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Meeting Report

Cancer Research

Moonshot Acceleration Factor: Medical Imaging

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Abstract

Medical imaging is essential to screening, early diagnosis, and monitoring responses to cancer treatments and, when used with other diagnostics, provides guidance for clinicians in choosing the most effective patient management plan that maximizes survivorship and quality of life. At a gathering of agency officials, patient advocacy organizations, industry/professional stakeholder groups, and clinical/basic science academicians, recommendations were made on why and how one should build a "cancer knowledge network" that includes imaging. Steps to accelerate the translation and clinical adoption of cancer discoveries to meet the goals of the Cancer Moonshot include harnessing computational power and architectures, developing data sharing policies, and standardizing medical imaging and *in vitro* diagnostics. *Cancer Res; 77(21); 5717–20. ©2017 AACR.*

Introduction

Over the past decade, the explosion of new analytic methods in cancer diagnosis and screening, (commonly referred to as "-omics" because genomics and proteomics are important players), along with molecular and immune therapies promises more personalized and precise cancer treatments. This creates an array of patient-centered care pathways that must be supported by a set of diagnostic data upon which treatment decisions are based. Medical imaging plays an essential role in Population Health, including screening, early detection, and monitoring responses to cancer treatments. When used together with clinical observations, pathology, and cancer -omics, imaging provides a cornerstone for effectively and efficiently choosing the cancer care pathway that maximizes survivorship and quality of life.

The Cancer Moonshot, which received $1.8 billion in federal funding over 7 years through the 21st Century Cures Act through bipartisan support from the 114th U.S. Congress, seeks to "make a decade's worth of advances in cancer prevention, diagnosis, and treatment, in five years." Although there are significant examples of and new opportunities to accelerate the translation of cancer discoveries through medical imaging, there are also hurdles that hinder the integration of accurate imaging with other diagnostic datasets to support treatment decisions in both academic medical centers and community practices where the majority of our nation's cancer patients are treated.

At a workshop in Rockville, MD, on April 12, 2017, the National Photonics Initiative (NPI) convened leaders from the medical imaging industry, academia, government agencies, and patient advocate stakeholders to identity key issues and propose solutions for more effective use of medical imaging to accelerate the translation of innovations into cancer care. The workshop, "Improving Early Detection of Cancer and Response to Therapies through Imaging Technologies," had a specific focus on expanded database infrastructures for data sharing, strategic computation and artificial intelligence, and standardized medical imaging data protocols to support widely distributed clinical trials. Workshop participants addressed gaps that involve photonics technologies and recommended actions to achieve the bold mission of the cancer moonshot initiative.

The NPI is a collaborative alliance of the American Physical Society (APS), the IEEE Photonics Society (IEEE), the Laser Institute of America (LIA), The Optical Society (OSA), and the International Society for Optics and Photonics (SPIE) that seeks to collaborate with industry, academia, and government to increase coordination to advance both conventional (nuclear, CT, MRI, US) and emerging biophotonics-driven medical imaging technologies and data management tools.

Report

The workshop consisted of 11 presentations in three sessions titled "Cancer Moonshot and Complementary Initiatives," "Evidence Development using Medical Imaging," and "Use of Diagnostics and High-Performance Computing to Provide Criteria for Treatment Decisions."

The first session began with a review of ongoing, independent efforts that can be leveraged to deploy medical imaging and diagnostic data for accelerating approval and clinical adoption of new cancer treatments. Eight of the 10 focus areas recommended by the Cancer Moonshot Blue Ribbon Panel (www.cancer.gov/brp) and implemented under the direction of the NCI (Rockville, MD), will require the support of medical imaging. As part of the Precision Medicine Initiative (https://syndication.nih.gov/multimedia/pmi/infographics/pmi-infographic.pdf), the NCI is establishing a national IT "cancer knowledge network" to house and integrate genomic information from tumors with clinical response data (e.g., tumor shrinkage) and outcomes information (e.g., length of survival) with privacy protections to advance the collection and analysis of clinical trial data. This resource for scientists, health care professionals, and patients

