimha Karanam, Ph.D., was awarded a

three-year AACR-Novocure Career Development Award, totaling \$225,000, for his project "harnessing E2F-Rb-CDK4/6 axis for novel combination therapy with TTFields."

Guo-Min Li, Ph.D., was awarded \$134,336 by the Hereditary Disease Foundation to investigate the role of mutant huntingtin in promoting CAG repeat expansion.

Debabrata Saha, Ph.D., was awarded \$250,000 by the AACR to evaluate the efficacy of TTFields and radiotherapy in preclinical tumor model.

Yiping Shao, Ph.D., was awarded \$75,780 in NIH-NIBIB supplementary funding to study advanced micro-PET/CT/RT system for translational radiation oncology applications.

Michael Story, Ph.D., was awarded \$749,479 by Galera for the examination of the radioprotection and anti-tumor effects of Galera Therapeutics GC4419 and GC4401. In addition, he received \$277,172 from NASA to investigate tumorsequencing addendum.

Jing Wang, Ph.D., was awarded \$48,145 by UTA-NHLBI-R15 to investigate attenuation correction strategies for myocardial perfusion imaging using dual-gated SPECT.

Awarded under Steve Jiang, Ph.D., Ken Kang-Hsin Wang, Ph.D., received \$4 million for CPRIT Rising Star Recruitment.

Kenneth Westover, M.D., Ph.D., was awarded an R01 grant – NCI Stimulus Award for \$75,000 and an additional \$1,873,462, also from the NCI, for the characterization and targeting of rapid nucleotide exchange RAS mutations. In addition, he received \$105,000 from CPRIT for the characterization of novel KRAS inhibitors.

Zhaogang Yang, Ph.D., and Wen Jiang, M.D., Ph.D., were awarded an NCI R21 grant for \$450,030 to study renal cell carcinoma surveillance by immuno-lipoplex nanoparticle platform.

Erlei Zhang, Ph.D., was awarded a \$100,000 fellowship by the American Heart Association to develop an artificial intelligence-based radiotherapy cardiotoxicity analysis platform.

You Zhang, Ph.D., was awarded an R01 grant from the NCI in the amount of \$1,498,885 for accurate 4D liver tumor localization for radiotherapy using contrast-agent-free X-ray imaging and liver biomechanical modeling.

### Awarded Research Funding FY15 - FY20



## FEATURED PUBLICATIONS

#### **Department News**

The Department of Radiation Oncology publishes more than 130 publications every year. Our Department's unique research cross-collaborates with our three divisions to contribute to the research advancement in the field of radiation oncology.

#### PHYSICS

Hrycushko B, van der Kogel AJ, Phillips L, Folkert M, Sayre JW, Vernino S, Hassan-Rezaeian N, Foster RD, Yamada Y, Timmerman R, Medin PM. Existence of a dose-length effect in spinal nerves receiving single-session stereotactic ablative radiation therapy. Int J Radiat Oncol Biol Phys. 2020 Apr 1;106(5):1010-1016. PMID: 31953062.

Iqbal Z, Nguyen D, Hangel G, Motyka S, Bogner W, Jiang S. Super-resolution 1 H magnetic resonance spectroscopic imaging utilizing deep learning. Front Oncol. 2019 Oct 9. doi. org/10.3389/fonc.2019.01010.

Nguyen D, McBeth R, Sadeghnejad Barkousaraie A, Bohara G, Shen C, Jia X, Jiang S. Incorporating human and learned domain knowledge into training deep neural networks: A differentiable dose-volume histogram and adversarial inspired framework for generating Pareto optimal dose distributions in radiation therapy. Med Phys. 2020 Mar;47(3):837-849. PMID: 31821577.

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Zhou Z, Li S, Qin G, Folkert M, Jiang S, Wang J. Multi-objective based radiomic feature selection for lesion malignancy classification. IEEE J Biomed Health Inform. 2020 Jan;24(1):194-204. PMID: 30835231.

#### MOLECULAR RADIATION BIOLOGY

Huang Y, Zhao J, Mao G, Lee, GS, Zhang J, Bi L, Gu L, Chang Z, Valentino J, Li GM. Identification of novel genetic variants predisposing to familial oral squamous cell carcinomas. Cell Discov. 2020 Jul 14;6(46). PMID: 32685192.

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Yenerall P, Das AK, Wang S, .... Lin YF, et al. RUVBL1/RUVBL2 ATPase activity drives PAQosome maturation, DNA replication and radioresistance in lung cancer. Cell Chem Biol. 2020 Jan 16;27(1):105-121.e14. PMID: 31883965.

#### CLINICAL

Avkshtol V, Ruth KJ, Ross EA, Hallman MA, Greenberg RE, Price RA, Jr., Leachman B, Uzzo RG, Ma C, Chen D, Geynisman DM, Sobczak ML, Zhang E, Wong JK, Pollack A, Horwitz EM. Ten-year update of a randomized, prospective trial of conventional fractionated versus moderate hypofractionated radiation therapy for localized prostate cancer. J Clin Oncol. 2020 May 20;38(15):1676-1684. PMID: 32119599.

Butler SS, Winkfield KM, Ahn C, Song Z, Dee EC, Mahal BA, Sanford NN. Racial disparities in patient-reported measures of physician cultural competency among cancer survivors in the United States. JAMA Oncol. 2019 Oct 31;6(1):152-154. PMID: 31670752.

Chao ST, Dad LK, Dawson LA, Desai NB, Pacella M, Rengan R, Xiao Y, Yenice KM, Rosenthal SA, Hartford A. ACR-ASTRO practice parameter for the performance of stereotactic body radiation therapy. Am J Clin Oncol. 2020 Aug;43(8):545-552. PMID: 32404596.

Khan SA, Gerber DE, Zhu H, Hughes RS, Mannala S, Rashdan S, Dowell J, Westover KD, Saltarski J, Harrah K. Phase II trial of clinical activity and safety of ceritinib combined with stereotactic ablative radiotherapy (SABR) in lung adenocarcinoma patients. J Clin Oncol. 2020 May;38(15). Epub online.

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#### **UTSouthwestern**

NCI



Department of Radiation Oncology

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Photos by Brian Coats

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