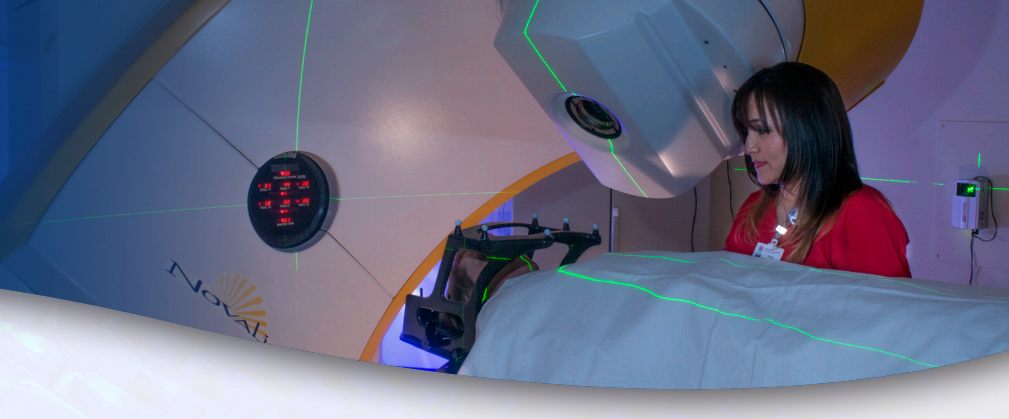
THE UNIVERSITY OF ARIZONA | COLLEGE OF MEDICINE



Radiation Oncology News

Winter 2013

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 reseach as well.

Inside this Issue:

Message from the Chair

Dear Friends and Colleagues

It's been an exciting year in Radiation Oncology at the UA! Our department has a great team of faculty that is working to bring this department to new levels. Our clinical trials have doubled in growth in the last year-largely due to variety of clinical trials that we have to offer our patients. Dr. Gonzalez, our breast cancer specialist, offers specialized treatment techniques that further reduce radiation doses to the heart. Many patients are seeking out the Breast Health Team at the UA because of the specialized treatments we offer that can't be found anywhere else in Arizona.

Our medical residents continue to have an unbroken streak of successful board passing. This year Dr. Tom Sroka and John Gordon, MS passed their oral board as well. We are very proud of their accomplishments. This year we graduated two physicians: Dr. Ben Slane and Dr. David Vonk and also Adam Turner, a medical physicist, all of whom have found jobs in Arizona.

In the research area, Dr. Weterings lab continues to study the biological effects of radiation therapy on both healthy and cancerous tissues. The ultimate goal of Dr. Wetering's studies is to find ways to maximize the effects of radiation on targeted tumors while minimizing the damage to healthy organs and tissues. Radiation kills cells by damaging their DNA. His lab continues to chart the activities to repair DNA, follow the benefits of epigenetic drugs, and dig into less mainstream ideas.

Our department continues to provide excellent patient care with the newest technologies. We are still one of the only facilities that offers patients an alternative to MOHs surgery with the Xoft treatment machine. Most recently, this fall we upgraded to the TomoHD system which will improve accuracy and efficiency in patient treatments.

One of the highlights of the year included being awarded a three-year accreditation in radiation oncology by the American College of Radiology (ACR). We are the only Cancer Center in Southern Arizona with this accreditation that reflects the highest levels of patient care and treatment, patient safety, personnel qualifications, facility equipment, quality control and quality assurance.

Thank you to all of those who have supported our department this year. We look forward to continued success in research and patient care in the upcoming year.

