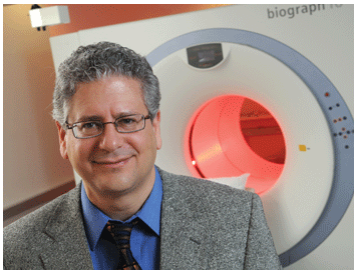
September/October 2010

IU researchers: Chemotherapy alters brain tissue in breast cancer patients

Researchers at Indiana University have published the first report using imaging to show that changes in brain tissue can occur in breast cancer patients undergoing chemotherapy.

The cognitive effects of chemotherapy, often referred to as "chemobrain," have been known for years. However, the IU research is the first to use brain imaging to study women with breast cancer before and after treatment, showing that chemotherapy can affect gray matter. The researchers reported their findings in the October 2010 edition of *Breast Cancer Research and Treatment*.

"This is the first prospective study," Andrew Saykin, PsyD, director of the Indiana University Center for Neuroimaging and


Saykin

a researcher at the IU Simon Cancer Center, said. "These analyses, led by Brenna McDonald, suggest an anatomic basis for the cognitive complaints and performance changes seen in patients. Memory and executive functions like multi-tasking and processing speed are the most typically affected functions and these are handled by the brain regions where we detected gray matter changes."

Dr. Saykin, who is Raymond C. Beeler Professor of Radiology at the IU School of Medicine, and colleagues studied structural MRI scans of the brain obtained on breast cancer patients and healthy controls. The scans were taken after surgery, but before radiation or chemotherapy, to give the researchers a baseline. Scans were then repeated one month and one year after chemotherapy was completed.

The researchers found gray matter changes were most prominent in the areas of the brain that are consistent with cognitive dysfunction during and shortly after chemotherapy. Gray matter density in most women improved a year after chemotherapy ended.

For many patients, Dr. Saykin said, the effects are subtle. However, they can be more pronounced for others. Although

relatively rare, some patients -- often middle-aged women -- are so affected that they are never able to return to work. More commonly, women will still be able to work and multi-task, but it may be more difficult to do so.

The study focused on 17 breast cancer patients treated with chemotherapy after surgery, 12 women with breast cancer who did not undergo chemotherapy after surgery, and 18 women without breast cancer.

"We hope there will be more prospective studies to follow so that the cause of these changes in cancer patients can be better understood," Dr. Saykin said.

Dr. Saykin and his colleagues started their research at Dartmouth Medical School before finishing the data analyses at IU. A new, independent sample is now being studied at the IU Simon Cancer Center to replicate and further investigate this problem affecting many cancer patients.

Other researchers included lead author Brenna McDonald, PsyD, MBA, assistant professor, Department of Radiology and Imaging Sciences, IU School of Medicine; Susan Conroy, MD, PhD student; Tim Ahles, PhD, professor of psychiatry, Memorial Sloan-Kettering Cancer Center, N.Y.; and John West, MS, an imaging researcher at the IU Center for Neuroimaging.

The study was supported by a grant from the Office of Cancer Survivorship of the National Cancer Institute, National Institutes of Health and the Indiana Economic Development Corp.

September/October 2010

Core spotlight

Tissue Procurement and Distribution Core

The Tissue Procurement and Distribution Core now offers three new services.

The core -- which specializes in the collection, preservation, and distribution of human solid tumor and hematologic malignancy tissues for the IU Simon Cancer Center research community -- now offers a hematological malignancy tissue bank, an Aperio imaging station, and tumor microarray.

In the hematological malignancy tissue bank, bone marrow aspirate, core biopsies, blood samples, and buccal swabs are collected for leukemia, lymphoma, multiple myeloma, and other hematological malignancies. This collection allows researchers, for example, to extract DNA from the buccal swabs or access plasma or serum from the blood samples. Researchers can do chemical or protein analysis with the bank's blood samples.