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should include medical images. The Department of Energy's National Strategic Computing Initiative (www.nitrd.gov/nsci) provides infrastructure for developing and utilizing high performance computing, and again through the Precision Medicine Initiative, toward data mining to accelerate discovery, regulatory approval, and development of medical evidence. The infrastructure for multicenter clinical trial design, conduct, and reporting developed by the Eastern Cooperative Oncology Group (ECOG) and the American College of Radiology Imaging Network (ACRIN) known collectively as ECOG-ACRIN, provides one example of ongoing efforts to develop databases that include medical imaging. Clinical trial image data management focused upon (i) early detection and diagnosis; (ii) biomarker-driven phase II and III therapeutic studies; and (iii) genetic, molecular, and imaging marker research is ongoing in over 7,000 ECOG-ACRIN sites. These efforts, along with ongoing activities from the Colon Cancer Alliance, Prevent Cancer Foundation, Lung Cancer Alliance, AdMeTech Foundation (Non-profit Corporation for the Advancement of Medical Technologies), Medical Imaging and Technology Alliance (MITA), and Society of Nuclear Medicine and Molecular Imaging provide opportunities for partnership. This session showed that the data sharing opportunities in the intensive processes of cancer discovery, clinical research, and postmarket data collection exist and can be developed through various efforts to continually evolve and accelerate translation of technological advances into clinical practice. Data sharing can mitigate research costs while enhancing cancer survivorship and quality of life.

The second and third sessions provided scientific and technical presentations that focused upon the key challenges to incorporate medical imaging into the "cancer knowledge network." Within these two sessions, discussions at the workshop focused upon three key themes, namely (i) the judicious development and use of imaging data as quantitative biomarkers to support discovery, medical evidence, and clinical care decision making; (ii) the development of protocols and standards and their facile clinical use in the "cancer knowledge network"; and (iii) challenges and opportunities for incorporating the diversity of medical image datasets into the cancer knowledge network for transparent and secure use by patients, clinical researchers, providers, and payers.

Tumor heterogeneity drives medical imaging

Tumor biopsy, biomarker analyses, and pathology are "gold standards" for cancer staging and delineation of treatment. Yet tumor heterogeneity mandates the need for numerous biopsies to accurately sample and characterize tumor potential, while practical issues make biopsy an inherent "sampling problem." Magnetic resonance (MR) and ultrasound image-guided biopsy of prostate tissues were presented as examples in which imaging allowed more accurate assessment of cancer progression risk than could be obtained from standard biopsy procedures (1).

"Active surveillance" by multiparametric MR (mpMR) can, when combined with computer-aided diagnosis, improve prostate cancer margin detection and guide biopsies to tissues with the most aggressive prostate tumor. This improved diagnosis of clinically significant prostate cancer allows for the more accurate decision making and impactful biospecimen assays that can change management plans for improved outcomes. Nonetheless, the restricted number of biopsies and repeat biopsies in most cancers will ultimately limit the amount and quality of genomic and immune biomarker information available throughout the course of cancer care.

The combination of genetics and medical imaging comprising the field of "imaging-genomics" is another research area to relate MR imaging features (i.e., radiomics) of cancer tissues to clinical, pathologic, molecular, and genomic markers. Referred to as "virtual" or "digital biopsies," these tools under development could overcome some of the perplexing problems of tumor heterogeneity and contribute to the array of data for early detection, more accurate cancer staging, and repeated assessments of treatment response, especially when actual biopsies are not practical. Medical imaging may also become an essential companion diagnostic for cancer immunotherapies where biomarkers may not always be assessed from tumor biopsies. For example, the success of cancer immunotherapies hinges not only on the heterogeneous expression of immune biomarkers on tumors, but also on the status of the regional lymphoid tissues where the immune system is molecularly manipulated to attack or tolerate cancer. The use of medical imaging to "virtually biopsy" anticancer immune responses, both in the regional lymphoid tissue and in cancerous tissues, needs to be further developed so patients who will and will not respond to these novel therapies and those who may have severe immune-related adverse events can receive the optimal treatment (2). Overall, the use of medical imaging as a biomarker has the potential to contribute significantly and efficiently to the "cancer knowledge network," advancing personalized medicine.