B. Dino Stea

Baldassare "Dino" Stea, MD, PhD
Department Head and Professor
Department of Radiation Oncology

Radiation Oncology Research – Research is Hope

This past year has been a year of excitement and growth in the Research Division of our Department. We have had very positive results from many of the studies that we have participated in. One trial in particular showed a more than doubling survival rate when the drug, Erlotinib, was given in conjunction with Radiation Therapy for the treatment of brain metastases from Non-Small Cell lung cancer. This study is reflective of the new, innovative approaches in studies we have available that go beyond the previous standards of radiation therapy and chemotherapy. We currently have an open vaccine study for Glioblastoma Multiforme. We are collaborating with pharmaceutical companies in the use of new ground breaking drugs that may inhibit the growth of cancer in certain diagnoses, as well as drugs that may be able to delay DNA repair. In addition to these studies, we are participating in many sub-studies that are aggressively looking at tumor cells to identify ways to utilize diagnostic-specific targeted agents with radiation therapy.

We have added many research studies this year to include the following disease sites:

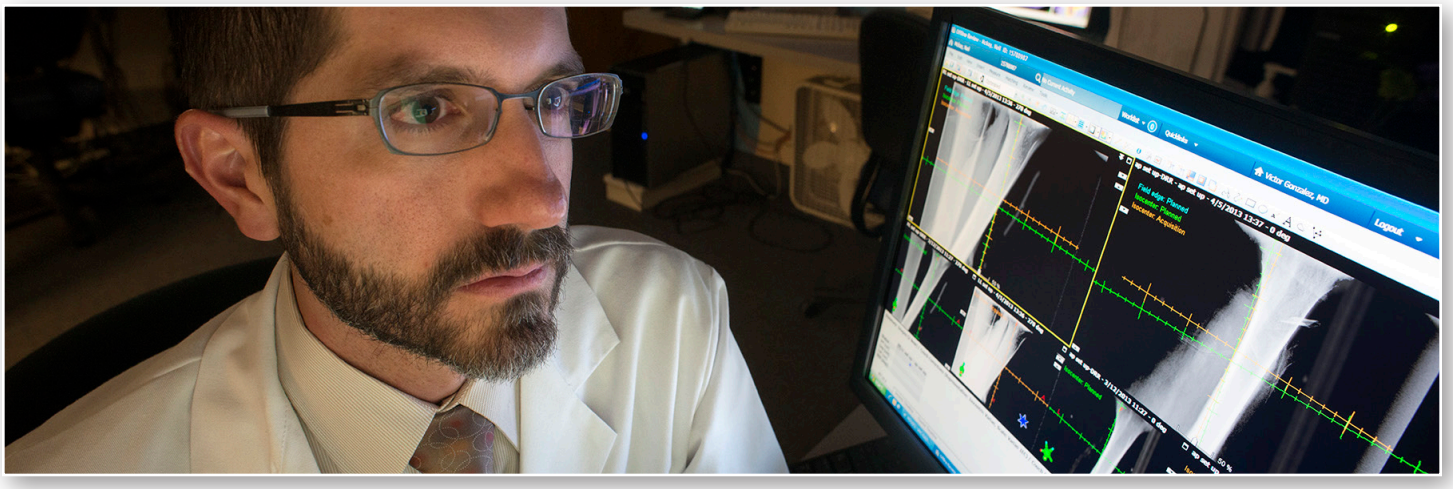
Brain Metastases from Non-Small Cell Lung cancer, Breast cancer, Cervical/Endometrial cancer, Esophageal cancer, Glioblastoma Multiforme (both newly diagnosed and recurrent), Head and Neck cancer, Liver cancer and Spine metastases. For more information on these studies, please visit our website at:

http://azcc.arizona.edu/research/clinical-trials

We've tripled our enrollment to research studies just in the first few months of this year compared to all of last year. Below is an extraordinary brain metastases study that we have open and are enthusiastic about being able to offer to patients:

M10-897 A Randomized, Double-Blind, Phase 2, Dose-Ranging Study to Evaluate the Safety and Efficacy of Veliparib and Whole Brain Radiation Therapy Versus Placebo and Whole Brain Radiation Therapy in Subjects with Brain Metastases from Non-Small Cell Lung Cancer

Please contact either Jamie Holt or Daniella Boros at 520-626-6800 for further information on any of our research studies.



