

Radiation Oncology News

Fall 2014



Baldassarre Stea, MD, PhD
Department Head and Professor

Most physicians enter the medical field because of a strong desire to help fellow human beings. These days, technological advances in radiation oncology have made our job ever more rewarding. We provide new and innovative technology at The University of Arizona Medical Center to allow radiation oncologists to improve clinical outcomes. This new technology provides fertile ground for innovative research as well.

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Message from the Chair

Dear Friends and Colleagues

I am happy to write this brief overview on behalf of the University of Arizona College of Medicine Department of Radiation Oncology. Since our last newsletter, we have both a new director of the University of Arizona Cancer Center, Dr. Andrew Kraft, who started in his position in September, and an interim dean of the UA College of Medicine – Tucson, Dr. Joe G. N. “Skip” Garcia, the UA Senior Vice President for Health Sciences who took over for Dr. Steve Goldschmid in February.

In other big news, just as we were wrapping up this fiscal year, it was announced that the University of Arizona Health Network is considering a merger with Banner Health, an Arizona-based non-profit and nationally recognized leader in patient care. As with any change, there’s some uncertainty. We are looking forward, however, to exciting developments with this partnership in all areas of our department, including academics, research, technology and most importantly facilities (with the planned building of new modern facilities at the University of Arizona Medical Center – University Campus and North Campus). Negotiations are under way, and we anticipate the merger to be effective February 1, 2015.

Our residency program continues to thrive under the leadership of Dr. Shona Dougherty. We now have, for the first time in two decades, a total of seven residents. We are very proud of our medical residents who continue to have an unbroken streak of successfully passing the board exams (both written and oral). This

year, resident alumni Drs. David Vonk and Benjamin Slane passed their oral boards and Dr. Kristen O’Donnell her written. We also successfully graduated Dr. O’Donnell, and a medical physicist, Bryan Dukes, M.S., both of whom have found jobs in private practice out of state. Our current residents have had a successful year in research. Three medical residents from our program presented their research at the ASTRO annual meeting in San Francisco in September and Dr. Steven Skolnik won a prestigious ASTRO award for his research on treatment of trigeminal neuralgia.

Also in academics, we were fortunate to host guest professor Dr. Albert Van Der Kogel, from the Netherlands, visit last February. He gave three lectures in the Arizona Cancer Center as well as met one-on-one with our faculty and residents. His lectures included “New Developments in Fractionation,” “Tumor Hypoxia and Microenvironment” and “Normal Tissue Response, Volume Effect, Retreatment Tolerance.” This January, we will be honored to host as visiting professor Dr. Paul Wallner, the ABR Associate Executive Director for Radiation Oncology.

We have a new addition to our faculty, Wen Li, PhD, who joined us in July from the Cleveland Clinic. He comes to us with an extensive research background in the joint field of medical imaging and radiation therapy. Congratulations also are in order for Dr. Dougherty who was promoted to full professor in August.

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Our clinical trials and research office continue to grow. We currently have many clinical trials open, ranging from studies on myeloma to liver cancer – and we continue to contribute to NRG trials.

Thank you to all of those who have supported our department this past year. We look forward to continued success in research and outstanding patient care in the coming year. Here's wishing you a wonderful Holiday Season and healthy New Year.



Baldassarre “Dino” Stea, MD, PhD
Department Head and Professor
Department of Radiation Oncology



2013-14 FACULTY SELECT PUBLICATIONS

Victor Gonzalez, MD

Book Chapters:

Gonzalez VJ Radiation Therapy. In Lee C., *Living and Thriving with Breast Cancer*. Provenir Press inc. 2013

Christopher Watchman, PhD

Published Abstract:

A Moghadam, K Hadad, C Watchman, R Hamilton. “CT-Based 3D Dose Calculation Method Using Artificial Neural Networks (ANN)”. *Medical Physics* 40(6) 474, 2013

Sun Yi, MD

He W, Luo J, Bourguet F, Xing L, Yi SK, Gao T, Blanchette C, Henderson PT, Kuhn E, Malfattie M, Murphy WJ, Cheng RH, Lam KS, Coleman MA. Controlling the Diameter, Monodispersity, and Solubility of ApoA1 Nanolipoprotein Particles Using Telodendrimer Chemistry. *Protein Science*; 2013; 22(8); 1078-1086.