The Aperio imaging station takes photographs of slides, which can then be e-mailed to researchers. "They can view the tissue before they purchase it," according to Colleen Mitchell, the core's operations manager. The imaging station also has software that grades immunohistochemistry stains, telling researchers how much antibody is attached.

Through tumor microarray, the core can provide researchers with15 to 20 slides with up to 40 different types of tissue -- either animal or human -- on each slide.

Tissue Procurement and Distribution Core

The Tissue Procurement and Distribution Core is located in the CTSI Specimen Storage Facility in Joseph E. Walther Hall (RIII).

Colleen Mitchell, the operations manager, can be reached at 274-2213.

Overall, the core contains more than 3,000 specimens that represent most types of adult solid tumors and blood cancers. It also has select non-malignant tissue (for example, inflammatory bowel disease) and some normal tissue (such as breast, colon, prostate, lung, liver, kidney, heart, skin). Specimens are collected from patients undergoing surgery at IU Hospital and Wishard. A significant number of other tissue specimens also are available to researchers.

Biospecimens are used in basic science projects and correlative laboratory studies associated with clinical research. All biospecimens can be used for pre-clinical drug development.

Any IU faculty members and CTSI researchers at academic institutions within the state may request tissue. All requests must be approved by an advisory board composed of representatives from IU.

The core also can assist researchers in fixation and processing tissues for cell lines, animal, and human tissues. Generalized histology services, which include frozen sections, common stains such as Hematoxylin and Eosin (H&E), unstained slides for immunohistochemistry and paraffin blocks, are also available.

Technician Dana Borneo cuts slides from a tumor microarray (TMA). TMA is one of three new services offered by the Tissue Procurement and Distribution Core. The core's two other new services are a hematological malignancy tissue bank and an Aperio imaging station.

September 2010

News briefs

David Wolf delivers Seminar Series, Grand Rounds addresses Sept. 30 & Oct. 1

NASA astronaut David Wolf is the keynote speaker at both the IU Simon Cancer Center's Seminar Series and Grand Rounds. Dr. Wolf will deliver "Tissue Engineering Utilizing Controlled Gravity" during the Combined Seminar Series from 3:30 p.m. to 4:30 p.m. Thursday, Sept. 30. During Grand Rounds, Dr. Wolf will present "Building and Utilizing Laboratories in Space." That presentation is 7:30 a.m. to 8:30 a.m. Friday, Oct. 1. Both will take place in Walther Hall (R3), Room 203.


Wolf

IUPUI renames 2 buildings

Two of IUPUI's longest-standing buildings have been renamed. The former Robert W. Long Hospital will now be Long Hall. The former Willis D. Gatch Clinical Building will be renamed Gatch Hall. These changes will eliminate confusion for visitors, who might think these are facilities for the provision of hospital or clinical care, while still preserving their historical associations for the campus, according to an announcement from IUPUI.

Miles for Myeloma is Oct. 8-9

Rafat Abonour, MD, is gearing up for his sixth annual Miles for Myeloma. This year, he'll embark on a 235-mile cycling tour, which begins in Muncie Oct.8 and ends with a finish-line celebration outside University Place Hotel at 4:30 p.m. Oct. 9. More than 300 myeloma patients and their family members are expected to gather to watch the trek end. All are welcome. Visit the Miles for Myeloma Web portal for more.

National Black Caucus focuses on cancer in Indy

The National Black Caucus of State Legislators convenes in Indianapolis on Oct. 1 to discuss policy surrounding cancer. The event will feature presentations on breast, lung, prostate,

and colorectal cancers as well as panels discussing cultural and legislative approaches to these diseases that disproportionately affect African Americans. From 8:30 a.m. to 4:30 p.m., you can view and listen in on the dialogue and presentations by visiting http://dialogueonhealth.nbcsl.org/. Via the site, there will be an opportunity for you to pose questions to panelists and other speakers. Rivienne Shedd-Steele, director of the cancer center's Office of Health Disparities and Outreach, talks about cancer disparities at 8 a.m.

