

THE MICHIGAN DIFFERENCE

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NEWS AND NOTES

ISSUE 4 2011

HIGH-DOSE RADIATION GIVES PANCREATIC CANCER PATIENTS MORE TIME

When Andy Reddick felt pain in his abdomen, he was sure his gastrointestinal troubles had returned. With a history of Crohn's disease and intestinal surgery in 1985, Andy's GI doctors initially agreed. But after an office evaluation and a colonoscopy the following week found nothing unusual, they ordered a CT scan.

"Around 8:00 p.m. in the evening after the CT scan, my local GI doctor called to say that he wanted me to come in the next day for a MRI. We could tell by the tone of his voice that he thought it was something serious," recalled Andy.

The CT scan and MRI revealed an enlarged pancreatic duct and a suspicious-looking mass, which a biopsy at Jefferson University Hospital in Philadelphia (in January 2008) confirmed was cancer. That year, Andy was one of the nearly 40,000 Americans diagnosed with pancreatic cancer. Compared to other types of cancer, pancreatic cancer is especially deadly, with a five-year survival rate of just four percent. The symptoms of pancreatic cancer are often vague, so the disease is frequently discovered at an advanced stage.

Dana (35 years old), Jenny, Andy, Julien (16 years old), and Andrea (33 years old) Reddick. Andy was instrumental in forwarding Dr. Ben-Josef's research, and his story highlights the powerful partnership between doctors and patients at U-M.

"I could tell by the way they looked at me, all the other specialists thought my case was hopeless—I could see the fear in their eyes. None of them wanted to be my doctor. But Dr. Ben-Josef never looked at me that way. From the moment we met him it was clear the man was on a mission. And because of that, he saw hope—Dr. Ben-Josef wanted to be my doctor."

—Said Andy Reddick, just a few months before he passed away in April 2011. His life was extended by three years after participating in a high-dose radiation trial at U-M.

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Photo: Andrea J. Bishop

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FROM THE CHAIR

July 2011

Dear Friends and Colleagues,



I am pleased to present the 2011 issue of the Department of Radiation Oncology *News and Notes*.

This edition of our newsletter features a profile of a patient, Andy Reddick, who participated in one

of our high-dose radiation trials, and whose life was extended because of it. His compelling story offers a wonderful example of how our research impacts patients, and in particular showcases how our department continues to push the envelope and lead the field in conducting high-risk, high-reward research.

You will also read about the leadership transition in our medical physics division. Long-time division head, Dick Fraass, has left the U-M after nearly 30 years of dedicated service. Randy Ten Haken has taken over as director of radiation physics and James Balter has become co-director of medical physics. We all look forward to the exciting work ahead for this dynamic and important group and for our department as a whole.

Finally, you will also learn about our department's recent purchase of a state-of-the-art MRI simulator. I hope you will become as excited as I am about the opportunity to utilize MRI as a primary modality in treatment planning.

Thank you for your continued support.

Sincerely,

Theodore S. Lawrence, MD, PhD,
FASTRO

*Isadore Lampe Professor and Chair
Department of Radiation Oncology*

cont. from page 1

The Reddicks met with renowned pancreatic surgeon, Dr. Charles Yeo, at Jefferson to find out if surgery, the treatment that offers the greatest potential for survival, was an option. Unfortunately, 80 percent of the time surgery is not an option because the cancer has invaded other tissue and there is no way to remove the tumor without causing fatal damage.

“We looked at a 3D image of the mass and even we could tell it was bad—the blood vessels around the mass were bulging and it was a mess of intertwined tissue,” said Andy. “Dr. Yeo told me that there wasn’t a surgeon in America that would touch it.” With no chance for surgery, Andy was referred to Dr. Alex Lin, a radiation oncologist at the same hospital.

“After reviewing the CT scan, Dr. Lin let me know there really wasn’t anything he could do for me there—he believed the standard radiation doses authorized for use at Jefferson weren’t high enough to help,” adds Andy. But, as luck would have it, Dr. Lin had completed his residency at the University of Michigan and knew about a pancreatic cancer prospective trial being led by radiation oncologist Dr. Edgar Ben-Josef. The trial was investigating the effectiveness of high-dose radiation in combination with full doses of systemic chemotherapy for inoperable patients with advanced pancreatic cancer.

Dr. Lin made a call and a week later the Reddicks, along with their youngest daughter, Julien, were headed to Ann Arbor.

