Contemporary Education Opportunities Improve Physician and Researcher Training

UAB Radiation Oncology is currently engaging in several novel and exciting educational and research opportunities. These opportunities are not limited to this department. In fact, several of our newest educational projects are focused on training with medical teams from outside this institution.

We have successfully completed our first Eclipse and TrueBeam training course. This course provides radiation oncologists, radiation physicists, surgeons, and dosimetrists a three-day didactic and laboratory course designed to train in advanced therapies with Eclipse and TrueBeam, including CNS radiosurgery and stereotactic body radiation therapy. After completing the course, participants will understand the workflow, advantages, and risks associated with SRS/SBRT and know how to technically and clinically evaluate SRS/SBRT treatment plans. Medical teams who attend the Eclipse/TrueBeam training course also receive access to our treatment planning manual, a living, wiki-like document which collects our most current procedures and processes into a central, easily-accessed location.

The improved treatment developments created alongside the training courses have made a large impact on our educational and research programs. Our research in treating brain metastases is poised to have a huge influence on how we will treat future patients.

For example, the UAB Departments of Radiation Oncology and Neurosurgery in partnership with Varian Medical Systems have examined a single-isocenter linear accelerator-based technique for brain metastases treatment. This approach boasts equivalent radiosurgical plan quality to Gamma Knife and can be delivered in a fraction of the time previously required with no need for anesthetic. After proper imaging, review, evaluation, and alignment, beam arcs are delivered with each full arc taking approximately one minute. For complicated plans, additional hemi-arcs are added, each of which is delivered in roughly 30 seconds. Even the most complicated treatment plans are typically completed within 20 minutes.

Our department is also focused on a long-term strategy to attract and train academic physicians. In 2008, the addition of the Clinical Trials Pathway and the Holman Research Pathway changed the curriculum to include specific training in clinical trials and translational research. Two residents have completed the Holman pathway, the results of which will aid us in the continuing evaluation and modification of our curriculum. We hope that exposing medical students and residents to research earlier in their career will foster greater interest in academic careers.

Our dedication to increasing educational materials access has culminated in an online training and research material archive. We have established a private YouTube channel to provide UAB residents, medical students, and other radiation oncology researchers the opportunity to view any of our lectures at any time from any location. This department is also emphasizing training in lifelong learning and quality improvement. Medical records training and quality improvement projects are being added to our curriculum to better satisfy new requirements from the American Board of Radiology.

These most recent developments are strong examples of the research culture we work tirelessly to maintain. We work to create a culture that values translational and clinical research, encouraging our physicians, researchers, and residents to value the creation of new knowledge that will help future cancer patients. Training our residents to not only work as skilled physicians, but also as skilled researchers, is an essential core principle of all our educational programs and research protocols.
RESIDENT SPOTLIGHT: ALEX WHITLEY

Holman Research Scholar and Chief Resident Dr. Alex Whitley is nearing the end of his residency while preparing for the next stage of his medical career.

"After working on my PhD for two years at MUSC in Charleston, I decided that I really liked clinical research and translational research. So, I joined the MD/PhD program there. After that, my wife finished her Pharm.D and did a two-year residency at MUSC in ambulatory care. When she finished, she got a faculty position with Auburn's College of Pharmacy," Dr. Whitley explained. "Because of that move, I transferred and finished up in the MD/PhD program here at UAB. I've been here since 2006. I started the residency program here in 2010 and will finish in June."

Dr. Whitley took part in a considerable amount of research and clinical work throughout his years at UAB Radiation Oncology.

"Through my residency at UAB, I did the Holman Research Pathway. That is an intense research pathway from a laboratory standpoint. I worked with Dr. Yang as my mentor on that project," Dr. Whitley began. "I worked on targeting DNA repair with novel combinations of therapeutics to improve patient outcomes. I focused on esophageal malignancies after an initial focus on head and neck malignancies. Dr. Bonner was a co-mentor for me on both the Holman application and my project."

Dr. Whitley's exemplary work and skills have led him to a new career opportunity nearby.

