

PRESENTATIONS

NCI Cancer Imaging Program Update

The mission of the Cancer Imaging Program (CIP) of the National Cancer Institute (NCI), a part of the National Institutes of Health (NIH), is to promote and support: (1) cancer-related basic, translational, and clinical research in imaging sciences and technology; and (2) integration and application of these imaging discoveries and developments to the understanding of cancer biology and to the clinical management of cancer and cancer risk. In short, the goals are to use cancer imaging to visualize problems and direct solutions. The CIP works to accomplish these goals using several strategic approaches, including but not limited to: (1) infrastructure and programs to support the discovery and development of molecular imaging for cancer care and understanding of cancer biology; (2) a set of imaging methods validated as cancer biomarkers, some of which are surrogate endpoints; (3) infrastructure and programs to support the discovery, development, and delivery of image-dependent interventions for cancer and precancer; (4) an implemented infrastructure based on standardized models for the design and conduct of clinical trials of or using imaging and image-guided interventions; (5) accelerated development and delivery of integrated imaging systems and methods for cancer care and research; (6) critical roles in NIH and NCI activities in emerging technologies, such as nanotechnology, proteomics, and high-throughput screening technologies; (7) an implemented informatics infrastructure to optimize the value of cancer imaging data; and (8) a strategy of imaging science and methods to detect, treat, and monitor response to therapy in precancer.

Supporting these far-reaching goals and already vigorous research efforts is challenging. Approximately 61% of the \$4.8 billion NCI budget goes to research. However, these funds are challenged by eroding purchasing power, rising salaries, and escalating costs. The bottom line is that fewer studies can be funded and that already funded studies sometimes find themselves struggling to meet budgeted costs.

Despite the somewhat unfavorable financial climate, this is a time of forward-looking planning for both NCI and CIP. A recent synopsis of the areas in which NCI hopes to encourage advances in 2009 includes personalized cancer medicine, much of which pertains directly to molecular medicine and molecular imaging. Under this heading are prognosis, prevention, and treatment, including the need for research to:

- Monitor changes in an individual's cellular function in order to detect precancerous changes and intervene to prevent those changes from progressing to disease;

- Use genetic profiles to identify subsets of cancer types that define prognosis;
- Choose targeted therapies that minimize side effects and are based on both the type of cancer and the individual's biological profile; and
- Use biospecimen tests and imaging techniques to measure the impact of interventions and refine treatment to improve outcomes.

Under the headings of detection and diagnosis, NCI hopes to encourage research to:

- Identify patterns of genes associated with the development of specific cancers;
- Study the ways in which genetic variations that change the function of proteins cause cells to function abnormally;
- Investigate the ways in which those changes are further affected by lifestyle behaviors and environmental factors; and
- Develop biomarkers (blood tests and other tests using human specimens, imaging techniques, and other new methods) to detect and measure changes in protein and cellular function associated with specific cancers.

Research: Review, Renewals, and Reissues

Research is under continuous review at CIP, and several large imaging projects or funding mechanisms with significance for molecular medicine are currently under review or have recently been renewed or reissued for new proposals. The following are among these:

- The American College of Radiology Imaging Network (ACRIN), an international cooperative clinical trials group, has a new chair (Mitchell Schnall, MD, PhD), and funding has been approved for renewal for years 10–15. The network's goal is to use clinical trials of diagnostic imaging and image-guided therapeutic technologies to generate information that will lengthen and improve the quality of the lives of cancer patients. ACRIN clinical trials address both existing and emerging technologies as they apply to cancer screening, diagnosis, staging, imaging as a biomarker, and image-guided treatment.
- In vivo Cancer Molecular Imaging Centers (ICMICs) facilitate interaction among scientists from a variety of

fields to conduct multidisciplinary research on cellular and molecular imaging related to cancer. Pre-ICMIC planning grants have provided time and funds for investigators and institutions to prepare themselves, organizationally and scientifically, to establish ICMICs. We are currently reviewing various products that have come from these programs to determine levels of continued support.