The University of Michigan is one of only a few cancer centers in the nation with a dedicated Multidisciplinary Pancreatic Cancer Clinic. Patients have access to experts from every applicable specialty for their entire spectrum of pancreatic cancer care. Eligible patients such as Andy may participate in one of U-M’s groundbreaking clinical trials.

Regarded as one of the best radiation oncology departments in the world, U-M’s team is well-known for their work on an innovative radiation technique called intensity-modulated radiation therapy (IMRT). IMRT allows oncologists to deliver a higher dose of radiation to a pancreatic tumor while minimizing side effects and sparing surrounding sensitive organs such as the stomach, liver, and kidneys, as well as the spinal cord.

Using IMRT, Dr. Ben-Josef’s innovative approach combines full-dose gemcitabine (the most common chemotherapy used for pancreatic cancer) with very high-focused doses of radiation. U-M laboratory researchers established that gemcitabine makes pancreatic cancer more sensitive to radiation. In addition, by studying the motion of the pancreas and identifying the changes in the shape of the pancreas associated with breathing during radiation, Dr. Ben-Josef devised a technique to freeze motion and target the radiation, allowing treatment with approximately 150 percent of the standard radiation dose used with pancreatic cancer. The radiation treatment lasts five weeks (25 total radiation treatments) and is followed by four months of additional chemotherapy.

Andy first received two pre-radiation doses of gemcitabine, treatment overseen by U-M medical oncologist and co-investigator of the high-dose radiation trial, Dr. Mark Zalupski. He then began the radiation treatments with Dr. Ben-Josef.

“After about the first 15 radiation treatments, I still felt pretty good, but was losing a lot of weight and my energy level was starting to fade. For the remaining 10 treatments my appetite was nearly non-existent and all I wanted to do was sleep,” recalled Andy. “It really helped that Jenny and I completely trusted Dr. Ben-Josef. He believed in what he was doing, so we did too.”

“The teamwork among everyone involved was better than we’ve ever seen it—and we’ve been to a lot of hospitals over the years,” added Jenny. “Everyone at Michigan understood that it wasn’t just the patient who needed support, but the whole family.”

In the midst of Andy’s treatment, the Reddicks’ daughter Julien, who was suffering from undiagnosed gastrointestinal symptoms, became very ill. “You can imagine, the stress was almost



Dr. Edgar Ben-Josef standing next to the linear accelerator used to administer his high-dose radiation protocol.

unbearable,” recalled Jenny. “We asked Dr. Ben-Josef for a referral and within an hour we had an appointment scheduled with pediatrician Dr. James Baker. He was painstakingly attentive to Julien and really helped ease her symptoms. It was such a blessing to have doctors who went above and beyond to support us.”

In May of 2008, after seven weeks in Ann Arbor, the treatment was completed and Andy and his family returned to Pennsylvania. He slept 16 to 20 hours a day for the first few weeks, but in a little over a month Andy began feeling better. “For the first couple of weeks after the treatment, I was completely wiped out. But then one day I sat up, put my feet on the floor, and felt energetic for the first time in months.”

Andy completed the follow-up chemotherapy regimen near his hometown in Pennsylvania with Drs. Zalupski and Ben-Josef providing telephone consultation with his local medical oncologists. In October, Andy had another CT scan at Jefferson in Philadelphia to assess what, if any, progress the treatment had made on his tumor.

“We requested that the CT scan be sent to Dr. Yeo, and he called us within 24 hours. We knew one of the world’s most accomplished pancreatic cancer surgeons wouldn’t have personally called if he didn’t think something was possible.”

Andy’s instincts were right. Dr. Yeo agreed to the surgery. “The scans looked promising, but before the surgery no one knew for sure if the cancer was gone. Dr. Yeo offered no guarantees that the surgery would be successful. He made sure we understood that there was a strong chance things wouldn’t look as good on the inside. That being said, he was willing to try, which meant a lot given that this same surgeon had turned me away six months earlier,” said Andy.

The surgery lasted nearly 12 hours, and was, by all measures, a great success. To everyone’s amazement, the radiation therapy had reduced the tumor almost entirely to noncancerous scar tissue, which could be completely removed.

“We just couldn’t believe it—Dr. Ben-Josef’s protocol actually worked,” recalled Andy, who became the first patient in the trial to have a pancreatic cancer tumor become operable—an extremely rare outcome. To date, a remarkable 12 other patients in Dr. Ben-Josef’s radiation trial have had surgery.