Imaging as a biomarker drives quantitation and decision making

The robust and impactful use of imaging biomarker data for clinical research and personalized care of cancer patients requires the ability to objectively compare data obtained from imaging acquisition and analysis systems from multiple vendors, from multiple sites, and across time. In contrast to common diagnostic measurement devices, such as thermometers and pulse oximeters that have specifications for reproducible and quantitative results, the historical evolution of medical imaging has been to provide the best image quality in the shortest amount of time. Yet as other diagnostic measurements and biospecimen preparations need to be validated and standardized before providing reliable and meaningful use in the cancer knowledge network, quantitative imaging biomarker measurements must likewise be standardized and the results reported in a consistent manner to make quantitative and statistical comparisons and guide decisions. Efforts by the Quantitative Imaging Biomarker Alliance (QIBA, www.rsna.org/qiba) of the Radiological Society of North America (RSNA) highlight the potential clinical impact of quantitative imaging on patient care and the importance of standardizing and harmonizing image acquisition, analysis, and reporting. The application of metrology principles to specify the bias and precision of quantitative imaging biomarker measurements is essential for sharing and using medical imaging data in the "cancer knowledge network" (3). The development of standardized imaging biomarker measurement tools and data sharing pipelines is an overarching goal of the NCI's Quantitative Imaging Network (imaging.cancer.gov/programs_resources/specialized_initiatives/qin.htm). Finally, the need for industry-standardized, application-specific standards and their deployment requires industry-government collaboration.

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Appendix: Participants and discussants other than authors

Carolyn "Bo" Aldigé	Prevent Cancer Foundation
Rick Avila	Accumetra
Sue Bunning	Medical Imaging and Technology Alliance
Peter Choyke	National Cancer Institute Center for Cancer Research
Bonnie Clarke	Society of Nuclear Medicine and Molecular Imaging
Laurie Fenton Ambrose	Lung Cancer Alliance
Claudia I. Henschke	Icahn School of Medicine at Mount Sinai
Edward Jackson	University of Wisconsin School of Medicine and Public Health
Maciej Mazurowski	Duke University
Robert Nordstrom	National Cancer Institute
Etta Pisano	Harvard Medical School, Beth Israel Deaconess Medical Center, and American College of Radiology
Berkman Sahiner	Food and Drug Administration, Division of Imaging and Applied Mathematics
Michael Sapienza	Colon Cancer Alliance
Faina Shtern	AdMeTech Foundation (Non-Profit Corporation for the Advancement of Medical Technologies)
M. Minhaj Siddiqui	University of Maryland Medical Center
Eric Stahlberg	National Cancer Institute Frederick National Laboratory for Cancer Research
Peter Weems	Medical Imaging and Technology Alliance
David Yankelevitz	Icahn School of Medicine at Mount Sinai

Once standardized for use in the "cancer knowledge network," medical imaging biomarkers will be an accelerant for evidence development that modifies treatment plans and improves care. For example, optimizing interdisciplinary application and integration of diagnostic tools, including standard approaches to screening and early detection (e.g., PSA, image-guided biopsy, and mpMR in prostate cancer) and emerging diagnostics (e.g., imaging, biomarkers, genetics/genomics, and molecular pathology) can end the current and unacceptable extent of unnecessary and failed biopsies and treatments and can enable a future of precision, personalized cancer care. Emerging opportunities to use standardized imaging datasets coupled with other diagnostics housed within the "cancer knowledge network" for artificial intelligence and "deep learning" will be necessary to guide health care providers through the myriad of patient-centered care pathways that embodies effective, precision medicine.