Baldassarre Stea, MD, PhD

Welsh JW, Komaki R, Amini A, Munsell M, Unger W, Allen PK, Chang JY, Wefel J, McGovern S, Garland LL, Chen SS, Holt J, Liao Z, Brown P, Sulman E, Heymach JV, Kim ES, and Stea B; Phase II Trial of Erlotinib plus Concurrent Whole-Brain Radiation Therapy for Patients with Brain Metastases from Non-Small Cell Lung Cancer. *J Clin Oncol*. 2013 Mar 1;31(7):895-902. doi: 10.1200/JCO.2011.40.1174. Epub 2013 Jan 22. PMID: 23341526

Yongbok Kim, PhD

Kim Y and Trombetta MG. Dosimetric evaluation of multi-lumen intracavitary balloon applicator rotation in high-dose-rate brachytherapy for breast cancer. *J App Clin Med Phys* 2014; 15(1):76-89. PMID: 24423837

Russell Hamilton, PhD

Nguyen NP, Nguyen ML, Vock J, Lemanski C, Kerr C, Vinh-Hung V, Chi A, Khan R, Woods W, Altdorfer G, D'Andrea M, Karlsson U, Hamilton R, Ampil F. Potential applications of imaging and image-guided radiotherapy for brain metastases and glioblastoma to improve patient quality of life, *Frontiers in Oncology*, Vol. 3, Article 284, 2013.

Our Research Efforts Have Been Growing!

We are excited to have so many different types of studies available to our patients. These studies are reflective of the new innovative approaches that go above the previous standards of radiation therapy and chemotherapy. We currently have studies open for the following disease sites:

Brain Metastasis

A Phase III Trial of Post-Surgical Stereotactic Radiosurgery (SRS) Compared with Whole Brain Radiotherapy (WBRT) for Resected Metastatic Brain Disease

Primary Brain Tumor (GBM)

Celldex ACT IV: An International, Randomized, Double-Blind, Controlled Study of Rindopepimut/ GM-CSF with Adjuvant Temozolomide in Patients with Newly Diagnosed, Surgically Resected, EGFRvIII-positive Glioblastoma

Esophageal

A Phase III Trial Evaluating the Addition of Trastuzumab to Trimodality Treatment of HER2-Overexpressing Esophageal Adenocarcinoma

Head and Neck

Randomized Phase II/III Trial of Surgery and Postoperative Radiation Delivered with Concurrent Cisplatin Versus Docetaxel Versus Docetaxel and Cetuximab for High-risk Squamous Cell Cancer of the Head and Neck

Liver Cancer

Randomized Phase III Study of Sorafenib versus Stereotactic Body Radiation Therapy Followed by Sorafenib in Hepatocellular Carcinoma

For more information, contact the Research Staff at (520) 626-6800

Upcoming Studies

The following studies are in various stages of approval and will soon be available for our patients:

Breast

Pilot Study for Prone Breath Hold Technique to Decrease Cardiac and Pulmonary Doses in Women Receiving Left Breast Radiotherapy

A Safety and Efficacy Study of Intra-Operative Radiation Therapy (IORT) Using the Xofigo® Axxent® eBX™ System at the Time of Breast Conservation Surgery for Early Stage Breast Cancer

A Randomized Phase III Clinical Trial Evaluating Post-Mastectomy Chestwall and Regional Nodal XRT and Post-Lumpectomy Regional Nodal XRT in Patients with Positive Axillary Nodes Before Neoadjuvant Chemotherapy Who Convert to Pathologically Negative Axillary Nodes After Neoadjuvant Chemotherapy (NSABP B-51/RTOG 1304)

Multiple Metastases

Testing the Safety and Effects of Radiation at Different Doses to Multiple Breast, Lung and Prostate Cancer Metastases

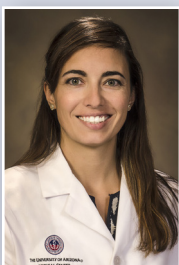
Prostate

Androgen Deprivation Therapy and High Dose Radiotherapy with or without Whole-Pelvic Radiotherapy in Unfavorable Intermediate or Favorable High Risk Prostate Cancer: A Phase III Randomized Trial

Phase III Trial of Dose Escalated Radiation Therapy and Standard Androgen Deprivation Therapy (ADT) with a GnRH Agonist vs. Dose Escalated Radiation Therapy and Enhanced ADT with a GnRH Agonist and TAK-700 for Men with High Risk Prostate Cancer

PHYSICIAN HIGHLIGHTS

Two of our physicians are worthy of individual recognition for their innovative design of a research study that is being done only at our institution:



Dr. Krisha Howell

Phase II study of vertebral augmentation and radiotherapy in painful or at risk of collapse spinal metastatic cancer/multiple myeloma.



