THE CANCER LETTER

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How Much is Enough?

Building Boom of Proton Beam Centers Flares Up in Washington and Baltimore

By Paul Goldberg

Health systems in the Washington, D.C., and Baltimore area are creating a massive capacity for delivering proton beam therapy.

Together, the three centers now under construction will be able to treat 3,225 patients per year.

By way of comparison, the MD Anderson Cancer Center proton beam center treated 700 patients in 2011. One of the pioneers of the modality, Massachusetts General Hospital, has treated 6,550 patients since the launch of its proton beam center in 2001 through 2012, according to the Particle Therapy Cooperative Group.

The Baltimore-Washington building boom is an excellent case study in proliferation of a therapy that costs significantly more than photon radiation to deliver, but which, overall, has not been conclusively shown to provide superior safety and efficacy.

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Conversation with The Cancer Letter

Proton Therapy: What's Known and What's Not

The Cancer Letter asked Walter Curran, chair of the Radiation Therapy Oncology Group, to describe the knowns and unknowns of proton beam therapy.

Curran, executive director of the Winship Cancer Institute and an associate vice president at the Woodruff Health Sciences Center, spoke with Paul Goldberg, editor and publisher of The Cancer Letter.

Paul Goldberg: *Are there any trials that can compare proton beam vs. other modalities? When do you expect the answers?*

Walter Curran: There are a number of ongoing as well as developing clinical trials comparing proton therapy to best non-proton therapy.

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In Brief

IOM Elects 70 Members at Annual Meeting

THE INSTITUTE OF MEDICINE elected 70 members and 10 foreign associates during its annual meeting Oct. 21.

The new members were chosen by current members through a process that recognizes individuals who have made major contributions to the advancement of the medical sciences, healthcare and public health.

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Construction Enables Treatment Of 3,225 D.C.-Area Patients With Proton Beam Therapy

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"It's a sad statement, but I think I can defend it: There is, as of today, no ironclad proof that protons are better than intensity-modulated radiation therapy photons for any site," said Theodore Lawrence, the Isadore Lampe Professor and chair of the University of Michigan Cancer Center Department of Radiation Oncology. "There is a widely held assumption—and I make this assumption—that for children, particularly for brain tumors, protons almost certainly make a lot of sense."

About 100,000 people have been treated with proton beam radiation, and about 85 percent of them received it for prostate cancer. Generally, proton beam therapy costs more than twice as much as IMRT.

The studies are only now getting started.

"While proton therapy has been around for a while, only now is there a critical mass of centers to truly conduct the randomized trials necessary to assess the clinical benefit of this new technology," said Walter Curran, chairman of the Radiation Treatment Oncology Group.

Curran's conversation with The Cancer Letter appears on p. 1.

While many radiation oncologists who treat adults are at equipoise and are able to randomize, pediatric oncologists generally believe that proton therapy is more appropriate that photon therapy for brain tumors and a small number of spinal tumors, particularly in situations where treatment is intended to cure the patient.

"If you have a modality that you know avoids radiating normal tissue, to do a randomized controlled trial between that and something that's radiating normal tissue would be a difficult thing to do, and it would be a difficult thing to ask a parent to do and it would be a hard thing for a parent to agree to," said Anne Reilly, medical director for oncology at Children's Hospital of Philadelphia and a professor of pediatrics at Perelman School of Medicine at the University of Pennsylvania, which has been operating a proton beam center for the past five years.

With or without randomization, comparative studies are being conducted, said Thomas DeLaney, medical director of the Francis H. Burr Proton Therapy Center and co-director of the Center for Sarcoma and Connective Tissue Oncology at Massachusetts General Hospital.

"Since the lifetime of these facilities is decades, the question is whether additional facilities should be built at this point for anything other than patients going on clinical trials," DeLaney said. "Once you have enough capacity to answer the questions of which patients are most appropriate, maybe some facilities should adopt a wait-and-see attitude."

To some extent, proliferation of the technology in Washington and Baltimore is exactly what one would expect to encounter in the haphazardly regulated U.S. system of healthcare.