Miss a Combined Seminar Series?

Did you miss a Combined Seminar Series? You can now watch it online. A full listing of past Seminar Series events is here. Also, speakers for the 2010-11 academic year have been announced. You can find the schedule here.

Summer Research Program ends successfully

Jennifer Schwartz, MD, and **Lindsey Mayo**, PhD, organized another successful IU Simon Cancer Center Summer Research Program. The two wrote about the program for *Life Sciences Indiana*. Their "Perspectives" piece is here. The Summer Research Program is also a success because of the dedication of Liz Parsons, Chasity Spears, and Rivienne Shedd-Steele. Kudos to all.

IUSCC social worker earns clinical licensure

IU Simon Cancer Center social worker V. Kay Guidry is now a licensed clinical social worker (LCSW). Guidry's office is in the cancer pavilion, room 226. She can be reached at 944-8735.

Walther Oncology Physical Sciences & Engineering Research Embedding Program begins; request for project proposals

The Oncological Sciences Center (OSC) at Purdue and the IU Simon Cancer Center announce the Walther Oncology Physical Sciences and Engineering Research Embedding Program. See full details.

CTSI accepting applications for Core Pilot funding

The CTSI Core Pilot funding opportunity is open for applications through Oct. 18. The guidelines and application are available on the Indiana CTSI hub at https://www.indianactsi.org/grants. Log in using your university username and password. The proposals are to come from investigators interested in up to $10,000 in services from one of the CTSI designated cores. Eligible cores are listed at http://www.indianactsi.org/research/cores and have the CTSI seal next to the core name. It is acceptable for the investigator and core to be from either the same or different campuses/schools. For additional information, contact Lilith Reeves (lreeves@iupui.edu).

Other grants available to researchers

For the latest grant opportunities, visit the Funding Opportunities page on the IUSCC Web site.

Cancer center members in the news

- Cost but not convenience plays a significant role in attitudes about vaccination for common human papillomaviruses for women over the age of 26, according to the authors of a recent article in the journal *Sexual Health*. Researchers from IU School of Medicine and Columbia University Medical Center surveyed 1,323 women between 27 and 55 years of age who represent a racial and demographic cross section of the United States to determine the willingness among adult women to be vaccinated. **Gregory Zimet**, PhD, served as senior author and co-principal investigator. Researchers found moderately strong interest in receiving the vaccination if it is available free of charge. As out-of-pocket costs increased, interest decreased for the vaccine, which typically costs $120 per dose and requires three doses.

- **George Sledge**, MD, and colleagues published "Poly(ADP-Ribose) Polymerase Inhibition: 'Targeted' Therapy for Triple-Negative Breast Cancer." It appeared online Sept. 21 in *Clinical Cancer Research*.

- **Ken Nephew**, PhD, and colleagues reported that several lines of evidence have suggested that estrogen receptor α (ERα)-negative breast tumors, which are highly aggressive and nonresponsive to hormonal therapy, arise from ERα-positive precursors through different molecular pathways. Because microRNAs (miRNAs) modulate gene expression, we hypothesized that they may have a role in ER-negative tumor formation. In the *Journal of the National Cancer Institute*, they concluded that their findings suggest that the negative regulatory loop involving miR-221-222 and ERα may confer proliferative advantage and migratory activity to breast cancer cells and promote the transition from ER-positive to ER-negative tumors.

- **Hal Broxmeyer**, PhD, is a 2010 faculty member of the American Society of Hematology's Clinical Research Training Institute (CRTI).CRTI is a unique year-long education and mentoring program for hematology, hematology/oncology, and hematology-related fellows-in-training, as well as junior faculty physicians at academic medical centers. The goal of ASH's Clinical Research Training Institute is to prepare hematologists for careers in patient-oriented clinical research. Broxmeyer is currently president of the society.


Broxmeyer