"I've taken a position at Montgomery Cancer Center. I finish here June 30 and I start there August 1. My wife works for the Auburn College of Pharmacy, but her current clinic location is in Tuscaloosa. She commutes to Tuscaloosa and I commute here. We will be moving to Montgomery," Dr. Whitley explained. "Her new clinic will be in Montgomery, so she can continue her work while I work in the Montgomery Cancer Center. A previous graduate of this program, Dr. Lee Franklin, is there, along with two other physician partners in Montgomery."

The new clinical environment will be different from what Dr. Whitley has experienced in his career, but he is looking forward to the new experience.

"The group in Montgomery is a private practice group, so I will treat a little bit of everything. My research efforts will all be on the clinical side. It will be mainly a clinical position," Dr. Whitley said. "I'll be seeing lots of patients versus a split type of work like Dr. Bredel, Dr. Yang, or Dr. Willey each do. There may be potential collaboration with some faculty and researchers at Auburn, but it will all be clinical research."

Dr. Whitley provided high praise for both our department and the UAB Health System.

"UAB Health System is a very good health system. The training here has been excellent. The atmosphere and the environment, from an attending standpoint, have been very collegial," Dr. Whitley said. "It has been an excellent learning environment. There have been ample opportunities for research and to see any type of pathology. This system provides good training in all modalities without needing to travel."

While he will be working in a different clinical environment, Dr. Whitley hopes to maintain strong connections to UAB Radiation Oncology.

"The environment here is very good. Maintaining a good relationship with this department, especially since I will be taking a position only an hour and a half away, is a strong desire of mine," he said. "Potential opportunities for clinical collaboration are of high interest to me."

Through his past and present work along with his future career path, Dr. Whitley stands as a strong example of UAB Radiation Oncology's commitment to training excellent physicians and researchers.
"Our past fifteen years of research has focused on malignant brain tumors. That research focuses on characterizing the molecular biology and molecular genetics of primary brain tumors, which are clinically a very challenging disease," Dr. Bredel said. "In particular, we are working on understanding genetic changes in brain cancer. Most of our projects focus on how certain genes and their aberration patterns are involved in brain tumor development, or how those genes relate to tumor progression, tumor resistance, or patient survival."

The laboratory has made several noteworthy discoveries. These discoveries have been published in high-impact journals like the New England Journal of Medicine, JAMA, and the Journal of Clinical Investigation. These publications display the laboratory’s transition from establishing the existence of particular genes to understanding and targeting the changes within those genes.

"We hope that since we have established a few important genes in brain cancer, we can move to targeting changes in brain tumors," Dr. Bredel said. "We are trying to find selective therapeutics which target these changes, and by doing so seeing if we can halt or change the growth or progression of a brain tumor."

The Bredel laboratory’s work usually begins with a basic, genome-wide view, but utilizes specific technologies and methodologies to focus on specific genetic changes.

"We will often start a project with a very global view utilizing technology known as genomics. With genomics, you don’t just look at one gene in a cancer cell or tumor, but you look at the entire genome, which encompasses around 30,000 genes," Dr. Bredel explained.

"We try to put these genes and their changes in a relationship of change to each other. From that very basic perspective, we use functional genetics tools," he continued. “These tools help us understand how the change in a certain gene impacts the function of a tumor, the mechanism behind that change, and why the tumor cell selects that genetic change.”

Dr. Bredel’s laboratory work is highly collaborative, commonly working with other labs. These labs can be found here at UAB, in other states, and even other countries.

“We have a very extensive network of collaborators across the United States and in Europe. This helps us in terms of lab work. There are certain aspects of our research where one lab simply cannot complete the necessary work alone," Dr. Bredel stated. "We are integrated into the NCI SPORE for Brain Cancer here at UAB. There is substantial networking among UAB researchers and we are collaborating with many investigators who focus on brain tumors."
Dr. Bredel always keeps his projects’ clinical applications in mind while working.

“Clinical endpoints are always a strong focus of our work. There is a strong translational component,” he said. “Our eventual endpoint is determining how this will affect clinic patients. Our projects usually have to go the whole nine yards, going from a basic perspective to a translational perspective, to looking at the clinic.”

This focus on clinical endpoints has prompted Dr. Bredel to expand the parameters of his current research.