Registries to accelerate translation of innovations into patient use

Today's translation of clinical discoveries occurs by sequential processes of (i) generating clinical evidence of benefit at specific clinical sites and then (ii) assessing quality measures such as outcome and costs that ultimately facilitate or derail future clinical adoption. Although important, these steps in the critical path employ outdated and uncoordinated, site- and provider-specific databases that delay (i) the realization of benefits to the patient and health care provider, that is, outcome and quality, and (ii) the benefit to the health care delivery network, that is, cost savings. The coordination of registries to rapidly gather and share information of benefit and quality outcomes across sites and providers provides a strategy to accelerate translation and clinical adoption of innovations (4). Unfortunately, despite being digitized and therefore ideally suited for machine learning from "big data," medical image data are not accommodated in these databases.

The benefit of registries is clear from the impact of the International Early Action Lung Cancer Action Program (I-ELCAP, http://www.ielcap.org) on the LungRADS criteria for referral of patients to biopsy of lung nodules. Analysis of the data from this registry revealed that the lung nodule size threshold for referral could be raised, thereby reducing the harms and costs of false positives without missing true cancers (5). The need for expansion of the registry concept was also emphasized in the meeting by representatives of Prevent Cancer Foundation who pointed out that a vast percent of clinical data from oncology protocols, not only imaging data, is wasted and for two reasons: it is not collated into a widely accessible database, and much of it is unstructured (i.e. it does not a defined data model or is not organized in a predefined manner). Patient advocacy groups like the Lung Cancer Alliance (LCA, http://www.lungcanceralliance.org/) and the Colon Cancer Alliance (CCA, https://www.ccalliance.org/), play important roles in encouraging patient and clinical site participation in the process to generate medical evidence. The "National Framework of Excellence in Lung Cancer Screening and Continuum of Care" was designed by the LCA to provide guidance and criteria to implement responsible, high-quality screening programs and to encourage collaborative research. The "Clinical Trial Finder" designed by CCA was created to help patients get the care they need while also contributing to the advancement of clinical practice. Patient stakeholders who have the ability to contribute to and access their own medical images and clinical diagnostics within privacy guidelines will be essential to the evolution of the cancer knowledge network.

Recommendations

Because "an image is worth a thousand words," making medical imaging part of the "cancer knowledge network" is necessary for involving patient advocates and stakeholders. Too often, patients have to hand-deliver CDs containing medical images to the partnering providers, or repeat imaging tests because medical imaging is currently not part of the national IT health infrastructure and because electronic health records are not interoperable across vendors. Today more than ever, there are new opportunities to design and implement a national IT health infrastructure (i.e., the "cancer knowledge network"), so that it supports patient care while advancing medical discoveries and innovations into the clinic and accelerating their clinical adoption. This cloud-based, biomarker data and medical image resource could be established as a vendor-neutral utility and, when coupled with an enhanced national broadband infrastructure for secure and private patient access, could be scaled to support impactful deep learning for decision support in precision medicine as a

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nation-wide resource. In tandem, steps to standardize data acquisition protocols and analysis methods should be implemented early on when developing new diagnostic technologies, including optical imaging, computer-aided pathology, and others, again to hasten the timeline for clinical adoption. We believe these infrastructure development steps are essential for using medical imaging and diagnostic –omics to support individual cancer patient care decisions and accelerate the adoption of 10 years of discoveries in the Cancer Moonshot timeframe of 5 years.

Disclosure of Potential Conflicts of Interest

E.M. Sevick-Muraca reports receiving other commercial research support from Kimberly Clark Corporation and Tactile Medical Systems, has received speakers bureau honoraria from Lymphedema Seminars, and has ownership interest (including patents) in NIRF Imaging. R.A. Frank is the chief medical officer at and has ownership interest (including patents) in Siemens Healthineers. M.L. Giger has ownership interest (including patents) in Quantitative Insights. No potential conflicts of interest were disclosed by the other author.

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