Dr. Gonzalez, MD

New Study Reveals Benefits of Radiation Therapy for Breast Cancer Outweigh Risks

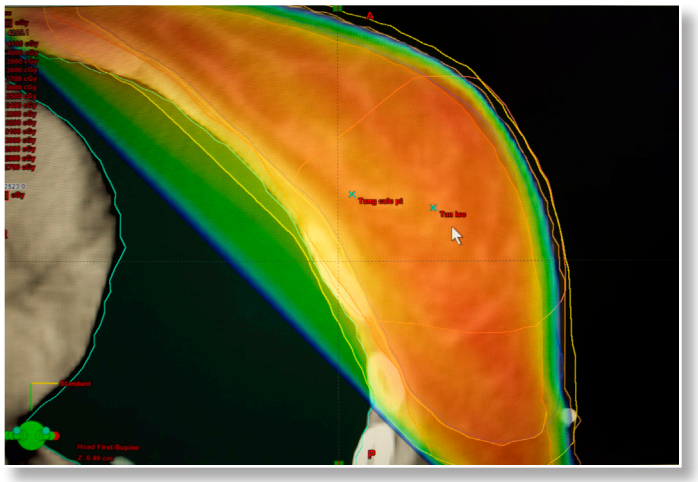
In a recent article published in The New England Journal of Medicine, the results of a study on the risk of heart disease to women who received radiation therapy for breast cancer spurred national headlines. This study is important for several reasons. On one hand, it shows us how far radiation techniques have advanced in breast cancer. The doses of radiation to the heart with modern techniques are dramatically lower than they were twenty years ago, when most of the women in this study were treated.

At the same time, it emphasizes the need for continued improvement and ongoing research. Right now, we don't know what dose of radiation is 100% safe for the heart. We can assume that the risk to the heart is going to be less with modern techniques, but we don't know if that will be enough to completely eliminate the risk.

At the UA Department of Radiation Oncology, we offer specialized treatment techniques that further reduce radiation doses to the heart. These techniques include intra-operative radiation therapy (where just a single dose of radiation is given to the tumor bed at the time of surgery), prone treatment (where the patient lies face down for the treatment and breast hangs down away from the heart), and respiratory gated treatment (see below) .

Patients at greatest risk for treatment are women with left sided tumors and women who require radiation to the lymph nodes close to the heart. In this situation, the heart can temporarily be moved away from the ribcage by having the patient take a deep breath. When you take in a deep breath, the ribcage and the breast move away from the heart. Special cameras located in the radiation treatment room track the patient's breathing cycle. This breathing trace is displayed to the patient on special video goggles. In this way, the radiation beam is automatically turned on, only after the heart had moved safely out of the way. The University of Arizona Cancer Center is the only center in Tucson to offer this technology and one of the few centers in the United States with this technology.

We have to balance the potential risks of treatment with the known benefits. After breast cancer surgery, radiation cuts the odds of the cancer returning in half. For most women, that's going from a 30 percent chance of cancer without radiation to a 15 percent chance of cancer with radiation. There is no doubt that radiation therapy for breast cancer is a life-saving treatment. Overall, the benefits far outweigh the risks.



TomoHD Upgrade

Christopher Watchman, PhD

At the end of September, our department upgraded our TomoTherapy machine to a TomoHD configuration. This upgrade significantly improves the system's capabilities and will increase our treatment options for patients. The TomoHD system includes traditional helical treatments (3D and IMRT) and TomoDirect. TomoDirect allows for 3D discrete angle treatments up to 135 cm in length. In addition the system includes a new 14 Blade computer server and the VoLo planning system which allows for faster treatment planning. Additional improvements in treatment delivery control will translate to faster patient treatment times. Both of these improvements will allow for greater patient volume and enhance the patient's experience in our department. Other improvements include greater dose delivery accuracy, more quality assurance options and remote software solutions that will improve treatments and staff workflow. All of these improvements are now available to all of patients.