Because the protocol is used with very late stage cancers, ultimately it does not yet offer a cure because the cancer spreads to other organs. But it does offer patients more time. For Andy, it gave him nearly three additional years with his family. On April 28, 2011, Andy passed away. While the high-dose radiation protocol prevented a recurrence in the pancreas, the cancer spread.

“Three years ago Andy was being advised to take Percocet for the pain and arrange hospice,” says Jenny. “And while the treatment wasn’t a cure, participating in the clinical trial extended his life and gave us three additional years together. I know it meant everything to Andy, and to all of us.”

“Andy was one of the very first known patients with a clearly unresectable tumor to have surgery. In other studies, most patients reported as unresectable (who later went on to have surgery) turn out to be ‘borderline-resectable,’ which is an intermediate category, not truly unresectable,” says Dr. Ben-Josef. “We selected only clearly unresectable patients for this trial. So far, 25 percent of patients on the protocol have had surgery, which is very encouraging.”

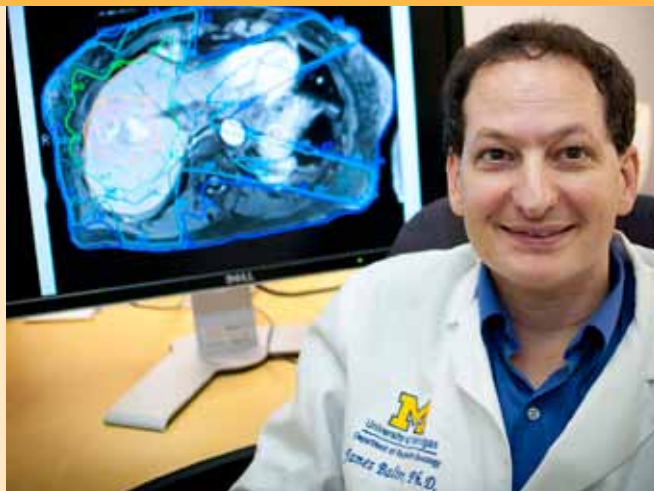
“What we’ve learned is that (1) radiation, in high enough doses, can sterilize unresectable pancreatic cancer and (2) a highly skilled surgeon can safely remove the tumor after such high-dose therapy. Andy was instrumental in the discovery of both these groundbreaking findings,” adds Dr. Ben-Josef.

Based on his findings so far, Dr. Ben-Josef is planning another trial that will combine the high-dose radiation and chemotherapy protocol with additional drugs designed to weaken cancer cells.

U-M’s Pancreatic Cancer Program

The University of Michigan is an internationally recognized leader in pancreatic cancer research and treatment. Because our clinical faculty members actively participate in research studies initiated both within the University and nationally, patients have access to both standard therapies and investigational treatments unavailable at other institutions.

The Multidisciplinary Pancreatic Cancer Clinic is one of just a few programs within the U-M Health System to be designated a “destination program” in recognition of both the advanced treatment options offered and the many steps taken to streamline care for patients and families coming from far away. For more information on U-M’s Multidisciplinary Pancreatic Cancer Clinic and Dr. Ben-Josef’s high-dose radiation trials, please visit www.med.umich.edu/cancer/cancertreat/pancreatic/the_clinic.shtml.



James Balter, PhD, anticipates the arrival of the department's new MRI in fall 2011.

Radiation Oncology's New MRI

The Radiation Oncology Department at the University of Michigan continues to pioneer the field of personalized oncology treatment by innovating MRI-guided radiation therapy. Over the last decade, U-M radiation oncologists have led the nation in the use of intensity-modulated radiation therapy (IMRT) and image-guided radiation therapy (IGRT) to more precisely target radiation. The department's MRI-guided radiation now promises to dramatically improve individualized cancer care by providing a much clearer picture of both tumors and the surrounding normal tissue.

"MRI-guided radiation offers an unprecedented opportunity to study the underlying structure, molecular composition, and physiological behavior of tumors, allowing doctors to closely monitor treatment progress and more precisely characterize how different kinds of tumors, and different kinds of people, respond to treatment," says James Balter, PhD, professor of radiation oncology and co-director of the physics division.

"MRI-guided imaging also has the potential to significantly reduce complication rates by allowing physicians to closely track changes in liver function, which is often an early indication of toxicity," adds Balter. "We have pioneered MRI and image analysis to learn individual patient responses to treatment and adapt treatment accordingly for maximum effectiveness. Providing this technology to patients will help make individualized therapy part of the routine practice of radiation oncology."