"England, for example, decided that their National Health Service is going to support two proton centers," DeLaney said. "At the moment, it's based on what the accepted indications are, with some additional capacity to do additional research studies. And if it proves to be a technology that offers a clinically significant improvement in patient care, they would go ahead and adopt additional capacity."

Meanwhile, Oklahoma City is getting two proton beam facilities, and economically depressed Flint, Mich., is getting one as well.

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The Question of I-95

In the Washington-Baltimore area, the controversy over proton beam therapy is playing out in all its complexity.

Approval of the three facilities located so closely together in the Washington and Baltimore markets illustrates the absence of a mechanism for regional planning for adoption of expensive technology.

Here is what the chessboard looks like:

Two of the proton beam systems approved by the District of Columbia State Health Planning & Development Agency will be located a couple of miles apart, one at Georgetown University Hospital, the other a couple of miles up Reservoir Road and MacArthur Boulevard, at Sibley Memorial Hospital, a unit of Johns Hopkins University.

Meanwhile, a much larger five-room facility is being constructed in the Baltimore area, and will be owned by a for-profit firm and operated by the faculty of the University of Maryland Marlene and Stewart Greenebaum Cancer Center.

The approval letters are posted on The Cancer Letter website.

Health authorities in D.C. routinely coordinate their decisions with officials from the counties that surround the capital. Baltimore isn't considered to be a part of that region, even though it can take a little as an hour to drive from Capitol Hill to the Orioles' stadium.

A lot of money is being invested.

The University of Maryland has made no investment of institutional funds in the $200 million facility that's being built across the street from its downtown Baltimore campus. MedStar health system, which operates the Georgetown Lombardi Cancer Center, is investing $32 million, and Sibley is investing $129.9 million.

Originally, Sibley sought approval to treat pediatric patients, but the D.C. State Health Planning and Development Agency said no, citing the absence of pediatric programs at the hospital. This prompted Sibley to regroup and forge an alliance with Children's National Medical Center.

While the treatment facilities at Sibley can be built based on an earlier approval, the institution is seeking a new approval to set up a program to provide radiation therapy to kids.

The program would include dedicating a bay at the Sibley proton center to treating children. If the program is approved, children referred to proton beam therapy from both Hopkins and Children's National Medical Center would be referred to Sibley.

Today, the closest institution that provides proton beam treatment to children is located at Children's Hospital of Philadelphia.

Opposing Pediatric CON

On Oct. 23, the D.C. health planning agency held a public hearing to hear plans for the pediatric program proposal from Hopkins and Children's.

At least one Georgetown official was in the audience, as was Kevin Cullen, director of the University of Maryland Cancer Center, and a member of the National Cancer Advisory Board.

While Georgetown officials were there to observe, Cullen's mission was to oppose the proposal.

Oppose a well-formulated program serving pediatric cancer patients?

Precisely, Cullen said later. Research questions—as well as all proton treatment needs in the area—could very well be addressed at the five-bay center being built across the street from the University of Maryland hospital by Advanced Particle Therapy, a San Diego-based company that is developing and operating the centers at the University of Maryland, Emory University, UT Southwestern, and Scripps.

"This is a great example of what's wrong with American medicine, and it's disheartening to me that three NCI-designated cancer centers that are within 40 miles of each other can't work together on a project like this," he said to The Cancer Letter.

At the public hearing, Cullen said he had failed in his attempt to preempt the building boom.

Cullen's testimony follows:

While I am specifically opposing the application of Johns Hopkins for treatment of pediatric patients at their proposed facility in the District, my opposition reflects a larger concern that the recent Certificates of Need approved for Johns Hopkins and MedStar would vastly overbuild capacity for proton therapy for this entire region.

By way of background, Advanced Particle Therapy, a private company, is building a five-treatment-room proton facility on the University of Maryland BioPark campus in West Baltimore. This is a privately funded facility being built at a cost of $200 million. Construction is already well advanced, the cyclotron will be installed early next year and the facility will be operational in 2015.

Neither the University of Maryland Medical System nor the University of Maryland School of Medicine have an equity ownership interest in the treatment facility being built by Advanced Particle

Therapy. Physicians from the University of Maryland Department of Radiation Oncology are contracted to provide professional and management services in the facility.