Dr. Sun K. Yi

A phase II randomized study of short-term dexamethasone versus placebo in patients receiving radiation and chemotherapy for the treatment of head and neck cancers.

IntraOperative Radiation Therapy (IORT)

A New Tool in the Fight against Breast Cancer



The UA Department of Radiation Oncology is pleased to announce the launch of its IntraOperative Radiation Therapy (IORT) program. This program was developed in close coordination with the other members of the Breast Health Team. The first patient was treated with intraoperative breast radiation

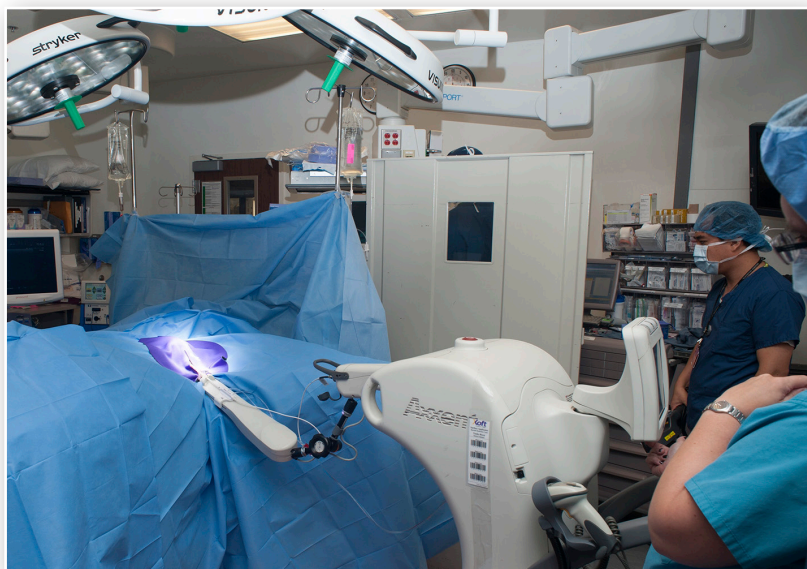
during an outpatient procedure performed Sept. 26 by Breast Surgery Program Director Michelle Ley, MD, at the UA Cancer Center - North Campus.

IntraOperative Radiation Therapy (IORT) is a technique in which radiation is delivered directly to breast tissue surrounding the tumor at the time of surgery. During surgery, the surgeon removes the tumor then places a special balloon catheter inside the surgical bed. The radiation oncologist and team then deliver the radiation treatment. Radiation treatment is performed with the XOFT Axxent device. This device uses a miniaturized X-ray source to produce radiation within the tumor bed. Unlike other forms of radiation treatment, the X-rays produced by this device have a very sharp drop-off. This allows for high doses of radiation to be delivered to the surgical bed while delivering very low amounts of radiation to surrounding tissues. The radiation treatment takes from 10 to 20 minutes to deliver. Afterward, the device is removed and the surgery is completed as normal.

IORT is being offered on a clinical trial at the UA Cancer Center. Women who qualify for this study will receive a single dose of radiation at the time of their surgery.

“Intraoperative radiotherapy has the potential to revolutionize breast cancer treatment. It is by far the most convenient form of radiation treatment possible for early-stage breast cancer. The patient wakes up from their surgery, and the radiation course is complete. In contrast, standard post-operative external radiation requires a minimum of three weeks of daily treatment,” said Victor Gonzalez, MD, UA assistant professor of Radiation Oncology.

One of the greatest breakthroughs in breast cancer treatment over the last decade has been the recognition that different subtypes of breast cancer respond better to different types of treatment. A one-size-fits-all approach is no longer



acceptable. IORT is an excellent treatment option for patients who have a low risk of having cancer develop in other parts of the breast.

“Not all patients are good candidates for IORT,” Dr. Gonzalez added. The key to successful treatment is proper patient selection. All breast cancer cases are reviewed at a multidisciplinary conference. Here, the breast surgeons, medical oncologists and radiation oncologists interact and determine the optimal treatment plan. I am excited to have another tool for treating breast cancer.”

Who is eligible to have intraoperative radiation therapy? Potential candidates for breast IORT are women with a new diagnosis of early-stage, low-risk, invasive ductal carcinoma who are planning to undergo lumpectomy. Our breast cancer specialists work in partnership with every patient to determine the best individual treatment options. IORT requires a discussion with a radiation oncologist prior to surgery to discuss the potential risks, benefits and alternatives to this form of treatment. Since IORT is a relatively new technique for breast cancer treatment, we only offer this treatment as part of a clinical study to patients who meet study eligibility criteria. Patients will be monitored over time to determine the long-term safety and effectiveness of the treatment.