“While around 90% of our research is linked to glioblastoma, we are now looking outside the box, at different cancer types. We are expanding beyond the rare brain cancer and are looking at how our genetic discoveries impact more prevalent types of cancer like breast cancer,” Dr. Bredel said. “Expanding to different types of cancer will give our lab the opportunity to expand and test new drugs, manage new experiments, and create new treatment options for our patients.”

Clinically applying brain tumor genetics information to other forms of cancer has been promising thus far.

“We have been trying to put one of our discovered gene changes into comparison with well-known genetic changes like those in breast cancer. From that perspective, we hope to find out if our work could help in understanding the pathogenesis of breast cancer,” Dr. Bredel said. “We have very intriguing findings on that so far. We have been examining genomic profiles in about 5000 breast cancers and we have consistently found that there may be a critical genetic similarity between our findings and breast cancer.”

The ongoing discovery and innovation of the Bredel laboratory is another powerful example of how UAB Radiation Oncology continues its outstanding work in cancer treatment research.

The Bredel laboratory’s work usually begins with a basic, genome-wide view, but utilizes specific technologies and methodologies to focus on specific genetic changes.
After years of work in radiation oncology, Dr. Popple began to notice the difficulties of creating practical and effective radiation therapy treatment plans using current treatment planning programs. In complicated or difficult cases, planned treatment trajectories could often cause collisions with patients, resulting in the complete reworking of the treatment plan.

“You can plan as much as you want, but if you can’t deliver the plan because it would lead to a collision, that’s useless,” said Dr. Popple. “Because these trajectories were arbitrary and computer-optimized, the planner couldn’t use their intuition. The ability to use these trajectories clinically would be limited by the fact that you couldn’t predict whether they were deliverable.”

As he progressed in his research, Dr. Popple made important discoveries concerning therapy planning. Creating treatments in which machine positions could dynamically change were becoming a possibility. However, such treatments were missing two key elements. The first was the ability to determine during treatment planning if the projected trajectories would result in patient collision. The second was developing a real-time collision-avoidance system.

Dr. Cardan came to similar conclusions through his own research.

“The more experience you have with doing radiation therapy delivery, you realize that the more you can potentially move the patient, the better potential the treatment could be,” Dr. Cardan said. “You’d have some scenarios where you’d have ‘sweet spots’ of treatment that are easier to get to. The problem is we’ve had to keep the treatments relatively simple over the past few decades because it’s a relatively complicated problem to find the collision that could happen in the room with this specific patient on the table.”

To determine potential collisions, the two are examining the use of the Microsoft Kinect to scan in patients and gather their three-dimensional geometry.

“We use [the Kinect] to solve this polygonal collision detection problem. This is the Kinect for Windows; it’s designed specifically to create applications,” said Dr. Cardan. “We go through all the possibilities of how those things can move. We create a collision map, basically where the gantry and couch can go at the same time to create a treatment.”

To model the very complex geometries involved in a collision map, the Kinect was used to create a polygon mesh. Polygon mesh was chosen as it can be more efficiently used to describe the surface of an object without requiring empty irrelevant data points of the interior, the availability of visualization tools for meshes is widely available due to the prevalent use of polygon...
meshes in electronic gaming [1] and film [2], and because of the need for fast and accurate collision detection in those industries, solid algorithms for polygon-polygon collision detection have been extensively developed [3-7].

The collision detection was achieved using the Robust and Accurate Polygon Interference Detection (RAPID) library [3] developed in C++. RAPID takes two polygon models as inputs and can determine if any triangles are overlapping. The RAPID algorithm can be divided into two parts: 1) creation of a bounding box hierarchy and 2) testing for overlap of the bounding boxes. The hierarchical bounding box (HBB) method essentially allows for a preliminary low resolution collision test using the outermost bounding box. If the test is positive, successive higher resolution tests can be performed, iterating down to a bounding box that encapsulates just a single triangle.

Drs. Cardan and Popple are expecting wide use and application of this method in the future.

“The future of radiotherapy is going to be in more dynamic treatments, where the couch is either moving or in more strange positions than it has been before, said Dr. Cardan. “So, as the work gets published, I think potentially more people would be interested.