Prior to the District's approval of the initial CON applications from Johns Hopkins and MedStar earlier this year, I approached the leadership at both Hopkins and MedStar and offered that their physicians could practice in the newly constructed facility in Baltimore under an arrangement identical to that afforded the physicians from the University of Maryland.

Since this is a five-treatment-room facility, we believe that the capacity in this new facility (designed for 2,000 patients/year) is more than sufficient to provide for the needs of adult and pediatric patients throughout the entire region.

In addition to more than adequately providing for the present and future needs of patients throughout this region for proton therapy, this arrangement would facilitate important research collaborations between the three NCI designated cancer centers in the region which would help speed research on the future applications of proton therapy, bringing future benefits to patients in this region and around the world.

While both Hopkins and MedStar engaged in discussions of this possible joint arrangement, once the initial CONs were approved by the District earlier this year they have indicated they would each proceed with building their own facilities.

Specifically, with regard to children, there is no unmet need for proton therapy. At present, a significant proportion of the pediatric patients from Children's National Medical Center are being treated in Baltimore at the University of Maryland.

Since 2011, 34 patients have come to Baltimore for their treatment because of the technical radiation therapy capabilities in our present facility and the strong pediatric and anesthesia support necessary to care for these children.

Such support will also be present in the proton facility at the edge of our campus and since there is significant precedent for treating patients from Children's National Medical Center at our facility in Baltimore, the need for additional proton capacity to treat children at Sibley Hospital is unclear.

Additionally, the large volume of adult and pediatric patients from the main campus at Johns Hopkins would be more conveniently served by treatment at a facility which is approximately two miles from that campus rather than more than 40 miles distant in the District of Columbia.

In the original CON application filed earlier this year by Sibley, the need for proton therapy for pediatric patients is significantly overstated. In that application, Sibley estimated it would treat 152 pediatric patients with proton therapy per year. In 2012, the combined population of Maryland, the District of Columbia and Virginia was 14.7 million.

Based on a total annual U.S. incidence of 11,630 pediatric cancers, we would expect approximately 540 new pediatric cancers per year in all of Md., D.C. and Va. From 2010 through 2012, 467 new pediatric cancer cases were seen at Johns Hopkins and 107 of those (23 percent) required radiation therapy. Importantly, not all of those patients would require or benefit from proton therapy as opposed to conventional radiation.

Based on the Hopkins experience, 23 percent of the 540 new patients diagnosed in Md., D.C. and Va. each year, implying approximately 124 children from the region will require radiation, and some smaller portion of those will benefit from proton therapy.

Given that that there is already an operational proton unit in Virginia and another under construction in Maryland, it is very hard to reconcile the estimate that the Sibley unit will treat 152 pediatric patients per year.

In 2011, MD Anderson Cancer Center, the largest cancer institute in the U.S., treated a little less than 700 patients in its proton facility, which serves a regional patient population of approximately 13.8 million.

In 2011 no proton facility in the U.S. treated more than 800 patients. In comparison, the Maryland, Sibley and MedStar facilities would have a theoretical capacity (APT 2000; Sibley 917; MedStar 308) of 3225 patients per year, more than four times that number from a comparable regional service population of 14.3 million. The single proton treatment facility being built by APT is more than adequate to serve the needs of patients throughout the region for the foreseeable future.

I believe the proposed cost for the Hopkins and MedStar facilities ($132 million for the Hopkins facility at Sibley and $32 million for the facility at Georgetown) represent an expense which does not serve an unmet need but is rather driven by entirely unrealistic assumptions of patient volumes and similarly unrealistic hope for income generation.

Indeed, it is my personal opinion that the projection of 2,000 patients per year at the facility already under construction in Baltimore will be similarly challenging, if not impossible, to achieve. Given the clinical and economic factors discussed here, I respectfully request that the District decline the Certificate of Need application presented by Johns Hopkins at the present time.

Further, I would again encourage leadership

from the University of Maryland, Johns Hopkins and MedStar to work together towards an equitable use of the Baltimore-based proton facility, which will meet the regional clinical needs without undue additional cost and without encouraging overuse of this expensive therapy.

The partnership concept we have proposed will allow physicians at MedStar, Johns Hopkins and Maryland to work side by side in a fashion which will be good for patient care and promote cooperative research while avoiding redundancy and containing cost.