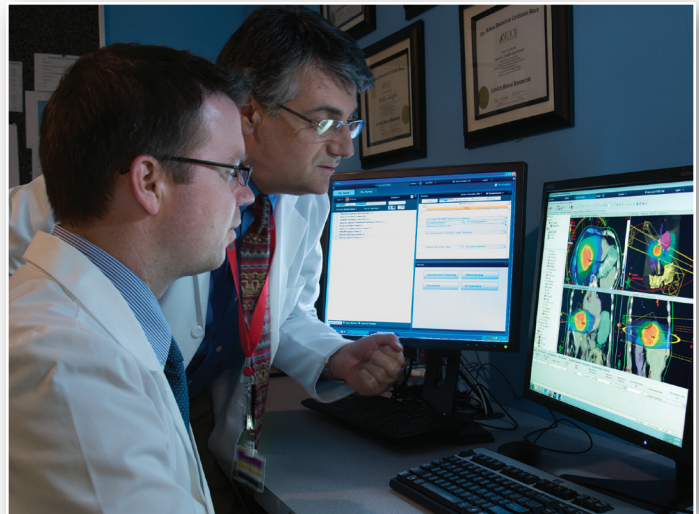
Education Programs in the Department of Radiation Oncology

The University of Arizona Department of Radiation Oncology has had a long history of educating oncology residents. This tradition continues with the expansion of the program to seven medical residents. Oncology resident education includes clinical teaching, a radiobiology course and a physics course. **Shona Dougherty, MD, ChB, PhD** continues to serve as the residency director.

In addition to the medical residency, the department also supports a medical physics residency with two residents in the program. **Russell Hamilton, PhD** serves as the program director. The radiation oncology physics residency includes all aspects of medical physics education and is in the process of seeking national recognition through accreditation with the Commission on the Accreditation of Medical Physics Education Programs (CAMPEP).

The Department of Radiation Oncology is committed to undergraduate education. The department regularly supports medical student electives. During the past year we have had 10 medical students of which 7 were UA medical students. **Sun Yi, MD** supervises this program.

Graduate education is also a big part of the department. The UA Professional Science Master's degree program in Medical Physics is a joint graduate program between our department and the Department of Physics. **Christopher Watchman, PhD** serves as the program director. The program received its CAMPEP accreditation in 2012. Currently there are 7 second-year students and three new students who entered the program this year. Over the past 5 years the program has graduated seventeen students who have gone on to



accept positions medical physics residencies, industry and regulatory agencies.

Eric Weterings, PhD supports radiobiology education by participating in the Undergraduate Biology Research Program (UBRP) which provides students with an opportunity to work on a full time basis in a biomedical lab during the summer months. The program pays 50% of their salary. Over the past summer Dr. Weterings had 3 participants in this program working in his lab.

The UA Department of Radiation Oncology is firmly committed to all aspects of education and we look forward to continued progress. If you have questions about any of these programs please contact the department at (520) 626-6723 or visit our webpage: rad-onc.arizona.edu.



About the Author

Christopher J. Watchman, PhD, DABR, is the graduate program director of the joint Physics and Radiation Oncology Professional Science Master's Degree program in Medical Physics. An assistant professor within the Department of Radiation Oncology, he teaches courses in radiation dosimetry, health physics, radiation therapy and clinical medical physics. He is an active member of the Radiation Oncology Medical Physics Residency program and is currently the head of the admissions committee. Dr. Watchman holds degrees in physics and exercise physiology from Brigham Young University (BS), health physics from Idaho State University (MS), and a doctorate in medical physics at the University of Florida (PhD). He completed residency training in radiation oncology physics at the University of Arizona Medical Center and is an American Board of Radiology certified medical physicist.

Unbridging the Gap – *Research May Show the Way Toward Retarding Radiation Repair*



The research branch of the Department of Radiation Oncology is headed by **Eric Weterings, PhD**, an established biochemist and radiation biologist who founded a brand-new laboratory at the University of Arizona Cancer Center in 2012, when he joined the UA College of Medicine as an assistant professor. Dr. Weterings' lab is staffed with a team of talented people: veteran researcher **Alfred Gallegos**, Chemistry junior **Trace Bartels**, Physiology junior **Siddhant Talwar**, and Biochemistry and Molecular & Cellular Biology senior **Lauren Dominick**. This multi-disciplinary team studies the biological effects of radiation on human tissue, hoping to find out how we can improve the efficiency of radiation therapy for solid cancers in the future.