As part of the MRI-guided radiation research effort, the department recently invested in its own state-of-the-art MRI technology. The Magnetom Skyra 3T, made by Siemens, has a 70 cm open bore design that will accommodate a wide variety of body sizes and physical conditions. The new equipment also features a multi-channel platform that accepts parallel signals from multiple parts of the body, significantly improving scan efficiency and facilitating functional imaging of patients.

"Our own MRI will enable us to optimize MRI scanning methods and patient positions specifically for radiation therapy," says Dr. Balter. "We also plan to investigate MRI as a primary modality for treatment planning, as an alternative to CT scans. The purchase of this incredible new equipment will be an invaluable asset to this work, and to the department's broader research in MRI-guided radiation."

Medical Physics Group Welcomes New Leader

After 27 years of leading the Department of Radiation Oncology's medical physics group, Benedick A. Fraass, PhD, stepped down from the post this year. Over his nearly three decades of dedicated service to the institution, Dr. Fraass played an instrumental role in establishing U-M as a world leader in the field of radiation treatment planning. He leaves a remarkable legacy in our department, and will be greatly missed. The new head of physics, and Dr. Fraass's longtime colleague, is Randall K. Ten Haken, PhD.



Randall K. Ten Haken, PhD

"Dick is not only a brilliant scientist, but he is also incredibly compassionate and a tremendous friend," says Ten Haken.

The two physicists first met at an American Association for Physicists in Medicine summer school in 1982. They both shared a technological, basic science approach to their work and hit it off immediately. Both men were recruited to U-M in 1984 by Dr. Allen Lichter, the department's legendary former chair, and former dean of U-M's Medical School.

"Back then, we were really creating a whole new field. There were no standards or protocols yet, and in fact, the physicians were looking to us to figure out how to establish them. But we weren't experts yet, we were young scientists in our 30s," recalls Ten Haken. "As the leader of our group, Dick never questioned our abilities—he always had faith that we would figure things out. I will forever be grateful to him for his vision and his incredible leadership."

As the new director of radiation physics, Ten Haken plans to continue pushing the department forward, ultimately forging new ground in the area of individualized oncology.

"Radiation treatment planning has come a long way in the last three decades. We started out using a combination of x-ray images and the physicians' knowledge of anatomy to figure out where to target the radiation beam. It was pretty basic," recalls Ten Haken. "The advent of CT scans ushered in three-dimensional treatment planning, which allowed us to create pretty good treatment models and begin to figure out how to safely escalate radiation doses and, ultimately, make them more effective."

The U-M team created treatment-planning software that streamlined the planning process and made it significantly more accurate. This work not only made radiation safer and more effective for patients, but also established U-M as a worldwide leader in the field.

“Today, we have a lot more confidence about how much radiation different parts of the body can tolerate, but there often remains a few percent chance of complication—for example, on some aggressive protocols this may be five percent or one out of every 20 patients. Of course, if you’re receiving radiation you want to know if you’ll be the one who’ll have a problem. Our work now is focused on creating methods to determine, in advance of and during the course of treatment, which patients are more vulnerable to toxicity or other complications, so that we can adjust the treatment plan accordingly.”

Ten Haken says that common health risk factors, such as diabetes, smoking, and obesity can play a role in making patients vulnerable, but alone are unreliable in predicting complications. “It’s really about identifying genetic and physiological differences, and understanding how each patient’s different organs and tissues and different tumor types respond to radiation,” adds Ten Haken.

Spectacular new technological advancements in both functional and anatomic imaging, as well as the discovery of biomarkers in the blood that can help indicate a predisposition to or early onset of toxicity, are making it possible for scientists to customize, plan, and adjust treatment based on the unique needs of each patient.

“Molecular ‘theragnostic’ imaging tools are giving physicians the ability to not only understand the genetic underpinnings of each incidence of cancer, but also to determine which parts of a tumor are more malignant. We can use this information in the treatment planning process to make radiation more precise and effective,” says Ten Haken.

“These same types of tools can be used to monitor individual responses to treatment over the course of their many fraction (session) treatments,” adds Ten Haken. “All of the new information is incredibly valuable, but as it becomes more abundant, our challenge is to create models and decision support mechanisms that can be used for defining and then making adjustments throughout the course of treatment, on an individualized basis, for large numbers of cancer patients. That’s our focus now.”