As an example, an analogous arrangement by the New York State Hospital Review and Planning Council resulted in the collaborative design of a facility by the five largest competing hospital systems in that region.

Indeed, at the time of the previous CON hearing, Mr. [Amha] Selassie [director of the DC State Health Planning and Development Agency] appropriately said, "I get asked one question I've not been able to answer and that is why don't these hospitals work together and invest together and have these types of services that would serve a lot of the hospitals."

As everyone involved in this CON process is painfully aware, there are dramatic and significant unmet healthcare needs in the District of Columbia, Maryland and the surrounding region. Additional proton therapy capacity is not one of them.

The proposed expenditure of more than $160 million by Hopkins and MedStar over and above the $200 million investment that has already been made by Advanced Particle Therapy is wasteful and redundant.

It is discouraging to me that I have been unable to convince the three largest health care providers in the region to work together in a collaborative fashion which will more than adequately meet the needs of all the patients in this region for this complex and expensive therapy while minimizing cost and duplication of services.

Hopkins Opted for Non-Profit Model

While no one expects that Cullen's opposition would derail the project, it triggered an hour of intriguing discussion by the state agency.

Altogether, Children's refers 65 children a year to radiation therapy and Hopkins refers another 75. Generally, 20 to 25 percent of these children would be likely to be offered proton therapy.

Discussion focused on the Washington kids who would be, hypothetically, spared a drive to Baltimore, presumably to the University of Maryland facility.

"For them Baltimore is a long, long way away," said Kurt Newman, president and CEO of Children's National Medical Center. "They get treated every day."

While Georgetown and Sibley were offered—and declined—to collaborate with the University of Maryland, Children's wasn't.

"With all due respect to the leadership of the University of Maryland, had we been approached to create that type of collaboration, perhaps we would have thought it through," Newman said.

However, the Hopkins offer to create a coordinated radiation oncology program was better. "The opportunity to be a pert of a world class pediatric oncology proton oncology program was too great to pass up," Newman said.

How far should patients be expected to travel to receive an exotic, expensive treatment? Pediatric patients and hypothetical drives to Baltimore similarly figured in Georgetown's announcement of regulatory approval for its proton beam center, which was finalized last May.

MedStar's strategy is to start small. The health system is building a single-vault unit and avoiding pressure to built a large program before the technology's utility is demonstrated.

In a statement at the time, Louis Weiner, director of Lombardi said that "accessing this cutting-edge treatment close to home will be particularly life-changing for our pediatric patients and their families."

Treatment to pediatric patients would be offered as part of pediatric services at Lombardi.

Expanding Utilization in Pediatrics

The number of pediatric patients eligible for proton beam may expand, Stephanie Terezakis, assistant professor of radiation oncology at Johns Hopkins, said at the certificate of need hearing.

"Twenty-five percent requiring proton therapy is an underestimate of the percentage that I would deliver proton therapy to if I had access," Terezakis said. "Those are 25 percent that we can't treat without proton therapy. That's not who would potentially benefit.

"I would say there is a much higher percentage of pediatric patients who I think would be eligible and might benefit from proton therapy, but can't guarantee it per se," she said. "There are so many other factors that prevent them from relocating that it's really hard to recommend this to families."

CHOP's Reilly said the Penn radiation center treats 30 to 40 kids at any given time, and about a third of them get protons.

"We have realized over the course of the last five years that we have been using proton in children here that there are many more uses," she said. "When you think about children and how they are growing, there are

a lot of tissues, the heart, the lung, the kidney that you would like to stay away from if you can with radiation beam."

According to a paper in the upcoming issue of the International Journal of Particle Therapy, utilization of proton beam therapy when up by a third in children with brain and spinal cancers.

The study by the Pediatric Proton Foundation and the National Association for Proton Therapy found that 694 pediatric patients were treated with proton therapy in 2012, compared with 465 in 2010, and 613 in 2011. Fifty-seven percent of pediatric patients treated with proton therapy in 2012 were less than 10 years old, with a curable brain tumor or axial sarcoma, the survey reports.