In order to change the way we think about radiation therapy, we first need to understand what radiation actually does to tumors and how it kills them. Radiation destroys human cells by damaging the DNA in those cells. DNA essentially holds the blueprint of the cell, controlling every essential cellular function and facilitating cell division. Radiation therapy bombards the cell with large amounts of energy, shredding the DNA to pieces. Usually, the cells (and, therefore, the tumor) won't survive this treatment or at least they won't be able to multiply anymore.


Evolution, however, has found a way to reduce the effects of radiation on DNA. This is not so surprising, given the fact that cells are constantly exposed to background radiation,

which has forced them to adapt for survival. In everyday life, we are lucky to have these protective mechanisms in place. But for radiation oncologists it is bad news. Protection against radiation is a good thing, but not for tumors. And some types of cancer actually have more active defenses against radiation than normal cells do. If we are to improve the efficiency of radiation therapy, therefore, we need to understand how cells prevent their DNA from being damaged permanently by radiation. That's where our research team steps in.

When a DNA molecule breaks as a result of radiation exposure, the cell activates a cascade of events at the molecular level. Ultimately, all these messaging and signaling events direct a group of enzymes to the site of the DNA break. Some of these enzymes will attach themselves to both ends of the broken DNA molecule and literally form a bridge that glues the pieces back together. In the end, this temporary bridge is replaced by a new chemical bond. For the past 10 years, Dr. Weterings has been involved in identifying key interactions between the enzymes that build the bridge between the DNA pieces and facilitate the final repair. At the core of this process is a triad of enzymes: Ku70/80, DNA-PK, and Artemis.

The Ku70/80 enzyme is the first to bind the broken ends of the DNA. It has the shape of a ring that literally slides over the DNA molecule. The Ku70/80 enzyme functions as the foundation of the bridge and attracts the other key players to the repair event. One of those players is called DNA-PK. This enzyme is essentially the mortar that holds the bridge together. The DNA-PK enzyme is unique in the sense that it actively regulates when and where the next step of the DNA repair process takes place. It coordinates this by controlling the transfer of a phosphate group from one DNA-PK molecule to another – via a complicated process called autophosphorylation. This autophosphorylation event opens the way for Artemis to come in and chemically modify the DNA ends to make them ready for permanent repair. Taking all this together, it appears that the coordinated teamwork between Ku70/80, DNA-PK, and Artemis forms the core of the machinery that protects human cells from radiation.

Now that we know how these enzymes collaborate, we can start designing ways to disrupt the teamwork between them. Ultimately, the researchers in Dr. Weterings' lab aim to apply those countermeasures to tumors in order