Achievements:

We are proud of the achievement of our residents (Dr Vonk, Dr Slane, and Dr O'Donnell) and junior attending/ physicists (Dr Yi, Dr Howell and John Gordon) who have successfully passed the written and /or oral ABR boards.

It was bitter sweet saying goodbye to three residents at the end of June. While we are proud of their many accomplishments they will be missed in our department. David Vonk, MD and Ben Slane, MD, with both be working for Arizona Oncology. Dr. Vonk will be working here locally and Dr. Slane will be working in the Phoenix office. Adam Turner, Ph.D, Arizona Center for Cancer Care, Medical Physicist

Presentations:

David Vonk, MD:

Arizona Oncology, Physician

- *Presentations during UA residency: Ocular Melanoma - ABS*

Ben Slane, MD:

Arizona Oncology (Phoenix), Physician

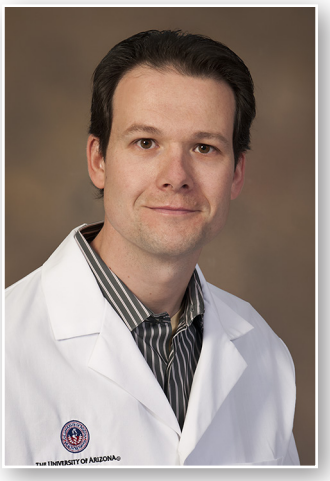
- *2013 American Brachytherapy Society LDR Prostate Brachytherapy Fellowship*
  Adjuvant cavity-directed radiosurgery following surgical resection of brain metastases- ACRO 2013
- *Comparison of three different linear accelerator based fractionation techniques for the treatment of vestibular schwannoma- ACRO 2012*
- *Improving detection of metastasis for sterotactic radiosurgery- Leksell GK Society 2012*
- *Increase radiosensitivity seen in cells with mutated succinate dehydrogenase subunits C or D is inhibited by overexpression of MnSOD and catalase- Society for Free Radical Biology and Medicine*
- *Succinate dehydrogenase subunit C deficient Chinese hamster fibroblasts demonstate increased steady state levels of superoxide production and metabolic oxidative stress- Society for Free Radical Biology and Medicine*

Adam Turner, PhD:

Arizona Center for Cancer Care, Medical Physicist. He had a number of presentations during his training and will be working in Phoenix at the Arizona Center for Cancer Care.

- *2012 AAPM Annual Meeting Research Presentations:*
- *Evaluation of Potential Effective Dose Estimates Using Values Included in CT Dose Reports. The Energy Dependence of Small Volume Ionization Chambers and Solid State Detectors at Diagnostic Energy Ranges for CT Dosimetry - Assessment In Air and In Phantom 2012 Arizona State Society of Radiologic Technologists*
- *Annual Meeting Invited Speaker:*
  Evaluating Dose from CT exams: The measurement and interpretation of the CT Dose Index 2013 AAPM Spring Clinical Young Investigators Symposium:
- *Evaluation of Gafchromic XRQA2 Film for Varian OBI KV Scanner Dose Measurements*

RadBio Research Updates



Eric Weterings, MD

The Weterings lab, part of the Department of Radiation Oncology, studies the biological effects of radiation therapy on both healthy and cancerous tissues. The overall goal of our researchers is to figure out how we can maximize the effects of radiation therapy on targeted tumors, while minimizing collateral damage to healthy organs and tissues.

Radiation kills cells by damaging their DNA. The energy deposited by the radiation literally shreds DNA molecules and chromosomes to pieces. Human cells, however, have developed a defense system that is capable of repairing such DNA breaks. Speaking from an evolutionary point of view, this is probably a good thing because it protects us from the damaging effects of cosmic radiation, UV light, background radiation, etc. Unfortunately, that same DNA repair mechanism can also restore the damage done to cancerous cells and thus reduce the overall efficiency of radiation therapy in solid tumors. The Weterings lab is devoted to obtaining a working understanding of how DNA repair works on a molecular level and how we can manipulate it in order to improve the outcomes of radiation treatment in the clinic.