Equipoise on Adult Uses

The current discussion regarding proton vs. photon is almost entirely about economics, MGH's DeLaney said.

"If X-rays and protons were the same cost, this would be almost a moot point—everyone would be using protons rather than photons," he said. "There are some technical issues in terms of protons being more sensitive to motion, and there are some physical issues that people who use the technology need to be aware of. But, at the moment, it comes down to the difference in cost between the two treatments."

In nearly all adult indications, the studies are ethical, DeLaney said.

"Protons are a great treatment for prostate cancer, but so is IMRT, so is brachytherapy, so is robotic surgery and so is active surveillance," DeLaney said. "For prostate, we did a study comparing IMRT with 3D protons, and IMRT were more conformal around the front of the rectum and the bladder than the protons.

"On the other hand, the protons gave less total pelvic dose. We don't know which of those are better, but most patients when they get a complication related to prostate cancer, it's usually related to the high-dose region around the bladder.

"For non-small cell lung cancer, the lung is a challenging area to treat with protons, because of the changes in density that there are enough uncertainties about the protons in the lung as well as the difference in capability to shape the proton distribution around the esophagus."

However, in adult some brain tumors—those with long survival—randomization can be problematic.

Recently, an MGH investigator proposed a pilot study to compare IMRT with proton in randomized phase II in low-grade brain tumors.

"Our IRB was uncomfortable with going ahead with randomization," DeLaney said. "If your sister has a low-grade brain tumor and she may live 10-15 years you are going to tell her that the whole brain is going to get 50 percent more radiation with X-rays than protons, it's hard to feel good about that.

"There is no way X-rays can be better. They can only be worse."

Rigorous studies of proton beam could have begun years ago, before the technology started to proliferate, the University of Michigan radiation oncologist Lawrence said.

"When you build a $170 million facility, it may be harder to run the trials that may limit the use of that technology," Lawrence said.

"I haven't been in the room when people had the conversation, but one might suppose that that would be the discussion."

Conversation with The Cancer Letter

Curran: New Trials Address Questions On Proton Therapy

(Continued from page 1)

WC: There is a trial ongoing for men with prostate cancer being conducted between Massachusetts General, University of Pennsylvania, and several other sites.

RTOG, soon to be integrated into NRG Oncology, has two phase III trials approved by NCI and to be activated in early 2014: one for patients with stage III lung cancer, and one for patients with glioblastoma.

There are many other trials ongoing: a randomized phase II trial for lung cancer being conducted by MD Anderson and Mass General, and randomized phase II trials for patients with liver cancer, esophageal cancer, and head and neck cancer. Results will mature over the next five years for these trials. Proton therapy is also allowed in several COG and other RTOG trials. It is expected that proton centers outside of the U.S. will also participate in the NRG Oncology and COG trials.

PG: *Are there any data to suggest that proton beam is better than photon in pediatrics? This seems to be a commonly held view, but is there a basis for it?*

WC: The pediatric data is very clear for patients receiving craniospinal radiation, in that the dose to normal tissues from proton therapy is clearly reduced and has resulted in less toxicity. The other areas are well described as better for some other brain tumors and sarcomas among children.

PG: *What about prostate and other adult indications?*

WC: Prostate data for proton beam is really about radiation dose response –for stages of disease where higher RT dose is better, there is good evidence that proton therapy can provide an advantage without increasing toxicity.

The lung cancer data from MGH and MD Anderson is promising as is the preliminary data from MD Anderson on head and neck cancer.

Base of skull lesions have a longer history of excellent results with proton therapy.

PG: *Why don't we have the answers, considering the number of people who have had proton beam therapy? Are urologists to blame? Are health systems?*

WC: While proton therapy has been around for a while, the latest units will offer a potential superiority in dose delivery, which now provide an outstanding dose distribution in target versus non-target tissues as compared with prior proton or photon technologies. This technology allows for intensity modulated proton therapy. Only now is there a critical mass of centers to truly conduct the randomized trials necessary to assess the clinical benefit of this new technology. The RTOG/NRG Oncology leadership and NCI are committed to testing this approach for a number of adult malignancies.