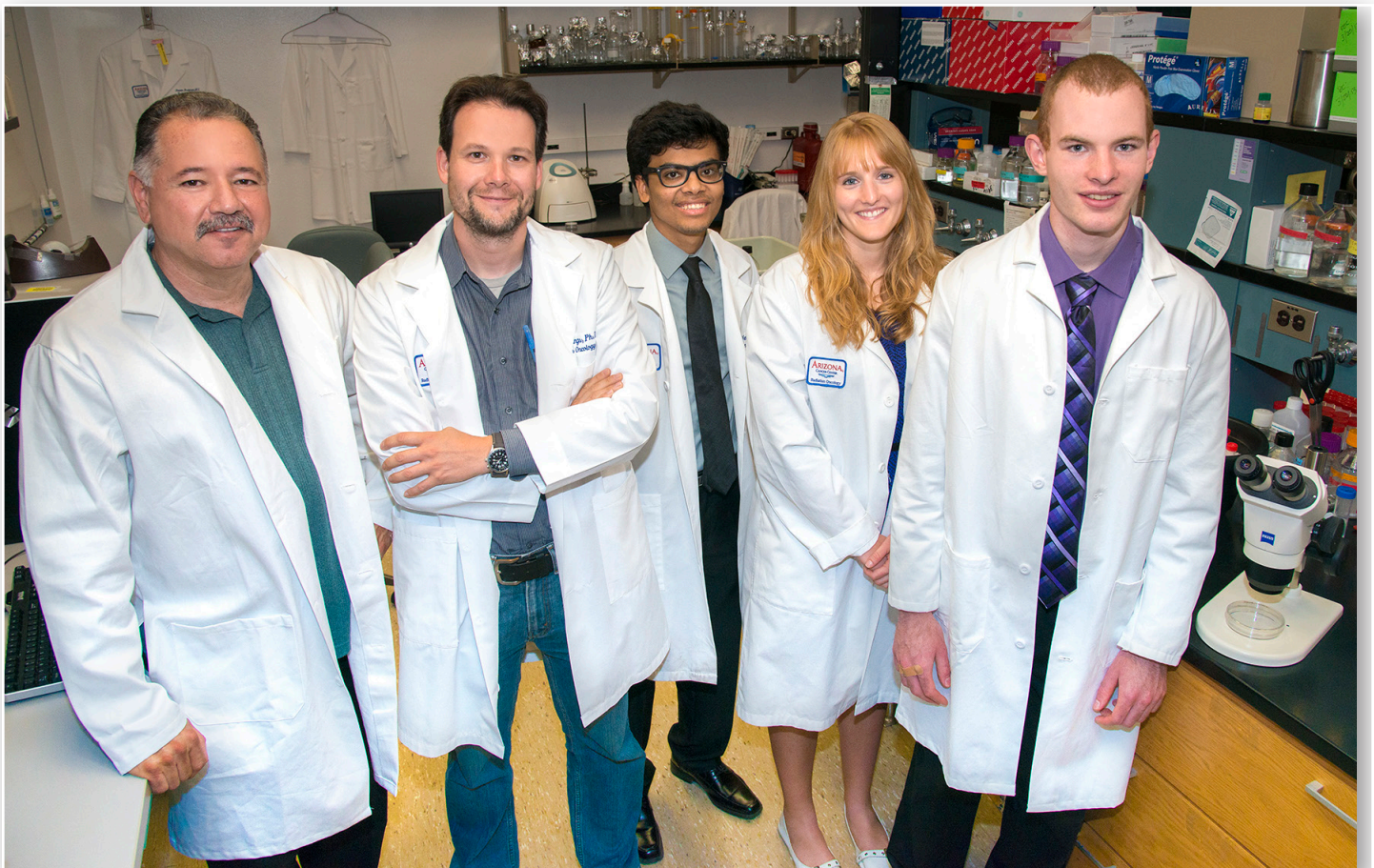


to make them more susceptible to the radiation therapy our oncologists provide. As part of an ongoing research project, Dr. Weterings' team has recently identified several experimental drugs that are capable of undermining the very foundation of the molecular bridge between the DNA pieces. Theoretically, these drugs should be capable of markedly increasing the sensitivity of cells to radiation and the department has therefore made moves toward patenting them. Now begins the arduous road to determine how well we can deliver those drugs specifically into tumors, while avoiding normal, healthy tissue.

In the meantime, our research team is also looking at other options to block the repair of radiation damage to cancer cells. For instance, we are trying to get a better understanding of how exactly the process of DNA-PK autophosphorylation works. As we have seen, this event basically determines whether or not repair of targeted damages will happen. If we can find a way to prevent DNA-PK autophosphorylation, that would effectively halt the repair of radiation damage and increase the sensitivity of tumors to radiation therapy. In addition, the Weterings

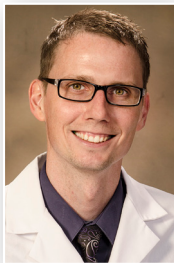
lab is also exploring more controversial ideas. By flooding cells with artificial pieces of DNA, the research team hopes to increase radiation sensitivity by depleting the available stores of Ku70/80 molecules. In that way, they are no longer available for DNA repair during subsequent radiation therapy.

Scientists have come to realize that the same enzymes that are involved in the repair of radiation-damaged DNA, may also play a role in the development of certain cancers. Some forms of cancer start by genes being cut-and-pasted into other parts of the DNA. These so-called oncogenic translocations are likely driven by enzymes that are able to do the "pasting" part of those processes, like Ku70/80, DNA-PK, and Artemis. Utilizing this knowledge, the Weterings' lab has recently started investigating how these enzymes are involved in certain gene rearrangements that are typically seen in early, aggressive prostate tumors. If it turns out that they play an important role, then perhaps it will be possible in the future to halt or slow down the development of aggressive prostate cancers. There's reason for optimism, but also for additional experimentation.



Residency Highlights

CONGRATULATIONS TO OUR RESIDENTS



Bryan Dukes, MS Physics

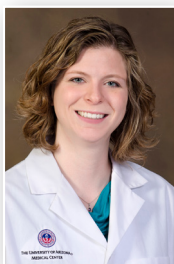
Bryan Dukes, MS Physics, June 2014 Graduate

Current employer: Radphys Oncology Services in Knoxville, TN.