- The NCI Small Animal Imaging Resource Program (SAIRP) is approaching its 10-year mark and is currently under review. Thirteen universities are funded through the SAIRP, which supports both shared imaging research resources to be used by NIH-sponsored cancer investigators and their research related to small animal imaging technology. These awards are intended to increase the efficiency, synergy, and innovation of preclinical small animal-based research and to foster research interactions that cross disciplines, approaches, and levels of analysis. The SAIRP has already enhanced functional and molecular imaging resources and advanced collaborative translational research across the spectrum of imaging modalities at institutions in the United States.
- The request for applications (RFA) to participate in the Network for Translational Research: Optical Imaging has been reissued with a new purpose: to develop, optimize, and validate imaging technology platforms and methods so that they can enter single or multisite clinical trials and eventually be incorporated into clinical practice. The response to the original RFA was much greater than early expectations, indicating the importance of optical and optical molecular imaging as the fastest-growing modality in cancer research. The new RFA focuses on translating innovations to clinical use across platforms through multisite teams that include broad national and international representation from academic, NIH intramural, and device and drug industry investigators.

Imaging Drug Development

CIP staff is actively involved in working with researchers on various aspects of drug development. The CIP has been creating Investigational New Drug (IND) applications for imaging agents to engage in multicenter clinical trials of these materials. Among agents under current investigation or consideration are: ^{18}F -D-cytidine, ^{13}N -gemcitabine, ^{11}C -SN-38, ^{18}F -paclitaxel, ^{18}F -DCFBC, ^{18}F -Her2 affibody, ^{18}F -FES, ^{18}F -fluorothymidine (^{18}F -FLT), ^{18}F -fluoromisonidazole (^{18}F -MISO), ^{18}F -galactose-RGD, ^{111}In -Herscan, ^{124}I -deoxyuridine, ^{64}Cu -ATSM, and ^{18}F -sodium fluoride. A subset of the documents filed for INDs is being made available to the research community to implement routine synthesis of tracers at their own facilities and to assist investigators with the filing of INDs. Sets of documents for ^{18}F -FLT, ^{18}F -MISO, and ^{18}F -FES are

currently available and include a full set of manufacturing and quality control documents and an Investigator Drug Brochure, all of which have been accepted by the U.S. Food and Drug Administration as part of the NCI IND. Templates, synthesis information, and other materials are available on the Web site at: <http://imaging.cancer.gov/programsandresources/Cancer-Tracer-Synthesis-Resources>.

The Development of Clinical Imaging Drugs and Enhancers (DCIDE) program is a competitive project to expedite and facilitate the development of promising investigational imaging enhancers (contrast agents) or molecular probes from the laboratory to IND status. Through the DCIDE program, the developer of a promising diagnostic agent or probe is given access to the preclinical development resources of NCI in a manner that is intended to remove the most common barriers between laboratory discoveries and IND status. CIP not only funds the toxicologic studies for these agents but provides guidance in the approval process. Despite the resources that CIP is able to contribute in this process, relatively few compounds have entered the DCIDE pipeline.

In addition, we have developed the Molecular Imaging and Contrast Agent Database (MICAD; <http://micad.nih.gov/>), an online source of information on in vivo molecular imaging agents based on recommendations from the extramural community. MICAD was established as a key component of the Molecular Libraries and Imaging program of the NIH Roadmap, a set of major interagency initiatives accelerating medical research. MICAD is edited by a team of scientific editors and curators at the National Library of Medicine and operates under the guidance of a trans-NIH panel of experts in the field. The database includes but is not limited to agents developed for PET, SPECT, MR, ultrasound, CT, optical, and planar gamma imaging as well as planar radiography. It contains textual information, references, numerous links to MEDLINE, and additional related resources at the National Center for Biotechnology Information and elsewhere. As of April 25, 455 agents were listed.