PG*: Is there anything unusual about the Washington-Baltimore situation? Overall treatment capacity here will exceed 3,000 patients per year. MD Anderson treats 700.*

WC: There are sufficient opportunities to offer proton therapy to patients as an outstanding therapeutic alternative or as a superior alternative to existing therapies to justify having a proton center in many large population regions. It is too early to know what the correct number of proton centers for any region, including the D.C./Baltimore area.

Self-Referral

Ownership of IMRT Centers Prompts Urologists to Refer Patients to Radiation Therapy

By Matthew Bin Han Ong

Urology practices that provide intensity-modulated radiation therapy are more likely to refer men with prostate cancer for IMRT than practices that do not provide such services, according to a paper published in the Oct. 24 issue of The New England Journal of Medicine.

The study, by Jean Mitchell, an economist and professor at the McCourt School of Public Policy at Georgetown University, is based on review of the Medicare claims of more than 45,000 patients from 2005 to 2010.

The NEJM paper provides an analysis of treatment patterns by urologists before and after they acquire ownership of IMRT services.

"I constructed two samples," Mitchell writes. "One comprising 35 self-referring urology groups in private practice and a matched control group comprising 35 non-self-referring urology groups in private practice, and the other comprising non-self-referring urologists employed at 11 National Comprehensive Cancer Network centers matched with 11 self-referring urology groups in private practice.

"I compared the use of IMRT in the periods before and during ownership and used a difference-in-differences analysis to evaluate changes in IMRT use according to self-referral status."

Mitchell concludes that "men treated by self-

referring urologists, as compared with men treated by non-self-referring urologists, are much more likely to undergo IMRT, a treatment with a high reimbursement rate, rather than less expensive options, despite evidence that all treatments yield similar outcomes."

The study was funded by an unrestricted educational research contract between the American Society for Radiation Oncology and Georgetown University.

Nearly all of the 146 percent increase in IMRT among urologists with an ownership interest in the treatment was due to self-referral, said a statement from ASTRO.

"Dr. Mitchell's study provides clear, indisputable evidence that many men are receiving unnecessary radiation therapy for their prostate cancer due to self-referral," said ASTRO Chairman Colleen Lawton. "While I am a prostate cancer specialist impassioned to eradicating the disease, I am equally dedicated to utilizing these powerful technologies prudently and in the best interest of each individual patient.

"We must end physician self-referral for radiation therapy and protect patients from this type of abuse," Lawton said.

The American Urological Association criticized the paper, saying Mitchell's selection of control groups may not be representative of general practice trends.

"Given its inherent biases and flawed methodologies, Dr. Mitchell's article does not contribute to the discourse," said the AUA statement.

"Prior studies using the SEER database (the data source considered most reflective of the U.S. as it includes roughly 25 percent of the U.S. population affected with cancer) have shown significant declines in the use of brachytherapy in the U.S. during the same time period, yet Dr. Mitchell's control groups fail to show any decline in brachytherapy use.

"As the methods used to select the control groups are poorly described, one cannot help but wonder whether Dr. Mitchell chose the control groups to arrive at results that were acceptable to the study's sponsors."

The study comes on the heels of a Government Accountability Office report released in early August, which also found that urology practices substantially increased the percentage of their prostate cancer patients they referred for IMRT after they began to self-refer.

An earlier July 15 report concluded that self-referred anatomic pathology services increased at a faster rate than non-self-referred services between 2004 and 2010 (The Cancer Letter, Aug. 9).

Three provider specialties—dermatology, gastroenterology, and urology—accounted for 90 percent of referrals for self-referred anatomic pathology services in 2010.

Self-referral occurs when providers refer patients to entities in which they or their family members have a financial interest. The practice is prohibited under the Stark Law.

However, an exception allows physicians to bill for some medical services where an ownership interest exists. It was intended to apply to services provided at the time of an office visit as a convenience to patients.

Over time, these services started to include pathology, advanced diagnostic imaging, and IMRT (The Cancer Letter, April 13, 2012).

The final report in GAO's four-part series on physician self-referral, expected by the end of this year, will detail self-referral for physical therapy services.

In Brief

IOM Elects 70 Members

(Continued from page 1)

The new members raise IOM's active membership to 1,753, and the number of foreign associates to 120. With an additional 93 members holding emeritus status, the institute's total membership is 1,966. The institute's charter stipulates that at least one-quarter of the membership is selected from outside health professions, such as the fields as the law, engineering, social sciences, and the humanities.