“Dr. Fiveash, long before this, thought about alternative prostate arrangements, which were at the time, fixed beam arrangements. It would have been kind of time consuming to deliver, so they weren’t really explored or implemented,” Dr. Popple continued. “[The arrangements] could be readily implemented as trajectories where everything’s moving. Patient-specific planning would require collision-avoidance tools. Although we’re not there yet, this work may integrate into trajectory research.

This research has already achieved success, being chosen as the Young Investigator Award winner at last year’s AAPN conference.

Cardan and Popple plan to demonstrate this procedure on patients within a year.

“This piece that we’re actually working on, it is a building block to better therapy in the future,” said Dr. Cardan.

REFERENCES

Currently, he is most proud of our department’s role as trendsetter and educator for the latest in radiation oncology technology and treatment.

“I’m very proud that we are the showcase for Varian. When people want to know how the treatment machines work, they don’t go to Stanford, they don’t go to Harvard, they go to UAB,” Dr. Brezovich said. “I would consider that a major accomplishment for us. As a group, we have been very active in getting all the treatment software to work so that we can actively work as a showcase.”

Dr. Brezovich is involved with far more than education and exhibition of our accelerators. He is also heavily invested in improving the accuracy and efficiency of patient treatment.

“We are trying to migrate the patient treatments as far as possible from Gamma Knife to our STx accelerator. We are measuring how accurately we can deliver radiation on the Gamma Knife. We are mainly interested in spatial accuracy or geographic accuracy,” Dr. Brezovich mentioned. “Once we have bench marked how accurate the Gamma Knife is, we can see how close to that level of accuracy we can get with our STx accelerator.”

Dr. Brezovich is also currently involved in the construction of devices and equipment to improve the overall accuracy of our accelerators.

“We built special QA devices which can measure the accuracy of radiation delivery within a small fraction of a millimeter. It allows us to measure how geographically accurate the ConeBeam CT and radiation treatment beams are,” Dr. Brezovich explained. “We are developing special phantoms for that purpose. We hope to have publications out of that. Some of the precision, I hope, is unique.”

“It’s important that when you set the patient up using the ConeBeam CT that the beam which you use to deliver the radiation accurately agrees with that setup,” Dr. Brezovich continued. “Our phantom will allow us to measure the capabilities of our machines within a fraction of a millimeter. I haven’t seen another phantom or QA device which allows us to measure in such a quick and practical way.”

The QA devices and phantoms are unique, custom builds, inspired by the needs of our department.

“We have the whole physics division involved with this work, but we also work with the radiation oncologists because we need to know what they need, what they consider important in terms of accuracy,” Dr. Brezovich stated. “This is a home-developed, home-built device, made partially in the UAB Physics Shop and partially by myself in our mold room downstairs.”

Dr. Brezovich is quite experienced with creating new tools and devices if current technology does not suit his needs.

“In many cases, I build things that are simply not available. We are trying to be more accurate than state-of-the-art. Over the years, we have done it many times. For example, going back to 1992, we were among the very first institutions in the nation that offered stereotactic brain radiosurgery to our patients. We were able to achieve and report on the highest level of accuracy available at that time. That treatment required a lot of development of equipment and procedures,” Dr. Brezovich said. “To assure patient safety, we developed a detailed checklist based on cockpit procedures in airplanes. Each step in the treatment procedure was called by one member of the treatment team, done by another member and read back as having been done, and checked off.” In the last few years, checklists have become the standard of care.

“We have also developed an improvement on the block cutting technique used in our mold shop to cast blocks with sub-millimeter accuracy. We have been using them for many years to help our patients, just like any other kind of accuracy,” Dr. Brezovich said. “If I can buy a device, I prefer to buy it, but sometimes that isn’t an option. I’m not building things to save money, but building devices is just part of being better than what’s available.”

Beyond his expertise in building new, more accurate machinery and devices, Dr. Brezovich is spending considerable time working in novel research and publications. One such
publication focuses on accelerator safety laws in the United States.

"Emergency off-switch tests are a major trauma for accelerators. When you press the switch, the machine may or may not come back to full operation," Dr. Brezovich explained. "That means you want to have a service provider or technician there to repair the accelerator if needed."