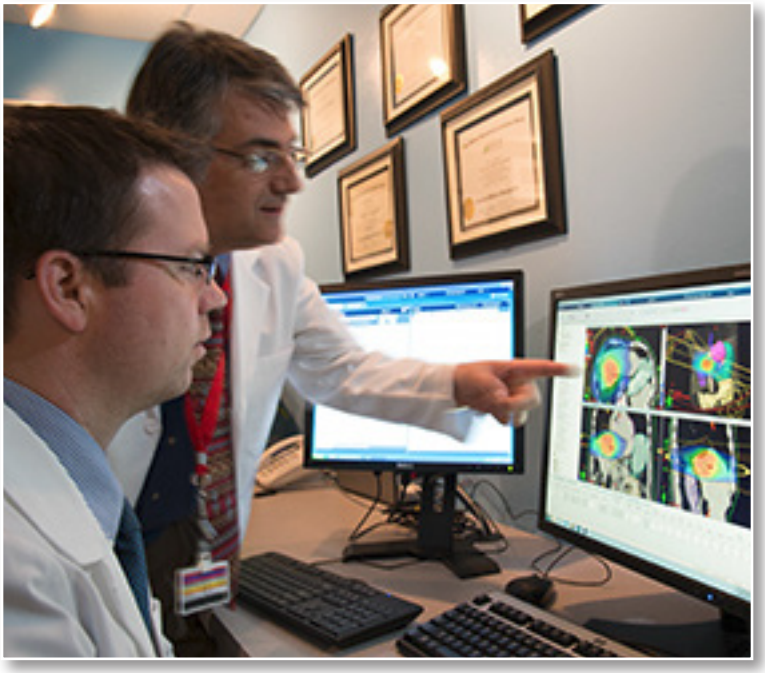
When DNA molecules break into fragments as a result of radiation exposure, human cells activate a cascade of molecular level events that eventually leads to the capturing and re-joining of the pieces. This rather amazing and intricate work is done by a team of proteins. Some of these enzymes will bind to the ends of the DNA fragments, other proteins will then come in and hold the DNA fragments together in what appears to be a sort of molecular bridge. Finally, a third group of proteins will enter the scene and glue the tethered DNA segments back together again.

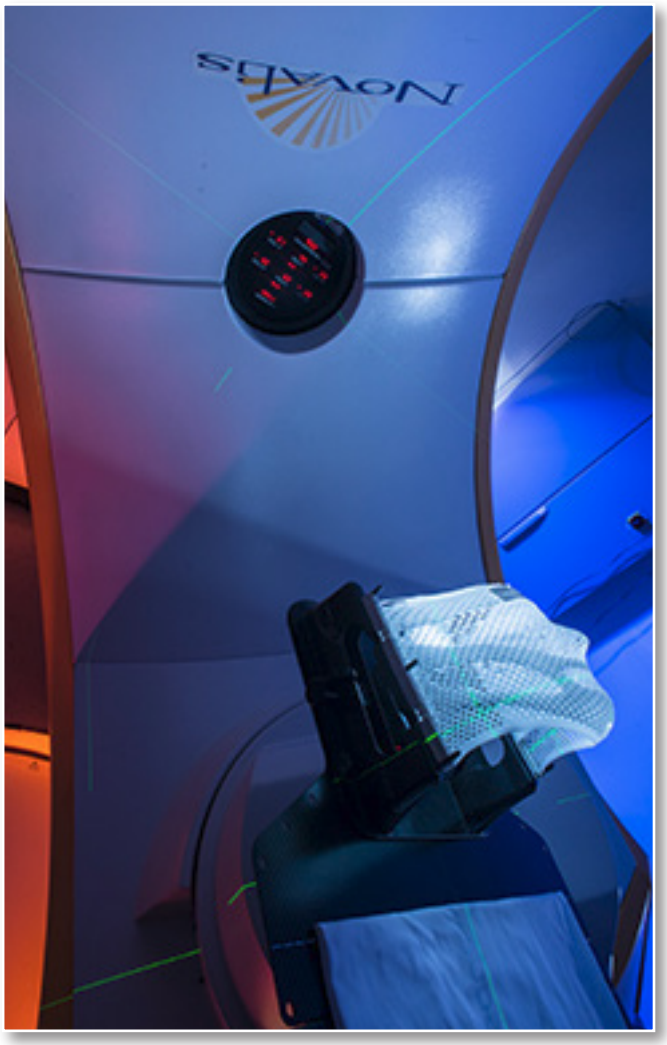
Researchers in the Weterings lab are currently charting the individual activities of four of these repair proteins. They are also trying to get an idea of how they interact with each other in order to get the job done. Besides satisfying an academic curiosity, this work is actively opening vistas for clinical application. For instance, in the past decade the Weterings lab has published a series of experiments which identified two rate-limiting steps in the repair of DNA breaks, both coordinated by interplay between three enzymes: Ku70/80, DNA-PK, and Artemis. Now that we have an understanding of the partnership between these factors, we also have an opportunity to design new drugs targeted at disrupting this partnership between repair proteins. These experimental compounds are expected to become powerful radiation sensitizers: drugs that increase the biological effects of radiation. In order to further this goal, the Weterings lab was awarded a Faculty Seed Grant by the University of Arizona Foundation Grants and Awards Committee of the Board of Trustees and the University of Arizona Office of the Senior Vice President for Research this year.