A full list of the institute's new members is available here.

MD ANDERSON CANCER CENTER and **VANDERBILT UNIVERSITY** will collaborate on drug discovery and clinical translation efforts to study novel pharmacological inhibitors, initially focusing on the bromodomain family of epigenetic regulators.

Bromodomains are commonly found in proteins that regulate chromatin structure. They bind to specific acetylated lysine motifs on histones reading the histone code, and participate in translating this code into action by effecting chromatin remodeling and gene expression. Several specific members of its family have been implicated in tumor growth. Recently, small molecule inhibitors of specific bromodomain proteins have been discovered and early clinical trials to treat cancer are already under way.

"When we realized that both of our drug discovery teams were pursuing the discovery of novel bromodomain inhibitors, we immediately sought

to determine if we could join forces," said **Giulio Draetta**, director of the MD Anderson Institute for Applied Cancer Science, professor of molecular and cellular oncology, and interim vice president for strategic research programs.

The collaboration combines the laboratory of Vanderbilt's **Stephen Fesik**, professor of biochemistry, pharmacology and chemistry, and the Orrin H. Ingram II Chair in Cancer Research, with IACS' drug development and translational medicine laboratories.

Fesik screens libraries of small molecules called fragments and subsequently combines these fragments with weak affinities that bind to different sites to generate new chemical matter with higher affinity for the protein target.

This approach relies on a technique pioneered by Fesik, known as SAR by NMR, structure-activity relationship by nuclear magnetic resonance, which led to the discovery of inhibitors against the previously undruggable Bcl-2 family of proteins.

SHELLEY FULD NASSO was named chief executive officer of the **National Coalition for Cancer Survivorship**.

Fuld Nasso previously served as senior director of public policy at NCCS. She will lead the management team with **Ellen Stovall**, senior health policy advisor, and **Nina Wendling**, who was recently named chief operating officer.

Previously, Fuld Nasso served as director of public and medical affairs and director of public policy at Susan G. Komen for the Cure. Prior to her tenure at Komen, she was director of community philanthropy at The Dallas Foundation.

THE LEUKEMIA & LYMPHOMA SOCIETY named nine researchers who will receive The New Idea Award, a grant program designed to identify research strategies with high potential for significant impact on blood cancer treatments.

The researchers, who will each receive a $100,000, one-year grant, are:

• **Hilary Coller**, of Princeton University, for her work in quiescent cancer cells, which are typically resistant to chemotherapy. Preliminary data suggest that the transcription factor Nrf2, a protein that helps control the activity of genes, is important for quiescence. Coller proposes to determine the level of Nrf2 in proliferating and quiescent populations in three different B cell tumor types.

• **Joaquin Espinosa**, of the University of Colorado, and his team will use a screen to knock out individual genes and pathways in cancer cells. This approach will identify those critical genes that, when inhibited, will potentiate the action of certain anti-cancer agents.

• **Irene Ghobrial**, of Dana-Farber Cancer Institute, and her team will use a genetic screen to identify genes involved in the spreading of multiple myeloma cells. They will also perform a drug screen for inhibitors of MM dissemination.

• **Nora Heisterkam**, of the Children's Hospital Los Angeles, is focused on targeting the carbohydrate portion of a glycoprotein on the surface of a cancer cell. This glycoprotein is associated with drug resistance in acute lymphocytic leukemia.

• **Robert Hromas**, of the University of Florida, believes that the protein PARP1 is responsible for secondary acute myeloid leukemia following chemotherapy, and seeks to better understand the mechanism. His team will also identify which of the available PARP1 inhibitors best prevents translocations, and determine if PARP1 levels are predictive of secondary AML formation in a retrospective analysis of stem cell transplant patients.

• **Robert Orlowski**, of MD Anderson Cancer Center, proposes to identify genes essential for the survival of tumors in patients with high-risk multiple myeloma. Since some gene products can be inhibited with known chemotherapies, they will evaluate the effectiveness of these drugs, alone or in combination with current myeloma therapies.