Kristen O'Donnell, MD, June 2014 Graduate

Research focus during residency: Patient symptoms levels during treatment and contouring the prostatic fossa.

Current employer: Providence St. Mary Hospital in Walla Walla, Washington.



Kristen O'Donnell, MD

Michael Cheung, MD, Chief Resident

Cheung M, Kim YB, Skolnik SE, Grow J, Slane BG, Gordon JD, Stea B. *Acute Skin Toxicity using High Dose Rate Electronic Brachytherapy for Non-Melanomatous Skin Cancer.*

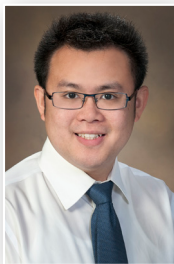
American Society for Therapeutic Radiation Oncology 56th Annual Meeting, San Francisco, CA

Cheung M, Ong S, Goyal U, Kratz S, Gernon TJ, Avery R, Aly F, Kuo P, Erman A, Khan R, Yi S. *Optimal Fractionation Regimen for Electronic Brachytherapy for Treatment of Non-Melanomatous Skin Cancers.*

American Society for Therapeutic Radiation Oncology 56th Annual Meeting, San Francisco, CA

AANS/ASTRO Stereotactic Radiosurgery Course for Neurosurgery and Radiation Oncology Residents.

Rockefeller Research Labs, Memorial Sloan Kettering Cancer Center, New York, NY



Michael Cheung, MD

Uma Goyal, MD

Goyal U, Ceizyk M, Locke A, Thai H, Hine C, Bowers K, Mignault A, Castillo L, Smith-Raymond L, and Georgiev G. *Prone lead shield to reduce scatter radiation to the contralateral breast during radiation therapy for breast cancer: Physics results.*

American Society for Therapeutic Radiation Oncology 56th Annual Meeting, San Francisco, CA

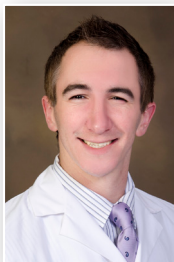


Uma Goyal, MD

Steven Skolnik, MD

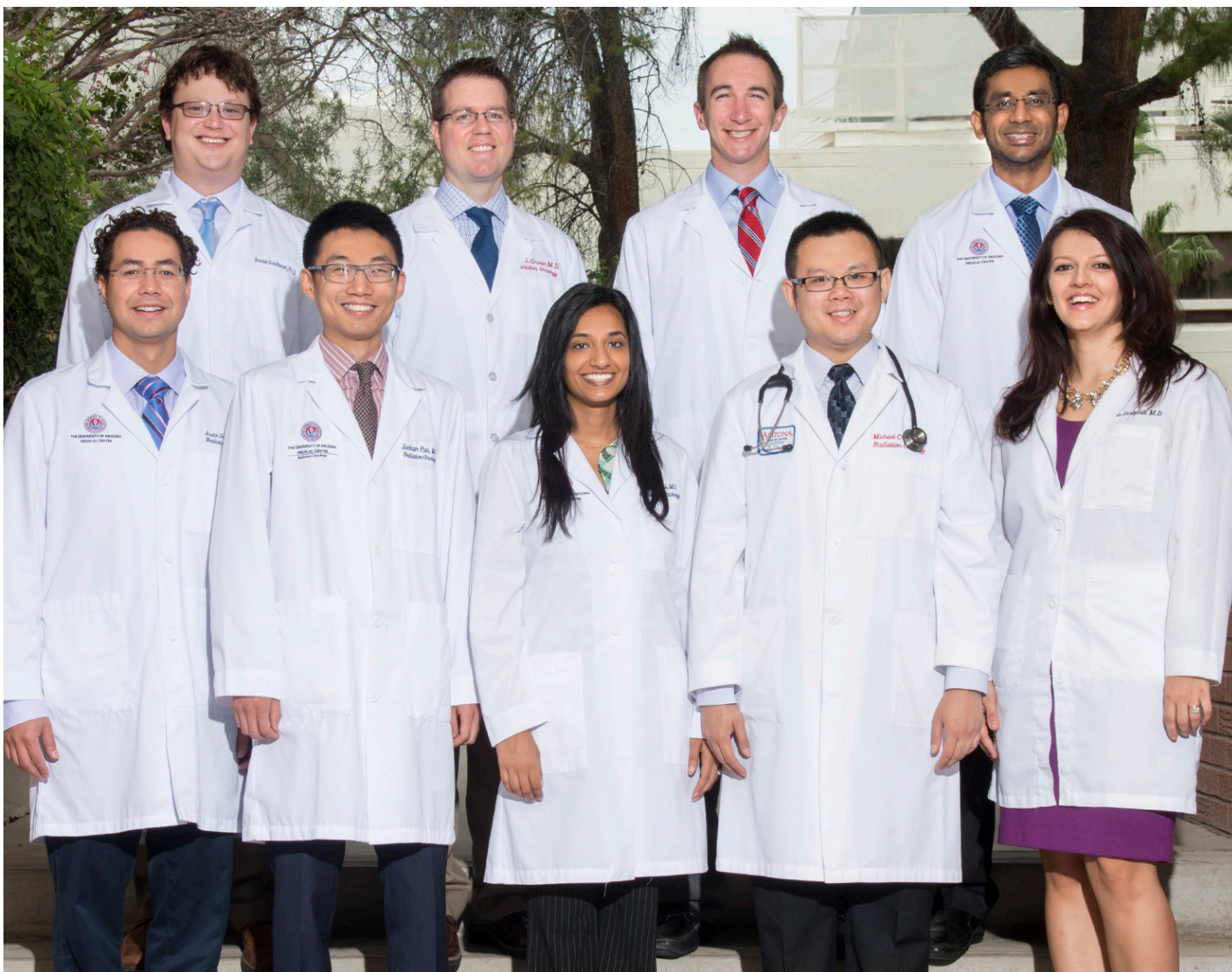
Baldassarre S, Desai A, Kruse J, Skolnik S. ASTRO- Resident Poster Viewing Award in the Clinical category for your abstract titled. *Frameless LINAC Image Guided Radiosurgery for Primary and Recurrent Trigeminal Neuralgia.*

