

National Cancer Institute and Imaging—Intersecting Scientific Opportunity With Clinical Need

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Our vision at the National Cancer Institute (NCI) is to stimulate and support scientific discovery and its application to achieve a future when all cancers are uncommon and easily treated. Cancer researchers have made significant progress but extensive work remains. In 2003, in USA alone, 1.3 million people were diagnosed with cancer and over 500 000 deaths occurred because of cancer. Technology continues to help us make major strides in understanding the molecular basis of cancer, and will be a major force in developing new diagnostics and interventions.

A critical technology in the fight against cancer is in vivo imaging. Detection through imaging of the molecular changes associated with a tumor cell will improve our ability to detect and stage tumors, select appropriate treatments, monitor the effectiveness of treatment, and determine prognosis.

The role of imaging in cancer research is changing. Historically the focus was on anatomic imaging, with an emphasis on developing clearer and more detailed pictures of organs and tissues. Now the focus is on functional imaging, emphasizing the physiological, cellular, or molecular processes in living tissues, as they take place. (As Richard Klausner noted when he was the NCI Director, imaging used to be “location, location, location,” in the future it will be “information, information, information.”)

The NCI has developed programs to move imaging into roles such as determining the pathogenesis of risk, identifying preclinical disease, enabling drug discovery, and facilitating tumor-selective image-guided interventions (<http://cip.cancer.gov>). Clinically, imaging will have a greater role in noninvasive diagnosis, identifying disease subsets in patients, assessing therapeutic response, disease progression, and monitoring of treatment.

We created the NCI Imaging Program in 1996, and its resources and initiatives extend internationally. The spectrum of research ranges from cellular to small animal to individuals to populations. Integrating scientific disciplines such as radiology, bioengineering, biology,

chemistry, and physics into a team approach was essential. For example, the In Vivo Cellular and Molecular Imaging Centers bring together a variety of investigators to develop molecular (functional) imaging methods and techniques for animals and humans. The Small Animal Imaging Resource Programs make these techniques available to researchers who need to use these imaging tools in their laboratory experiments on living animals. The use of molecular imaging techniques in small animals allows researchers to make serial measurements in the same animal over days, weeks, or months. The recently formed Network for Translational Research in Optical Imaging brings together groups of investigators who are developing diverse optical imaging methods. Optical methods hold the promise of providing molecular information with devices that are relatively inexpensive, and that do not use ionizing radiation.

NCI also has programs to help individual investigators develop novel imaging agents or new technologies. The Development of Clinical Imaging Drugs and Enhancers Program provides academic or industry researchers with a means to acquire the preclinical data needed to obtain regulatory approval to test new imaging agents in humans. For imaging device development, investigators can apply for grants from the Exploratory/Developmental Grants for Diagnostic Cancer Imaging initiative, or the Phased Innovation Award (R21/R33) Program.

When new methods, devices, or imaging agents are ready for multicenter clinical trials, investigators can submit a protocol proposal to the NCI-sponsored American College of Radiology Imaging Network (ACRIN). For example, ACRIN is carrying out two large screening trials, one in women at risk for breast cancer, and the other in collaboration with the NCI Division of Cancer Prevention in individuals at risk for lung cancer. Both trials have completed their 50 000-person accrual. The screening trial for lung cancer, the largest cancer killer, will determine if lung cancer screening using two different imaging modalities, spiral CT or CXR, reduces lung-cancer-specific

mortality. The screening trial for breast cancer will determine the screening efficacy of conventional screen-film versus digital mammography. Novel aspects in the design of the mammography trial included the willingness of four competing device manufacturers (GE, LoRad, Fischer, and Fuji) to pool the data on this technology, and the collaborative interactions of the ACRIN investigators with Food and Drug Administration (FDA) and Center for Medicare and Medicaid Services (CMS) staff. Well-annotated image archive databases will be available from both of these trials. Tissue and fluid specimens banked for biomarker research will also be available from the lung screening trial.

In addition to ACRIN, NCI has a program called the Early Clinical Trials of Imaging Agents to provide funds and infrastructure for phase 1 and phase 2 clinical trials of new imaging agents. NCI also supports several cooperative groups for therapeutic clinical trials, and these groups provide a resource to perform correlative imaging studies, for example to test the ability of imaging methods to measure tumor response to therapy.

We also recognized the need to integrate the various aspects of the environment in which technology developers had to work to bring promising products to testing and eventually to the market place to achieve an impact on the public health. The NCI works with scientists, clinicians, technology developers from academia and industry, and other federal government agencies critical to this effort, such as the three centers—Devices, Drugs, and Biologics—of the FDA and the CMS.

We created the National Forum on Biomedical Imaging in Oncology to facilitate partnerships with the imaging industry and government agencies to address new biomedical opportunities and challenges in oncology and to focus on the regulatory, coverage, and reimbursement issues for more developed and established technologies. From 200 to 250 technology developers from academia and industry, scientists, clinicians, and staff from NCI, FDA, and CMS have met in an open forum since 1999, with the most recent meetings on January 29–30th, 2004 in Bethesda, Maryland, USA.

A new multiagency group from the NCI, FDA, and CMS—called the Interagency Council on Biomedical Imaging in Oncology—was created in 2000 to serve as a confidential sounding board for technology developers from academia or industry, attempting to take emerging medical imaging technologies to market. These confidential meetings are held three times per year, and provide multiagency advice on scientific, clinical, regulatory, and reimbursement issues. Requestors have come from large or small companies and academia, with projects in various stages of development. The scope is broad and includes molecular probes, contrast agents, and imaging and optical technology devices. Feedback suggests the discussions have been instrumental in helping developers make informed decisions. The venue has also focused interagency discussion and heightened awareness of interagency perspectives as well as stimulated discussion of new

and novel issues such as those associated with the development of artificial intelligence algorithms. The next due date for requests is June 8th, 2004 for the July 20th meeting.

NCI also provides researchers in the imaging community with a variety of resources. The Mouse Models of Human Cancers Consortium (<http://emice.nci.nih.gov>) provides investigators with genetically engineered mice. A database of all imaging agents, an image archive of spiral CT lung scans from screened patients (Lung Image Database Consortium), and image archives of small animal imaging experiments are all under construction and will be publicly available soon.

Noninvasive or minimally invasive imaging as a means to obtain molecular information from and direct therapy in living animals and patients is in the midst of an exciting revolution. The entire spectrum of the clinical cancer problem, from risk assessment through detection, diagnosis, delivery and monitoring of therapy, and surveillance for recurrence, will be significantly altered by advances in imaging during the next decade.

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