Imaging-Related Clinical Trials

As part of its mission the CIP takes the lead in planning and recruiting for a number of imaging-related clinical trials, as summarized on the Web site at: <http://imaging.cancer.gov/clinicaltrials/>. These include screening and interventional trials, trials assessing imaging response criteria, single-institution feasibility trials (R21), phase 1 and 2 trials, and ACRIN trials. Current phase 3 ACRIN trials all involve PET, including PET to: monitor treatment for malignant gastrointestinal stromal tumors, predict treatment response in lung cancer, and evaluate treatment response in lung cancer.

Facilities

CIP is involved in 2 facility improvements that will enhance our collaborative abilities in both basic and clinical translational imaging. The NCI-Frederick Small Animal

Imaging Program (SAIP) was established to provide NCI investigators with a state-of-the-art in vivo imaging facility. The SAIP became operational in October 2006 with the installation of a 3.0-T MR imaging unit and now includes microPET, microSPECT/CT, optical, bioluminescence, and fluorescence imaging capabilities as well as real-time sonography. The NCI laboratory includes a very large mouse repository, with mouse models of human cancer. Much of the small animal instrumentation that has been installed at Frederick and is planned for the future will be used in experiments aimed at drug development for NCI.

NCI is also participating in renovations to Building 10 in the Clinical Center on the main NIH campus in Bethesda, MD. The result will be that NCI will have a separate imaging facility in support of clinical trials in cancer.

Information Technology: Integrating Data

One of the results of the rapidly expanding numbers of imaging modalities and their potential applications in molecular medicine is an accompanying and exponential increase in the amount of data. CIP, together with NCI and the rest of NIH, is participating in efforts not only to collect these data but to harness their collective power in support of synergies of knowledge and efficiencies of research that can advance the translation of scientific discovery to patient benefit. Among these efforts are the following:

- caBIG (cancer Biomedical Informatics Grid) Cancer Central Clinical Database (C3D), a next-generation computer implementation and clinical trials data management system, is designed to aggregate imaging results from trials. C3D collects clinical trial data using standardized case report forms based on common data elements.
- The Virtual Imaging Endpoint Workspace (VIEW) will be made up of a consortium of participating groups that will provide imaging core laboratory services to NCI-sponsored cooperative groups and other NCI-sponsored clinical trial programs, including developing cross-network information technology infrastructures and standardized operating procedures.
- Visually Assembled Access to Rembrandt Images (Vasari): The Rembrandt (REpository of Molecular BRAin Neoplasia Data) database contains images and

tumor specimen information, including SNP array, expression array, proteomics, and clinical data from approximately 300 gliomas (<https://caintegrator.nci.nih.gov/rembrandt>). Vasari incorporates access to the images of the Rembrandt collection.

- Database development for computer-assisted diagnosis (CAD) is targeted at efforts to create uniformity in imaging across platforms and institutions, particularly in those images in which CAD is most suitable as an investigational tool. Among the current efforts are the following: (1) The National Cancer Imaging Archive (NCIA) is a searchable repository of in vivo cancer images in Digital Imaging and Communication in Medicine format. Images are available at no cost over the Internet in an open source format. The NCIA currently houses almost 1,000 images, and curators are gathering the metadata that will support research using these images. (2) The Reference Image Database to Evaluate Response (RIDER) is a Web-accessible public resource of validated image data for different organs/diseases and different modalities that facilitates the investigation of appreciable differences and sources of variance of imaging techniques as well as the assessment of changes over time in the course of treatment.

More Information from CIP

For more information on CIP and its activities, as well as on the ways in which it interacts with other groups and agencies within and outside of NIH, visit <http://imaging.cancer.gov>. CIP staff members are often available in information booths on the exhibit floors at the annual meetings of SNM, the Radiological Society of North America, and the Academy of Molecular Imaging and at other imaging-related events. *The CIP Newsletter*, distributed by e-mail, provides regular notification of funding opportunities and other issues related to imaging research, including relevant information from NIH Web pages and the NIH Guide. To sign up to receive the newsletter, send an e-mail message to: bc129b@nih.gov.

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