American Society for Therapeutic Radiation Oncology 56th Annual Meeting, San Francisco, CA



Steven Skolnik, MD

Meet the Current Radiation Oncology Medical and Physics Residents



(top) Dan Goldbaum, PhD; Joel Grow, MD; Steven Sckolnik, MD; Rajayogesh Davulrui, MD; (bottom) Justin Suszko, MD; Junhan Pan, MS; Uma Goyal, MD; Michael Cheung, MD; Tijana "Tina" Skrepnik, MD.

Meet our New Residents & New Faculty



Justin Suszko, MD, PGY II

Dr. Suszko is a first year resident in Radiation Oncology. He received his M.D. at the University of Nevada School of Medicine in Reno, NV. He completed a residency in Diagnostic Radiology at the University of New Mexico Hospital in Albuquerque, NM. He hopes to become double-boarded in both specialties and use his imaging background to further the field of radiation therapy.



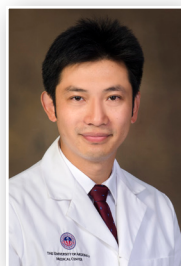
Dan Goldbaum, PhD Clinical Physicist Associate

Dr. Goldbaum earned a BA in physics and mathematics from Ohio Wesleyan University. He then earned a PhD in theoretical physics from Cornell University. After graduation he served as a postdoctoral research associate in the physics department at the University of Arizona, where he went on to earn a PSM in medical physics. While pursuing his PSM, Dr. Goldbaum investigated the effect of window and level settings on the accuracy of image fusion achieved via the ExacTrac patient positioning system. He also investigated the use of a normoxic shell model to predict tumor control probability.



Tijana "Tina" Skrepnik, MD, PGY II

Dr. Skrepnik is a first year resident in Radiation Oncology. She received her MD at the University of Arizona in Tucson, AZ. She completed her PGY-I Transitional year at the Tucson Hospitals Medical Education Program through Tucson Medical Center.



Wen Li, PhD New Physics Faculty

Dr. Li earned his bachelor degree in physics at Nanjing University in China. He received a master degree in physics at Arizona State University. His doctorate degree was in biomedical engineering from Case Western Reserve University, with his thesis focused on the development and application of quantitative Magnetic Resonance Imaging (MRI) techniques. Prior to his appointment as assistant professor at the University of Arizona Cancer Center in 2014, Dr. Li completed a three-year residency training in radiation oncology physics at the Cleveland Clinic.

Visit our website at,

<http://rad-onc.arizona.edu/>

GIVE A GIFT

By giving to the Department of Radiation Oncology at the University of Arizona College of Medicine, you are helping our efforts to recruit and retain key faculty, support promising research doctors, and maintain laboratories and lectureships. Your donation is fully tax-deductible.

For more information, please contact us by phone at 520-626-6724, or mail your tax-deductible contribution to:

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THE UNIVERSITY OF ARIZONA
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Radiation Oncology News

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