• **Tomasz Skorski**, of Temple University, proposes using genetic profiling to determine which primary leukemia patient samples have defects in the BRCA-dependent DNA repair pathway. The effects of inhibiting the second, alternative DNA repair pathway will then be tested.

• **Anthony Sung**, of Duke University Medical Center, and his team have developed a nanoparticle that induces clotting, and preliminary data show that it reduces bleeding and increases survival in a mouse model of thrombocytopenia. The innovation is in the use of a nanoparticle as an alternative to platelet transfusions.

• **Shobha Vasudev**, of Massachusetts General Hospital, proposes to identify all the genes involved in maintaining the quiescent state of cancer cells, searching for biomarkers as well as targets for future therapeutic intervention of hard-to-kill quiescent leukemia stem cells, which are often the source of resistance to targeted chemotherapy.

THE MELANOMA RESEARCH ALLIANCE named **Cindy Hensley McCain** and **Elliott Sigal** to its board of directors, effective Nov. 4.

McCain is a member of the board of trustees for HALO Trust, a non-profit organization dedicated to landmine removal, a board member of the 2015 Special Olympics in Los Angeles, and serves as co-chair of the Arizona governor's task force on human trafficking. She is the wife of Sen. John McCain from Arizona.

Sigal was former executive vice president and director of Bristol-Myers Squibb, and served as chief scientific officer and president of research & development from 2004 until 2013. During his tenure, BMS brought 14 new therapies to market, including the immunotherapy drug ipilimumab (Yervoy) for metastatic melanoma.

Funding Opportunity

NCCN and Pfizer Issue RFP In Renal Cell Carcinoma Or Hematologic Malignancies

THE NATIONAL COMPREHENSIVE CANCER NETWORK announced a collaboration with **Pfizer's Independent Grants for Learning & Change** team to offer a grant opportunity focused on improving care for patients with renal cell carcinoma and certain hematologic malignancies.

The intent of this grant is to fund concepts that close clinical practice gaps and improve the care of patients with rare cancer types through the establishment of education and support mechanisms for community oncologists. Up to $2 million is available to fund these grants.

Letters of intent are due Dec. 5. Any questions can be directed to grant officer Jacqueline Waldrop, at jacqueline.waldrop@pfizer.com, with the subject line "Oncology Communities RFP."

FDA News

FDA Grants 510(k) Clearance To HER2 Digital Imaging System

FDA granted 510(k) clearance to a digital imaging system that allows pathologists to assess stained breast tumor slides for HER2 status using a computer monitor.

The Her2/neu IHC Digital Manual Read product, marketed by Royal Philips, digitizes HercepTest stained tumor tissue slides and makes them accessible through an image viewing and analysis management system.

The system is based on the Philips Digital Pathology Solution platform, and was commercially introduced in Europe and Asia in 2012. HercepTest is a semi-quantitative immunohistochemical assay for determination of HER2 protein. HercepTest is a trademark of Genentech Inc. subject to licenses held by Dako Denmark A/S.

FDA and the European Medicines Agency granted orphan drug designations to IMAB362 for the treatment of pancreatic cancer. IMAB362 is a monoclonal antibody currently in phase IIb clinical trial for gastroesophageal cancer.

Orphan drug designation is given to investigational new drugs that are under development for the treatment of life-threatening or very serious diseases that affect fewer than 200,000 patients in the U.S. or less than 5 in 10,000 individuals across Europe.

IMAB362 selectively binds to the tight junction protein CLDN18.2 which is expressed in approximately 60 percent of primary and metastatic pancreatic cancers. CLDN18.2 is also expressed in up to 80 percent of gastroesophageal cancers as well as in other solid tumors. However, the protein is absent from the vast majority of healthy tissues. IMAB362 is developed by Ganymed Pharmaceuticals AG.

FDA announced the requirement of a boxed warning for the immunosuppressive drugs Arzerra (ofatumumab) and Rituxan (rituximab). The warning is specific to the risk of reactivating hepatitis B virus in patients who were previously infected with the virus. Use of these drugs in patients with prior HBV infection can result in severe liver damage if the virus is reactivated.

The agency also released recommendations to decrease the risk of HBV reactivation when these drugs are used.