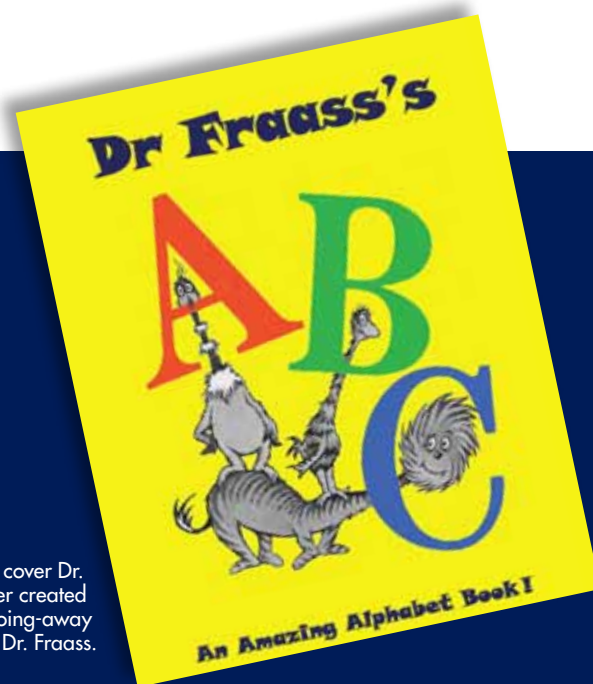
Since joining the department in 1984, Dr. Ten Haken has risen through the ranks to professor and director of the radiation physics division. He is a fellow of the Institute of Physics as well as of AAPM, ASTRO, and ACR. He is the author of more than 160 peer-reviewed publications, and is nationally known for his work in 3D planning and biological modeling of dose.

Radiation oncology chair Dr. Ted Lawrence says, “Randy’s previous position as co-director of the physics division, his outstanding leadership skills, and his deep knowledge of the department made him the perfect choice for this position. The new title of associate chair reflects his leadership role not just within physics, but for the whole department.”

For more information about the medical physics group or Dr. Ten Haken, please visit the department’s website at www.med.umich.edu/radonc/.



The book cover Dr. Mark Kessler created as a going-away present for Dr. Fraass.



A farewell reception honoring the service of Benedick A. Fraass (at right) PhD, was held on April 27, 2011, in the Towsley Center Lobby. He is pictured here with Dr. Avraham Eisbruch.

Dr. Ted Lawrence Named Taubman Institute Scholar

Dr. Ted Lawrence, Isadore Lampe Professor and chair of radiation oncology, was recently named an A. Alfred Taubman Medical Research Institute Scholar for his revolutionary work in the field of individualized cancer care. Continuing his groundbreaking work to develop new treatments for patients with liver and pancreatic cancer, Dr. Lawrence's Taubman-sponsored research aims to effectively combine molecularly targeted drug therapy with the most powerful, safe radiation approach.

"Cancer cells often hijack one of many normal growth signals and use that one signal to grow out of control," says Lawrence. "This new generation of molecularly targeted drugs can block the hijacked signal, which tends to shut down the cancer cell, but leave normal cells relatively unaffected. But the drug alone cannot kill a cancer cell. Radiation (or chemotherapy) is required to eliminate the cancer."

To develop the most powerful, safe approach that includes radiation, Lawrence and his team are now incorporating "functional" imaging techniques, which can identify whether a tumor has more aggressive regions; or similarly, whether some normal tissues function better than others, making them more likely to resist toxicity. Functional imaging offers the potential to target the highest doses of radiation to the regions of a tumor that are most aggressive and away from sensitive normal tissues that may be showing injury.

"I am convinced that combining molecularly targeted drugs with functional imaging, to both enhance and guide radiation therapy, will greatly increase our ability to control and cure pancreas and liver cancers. This approach holds great promise for improved treatment and, I believe, is the future of our field."

Traditional sources of medical funding are often not enough to yield transformative, cutting-edge research. The Taubman Medical Research Institute seeks to provide senior level medical scientists at U-M with the financial means to pursue ideas that otherwise they are unable to adequately explore.

"I am honored to have been selected as a Taubman Scholar. This support will help ensure that U-M's Department of Radiation Oncology continues to lead the field in innovation and research. I look forward to the opportunity to report back on all that we've accomplished as a result of this generous scholarship," adds Lawrence.

Now in its fourth year, the Taubman Institute was made possible by the historic generosity and expansive vision of A. Alfred Taubman. With a focus on translational research, designed to reach the patient as quickly as possible, the Institute supports physicians who are highly motivated to find effective treatments and cures.