In addition, research in the Weterings lab has provided elegant evidence that a certain class of medications, called epigenetic drugs, is quite capable of suppressing DNA repair. Epigenetic drugs exert their activity by altering the levels at which DNA repair enzymes are produced by cells. Experiments have already shown that an epigenetic modulator known under the trade name Vidaza effectively increases the effects of radiation therapy on (xenografted) prostate tumors. This research is currently supported by an Idea Development Award, granted by the Department of Defense's Congressionally Directed Medical Research Programs (CDMRP). An investigation of the efficiency of 5-azacytidine in sensitizing glioblastoma cells to radiation is on its way and has been awarded with the University of Arizona's Cancer Center Support Grant Pilot Project Program Grant 2013.

In the mean time, the Weterings lab is also exploring less mainstream and more controversial ideas. For instance, what would happen if we flood cells with artificial pieces of DNA prior to radiation treatment? These foreign DNA fragments mimic the presence of DNA breaks and should, at least in theory, trick the cells into prematurely activating their DNA repair proteins. In other words, it would deplete the cells resources to deal with the effects of an actual radiation exposure and reduce the striking capability of the cells' natural defenses against radiation. Food for thought. And for further experimentation.

The Weterings lab is lead by biochemist Dr. Eric Weterings and has been a part of our department since February 2012. The lab is currently staffed with two veteran Research Specialists, Alfred Gallegos and Suzanne Regan, as well as three upcoming talents of the University of Arizona: undergraduate students Trace Bartels, Lauren Dominick, and Siddhant Talwar.

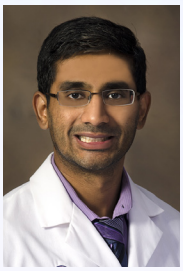




Meet our New Residents

Uma Goyal, M.D., PGY II

Dr Goyal is a second year resident in radiation oncology. She received her MD at the University of Arizona College of Medicine in Tucson, AZ. She completed her internship in Internal Medicine at Loma Linda University Medical Center in Loma Linda, CA.



Rajayogesh Davuluri, M.D., PGY II

Dr. Davuluri is a second year resident in radiation oncology. He received his MD from Baylor College of Medicine in Houston, TX where he also completed his internship in Internal Medicine.

Physics Resident

Junhan Pan
Clinical Physicist Associate

Junhan received his Master's degree in Medical Physics from University of Arizona. His research project during graduate studies focused on developing image based alpha particle emitter dosimetry model in bone marrow by using autopsy spongiosa samples and Monte Carlo simulation.

Visit our website at,

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

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