"By law, you have to test the emergency off-switch of an accelerator every three months in the state of Alabama. In some states it's monthly, in some states its weekly. In some states, there is no testing requirement. One time, many years ago, we were cited because we didn't complete our test within three months, but within three months and one day. We were one day past."

This citation prompted Dr. Brezovich and Dr. Richard Popple to examine the current state of accelerator safety laws.

"We completed a statistical analysis to see just how much of a loss in safety occurs if we do the tests not once every three months, but once every three calendar months. The difference would be that you could complete the testing any time within one of the listed calendar months. The analysis showed that any loss in overall safety was negligible."

Dr. Brezovich hopes that this new insight into accelerator safety will impact more than this department.

"This would really make life easy on us, since we could hold the test whenever a technician or service engineer is available, rather than having the test exactly at one time," he said. "The paper is now in press. I hope it will have some impact and have people rethink what medical physicists can really do."

Dr. Brezovich is also taking part in research and trials beyond HSROC. One such project was brought to his attention by UAB Hematology & Oncology professor Dr. Boris Pasche. This project's focus is the application of specific frequencies which have cancer-inhibiting effects.

"You give the patient a radiofrequency, about 100 milliwatts, which is less power than transmissions from a cellular phone. This is given to the patient through a spoon-like electrode device connected to a radiofrequency device which is about the size of a cellular phone. The device emits waves at 27.21 megahertz, which are modulated at specific frequencies," Dr. Brezovich explained. "Dr. Pasche found those specific frequencies by administering the radiation to patients and measuring their pulse amplitude. When the modulation frequency hits certain tumor-specific frequencies, the pulse amplitude goes up."

Initial research and publications are positive. Dr. Brezovich hopes that his additions to this project will lead to greater discoveries.

"Publications in the British Journal of Cancer have shown that those frequencies do inhibit cancer growth. This treatment has been administered to patients who were maxed out in every conventional treatment of many cancers. In some cases, the cancer no longer progressed, in some patients the cancer actually went back and got smaller, and some patients lived for several years after an initial chance of only a few months, so it seems to be working," Dr. Brezovich said. "I built some devices for his team so they can now expose cancer cells in the lab to these specific frequencies. It turns out that yes, those specific frequencies can inhibit the proliferation of cancer cells in the petri dish. That was a very interesting discovery and I'm very happy that I can participate and work with this group."

In addition to his current work, Dr. Brezovich also has his eye on the future. He works to train the physicians, physicists and researchers of the future and create stronger treatment methods for the Birmingham area.

"I have always made myself available to help with the PhD students," Dr. Brezovich mentioned. "I am very aware of the work they are doing. Specifically, I have been helping them in the machine shop with the phantoms they are using or will be using in their work."

Dr. Brezovich's decades of experience have given him the opportunity to see research interests from decades past be reconsidered. Dr. Brezovich believes that refocusing on these past ideas may push UAB's radiation oncology program to even greater heights.

"Right now, the potential for proton treatment is still being discussed in our department. It's interesting since the desire to treat with protons started at UAB back in 1969. At that time, one of the UAB physicists was doing some Monte Carlo calculations, trying to figure out what a proton beam could do that you could not do with x-rays," Dr. Brezovich stated. "We didn't get any grants to examine this, because at the time, the government felt that neutrons were the way to go. Not because of a lack of merit for the project, but it was felt that the neutron approach would be better. It turns out that it wasn't better. Neutrons for cancer treatment have all but disappeared. We didn't get the grant, but it was something we all wanted to do for decades. Maybe it is something we can do now. It would certainly give UAB the opportunity to stay on top of every research area that there is."
Graduate student Timothy Rohrbach has been pursuing his interest in cancer immunology for the past three years in Dr. Christopher Willey's laboratory.

“I’m pursuing my Ph.D. in Immunology, however, my real research interest and passion is in cancer immunology. My project investigates tumor-associated macrophages in lung cancer,” Rohrbach said. “The goal of this project is to better understand the signaling and communication occurring between tumors and macrophages.”

Rohrbach was not certain he would choose UAB for his graduate studies, but a visit changed his perspective on the school and its facilities.