The Institute provides its scholars with the freedom, resources, and collaborative environment they need to transcend the boundaries of medical research, to pioneer breakthroughs in disease cures and treatments, and ultimately to alleviate human suffering. To learn more about the Taubman Institute, please visit www.med.umich.edu/taubmaninstitute



"I am honored to have been selected as a Taubman Scholar. This support will help ensure that U-M's Department of Radiation Oncology continues to lead the field in innovation and research. I look forward to the opportunity to report back on all that we've accomplished as a result of this generous scholarship,"



A. ALFRED TAUBMAN
MEDICAL RESEARCH INSTITUTE
where scientists create cures

Faculty Achievements

Dr. Marc Kessler, world expert in image analysis, image registration, and treatment planning, was proposed as the next Allen S. Lichter Professorship honoree, effective summer 2011.

Dr. Lori Pierce received the prestigious Sarah Goddard Power Award from the University of Michigan Academic Women's Caucus for 2011, for her many contributions to women throughout the University community. Dozens of her mentees sent heartfelt congratulatory notes that confirmed how important she has been to the careers of a whole generation of radiation oncologists both here and abroad.

Dr. Pierce has recently been nominated for the Marie Sklodowska-Curie Award through the American Association for Women Radiologists (AAWR) Foundation, which is awarded to an AAWR member who has made an outstanding contribution to the field of radiology.

**Marc Kessler,
PhD**
*Associate
Professor*



**Lori Pierce,
MD**
Professor



New Appointments

**Aarif Ahsan,
PhD**
*Research
Investigator*



Dr. Aarif Ahsan obtained his PhD degree from the Institute of Genomics and Integrative Biology in Delhi, India, in 2006. Following the completion of his studies, he joined our Department of Radiation Oncology as a post-doctoral fellow. Dr. Ahsan has conducted insightful studies in EGFR degradation in response to chemotherapeutic agents in the treatment of head and neck cancer. Dr. Ahsan was appointed to the rank of research investigator effective June 1, 2011.

**Shyam Nyati,
PhD**
*Research
Investigator*



Dr. Shyam Nyati obtained his PhD degree in 2006 from the University of Zurich, in Switzerland. Prior to coming to the University of Michigan, Dr. Nyati worked as a research assistant at the Indian Institute of Science in Bangalore, India, and then held a research fellow position in our Division of Molecular Imaging. Dr. Nyati's research interests focus on combining cell-based imaging with high-throughput screening platforms in transforming growth factor-beta signaling. Dr. Shyam Nyati was appointed to the position of research investigator effective June 1, 2011.

**Eyad
Abu-Isa, MD**
*Assistant
Professor*



Dr. Eyad Abu-Isa completed his residency in 2011 at the University of Michigan, where he also served as chief resident. Dr. Abu-Isa will join our offsite practice at Providence Hospital in Southfield and Novi, Michigan. He will be involved in research projects related to improving the technical delivery of radiation therapy. Dr. Abu-Isa assumed the position of clinical assistant professor, effective July 1, 2011.

Radiation Oncology Residents

Graduating Residents

Terence Williams, MD, PhD



Graduating Residents: The graduating residents are Terence Williams, MD, PhD., Eyad Abu-Isa, MD; and Doris Brown, MD, PhD. Dr. Williams received the 2011 Roentgen Resident/Fellow Research Award from the Radiation Society of North America.

Eyad Abu-Isa, MD



Incoming Residents: This year's incoming residents include Dean Shumway, MD (University of Chicago); Corey Speers, MD, PhD (Baylor College); and Adam Liss, MD. (Penn State University).

Doris Brown, MD, PhD



Upcoming Residents: The residents who matched our program for the academic year of 2012–2013 include Joseph Evans, MD, PhD (Northwestern); Aaron Sabolch, MD (University of Michigan); and Stuart Samuels, MD, PhD (University of Miami).

Incoming Residents

Dean Shumway, MD



Corey Speers, MD, PhD



Adam Liss, MD



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“Never doubt that a small group of thoughtful, committed citizens can change the world. Indeed, it is the only thing that ever has.”

—Anthropologist Margaret Mead, 1901–1978, died from pancreatic cancer

Every day, nearly 600 people around the world lose their lives to pancreatic cancer. The Department of Radiation Oncology has taken a lead on changing that statistic through highly targeted therapies.

But we need your help. To learn how you can accelerate the research, please contact Ann Boyd-Stewart, Director of Development, at aboydst@umich.edu or at 734.936.5726.

With your thoughtful support, we will make marked progress.

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