“When I was applying for graduate school programs, I was interested in studying virology. My undergraduate mentor suggested that I apply to UAB because of their strong immunology and microbiology program,” Rohrbach said. “I applied to UAB, received an interview, and had a wonderful visit. All the employees and faculty members were very friendly.”

Rohrbach’s project is composed of two related aspects.

“I have outlined two related projects. The first project investigates the role the protein MARCKS plays in lung cancer biology. The second project investigates if there is a role for MARCKS in tumor-associated macrophages and the tumor microenvironment,” Rohrbach said.

“The majority of our data regarding MARCKS in lung cancer has been collected. We are in the process of drafting a manuscript. The project investigating MARCKS in the tumor microenvironment is in the early phases,” Rohrbach continued.

Rohrbach has been extremely pleased with his time in the radiation oncology labs, largely due to the excellent mentors and support he has found here.

“Dr. Willey has been a great mentor and very supportive. We were able to create a project that brought both the laboratory’s and my personal interests together. We formed a diverse committee that has been helpful in developing my project. Rohrbach explained. “I’ve been very fortunate to be trained by not only Dr. Josh Anderson, but also Dr. John Jarboe. They both taught me numerous techniques during my time in the laboratory. Our laboratory manager, Pat Hicks, has also been very supportive. She has helped with many experiments over the past few years.”

While Rohrbach has found his work as a researcher fulfilling, laboratory work is not his only professional goal. Once he completes his graduate studies, he is interested in pursuing educational positions.

“I see myself going into teaching in an academic setting. The next step forward will be looking into post-doc positions, especially at locations that have a teaching component. “

Rohrbach has been very pleased with his time at UAB and truly appreciates the unique and collaborative spirit of the radiation oncology department.

“UAB is very collaborative in nature,” he said. “It has been a pleasure getting to know and work with everyone in the department.”
The excellent care began with an early start for our radiation therapists, Nathan Jordan, Jason Schneider, Shashank Singh, and Brandon Beard. The therapists arrived at work early during several of the snowy days.Knowing that the weather would slow down patient arrivals and treatment, the therapy team took time from their busy schedules to make sure our facilities were ready to treat patients at any time.

"They all came in early on the late start days and began machine warm up to help get the schedule started sooner," said Kathy Bowman, director of radiation oncology. "No one asked them to come in early," she continued. "They just knew it would help everyone—patients and staff."

In addition to arriving early, many therapists stayed late or took on additional work to allow those who had to travel in the wintry weather ample time to safely travel home. Schneider and Singh volunteered to stay late, as did therapists Danielle Bentley and Freddie Ray.

Our nursing and reception staff also performed excellently, providing care and support to all patients who were inconvenienced or slowed by the weather. Laura Stewart and Lisa Moore stayed late, past the hospital-issued closing time, to make sure all patients who needed assistance with treatments or scheduling got the help they needed. Also, India Moore and Ruth Lewis organized all follow-up patients prior to the clinic closings, resulting in more efficient work for those who stayed behind.

"India and Ruth had it so well under control, it was easy to finish up," said Moore. "I just went into treatment and asked how I could help."

The staff did a great job working together as a team to ensure that all patients were called and rescheduled," said Ginna Blalock, operations director for Acton Road radiation oncology. "They all did their part.”

We at radiation oncology would like to thank our excellent therapy, nursing, and reception staff for providing excellent care and service to all patients in need during the severe winter weather.
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RADIATION ONCOLOGY HIGHLIGHTS

Craig Baden, M.D. has been awarded the ARRO Global Health Scholar travel grant for his radiation oncology projects overseas.

Lisa Moore won 2nd place in the UAB 2015 Safety Fair Slogan Contest. Moore, along with the 1st and 3rd place winners were recognized during the 2014 Safety Fair on Wednesday, March 12.

Javida Yow won the 3rd Annual Bowl Selection Game.

Dr. Ivan Brezovich and Jill Caranto were recently honored with the naming of the Brezovich-Caranto Endowed Support Fund for Research. The resolution was named to honor the decades of work Dr. Brezovich and Caranto have provided to this department.

For more Radiation Oncology news visit our website at www.uab.edu/radonc