QUANTITATIVE IMAGING WORKSHOP

prevent cancer® FOUNDATION

James L. Mulshine, MD, Rush University, engages with leading stakeholders from industry, academia, clinical practice, government and patient advocacy on the best ways to communicate the value of quantitative chest imaging. Panel pictured left to right: Andrea McKee, M.D. – Lahey Hospital and Medical Center; Anita McGlothlin – Lung Cancer Alliance; Robert Nordstrom, Ph.D. – National Cancer Institute; Bruce Pyenson, FSA, MAAA – Milliman, Inc.; and Albert Rizzo, M.D. – American Lung Association.

On November 5 and 6, 2018, the Prevent Cancer Foundation hosted the 15th Quantitative Imaging Workshop (QIW) in Alexandria, VA. The Workshop is a high-impact, multi-disciplinary forum for the advancement of quantitative CT imaging biomarkers for early thoracic disease management. The Workshop explored how a revolution in biomedical imaging, which enables radiologists to detect the pathological process earlier than ever before, can be leveraged to improve outcomes in managing early lung cancer. Our goal was to introduce robust approaches to allow quantitative assessment of the growth of pulmonary nodules, as this turns out to be a sensitive and specific way to find early lung cancers.

Included in the opening session is an annual award to an individual who has made a remarkable contribution to all people whose lives have been touched by lung cancer. The 2018 award honored brilliant trial lawyer Sharon Eubanks, for her inspired leadership of the US Department of Justice legal team in prosecuting the US tobacco industry.

Quantitative Imaging Workshop XV: Lung Cancer, COPD and Cardiovascular Disease - Quality is a Gateway to Deep Learning

November 5-6, 2018
Hilton Alexandria Old Town
Alexandria, Virginia

STEERING COMMITTEE

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Sharon Y. Eubanks accepts the James L. Mulshine, M.D., National Leadership Award in recognition of her transformative work as lead counsel for the US Department of Justice in convicting the tobacco industry of fraudulently informing the public about the danger of their products. The sterling example of Sharon Eubanks reminds lung cancer patients that seemingly impossible change can happen.

OPPORTUNITIES WITH NEW FDA CT IMAGE QUALITY STANDARDS

Within the framework of the Quantitative Imaging Workshops, there has been a persistent focus on data standards, including improving data quality and data reproducibility. This has been a shared concern of the Quantitative Imaging Biomarker Alliance (QIBA). Past Workshop efforts have resulted in the development of new image archives, such as the Reference Image Database to Evaluate Therapy Response (RIDER), with the National Cancer Institute, and Give-A-Scan (donation of images), with Lung Cancer Alliance. A variety of approaches to enhance data sharing (Interactive Scientific Publishing environment, ISP) are being explored with the Optical Society of America. This includes a long-term interaction with QIBA, as both share a focus on standardization of optimal imaging processes with a goal of allowing more efficient and economical integration of image biomarkers in routine care as well as clinical trials.

The topic of biomarker review was a focus of discussion at the Workshop, as it is fundamental to creating a strong foundation for enabling integration of imaging biomarkers into new approaches for early lung cancer management. Creating momentum for developing new imaging tools will also help, since new regulatory approaches have been developed with the passage of the 21st Century Cures Act. This law explicitly defines the biomarker approval process to facilitate such efforts. Discussion at the Workshop addressed the challenge of applying biomarkers to clinical practice, i.e., ensuring that the measurement of the relevant biomarker is performed in a consistent, accurate and reliable fashion to guide responsible clinical management.

The process for formally approving imaging biomarkers for clinical decision making is complex. Workshop XV laid groundwork for engaging the US Food and Drug Administration (FDA) in a new regulatory process for evaluation of imaging devices, software and imaging biomarkers for safety and effectiveness. This is a remarkably challenging bar, as no imaging biomarkers have been formally approved for clinical decision making. In light of this, the FDA has developed new regulatory processes, potentially separating the biomarker qualification process into two discrete steps, with the first step being a focused analysis of the performance dynamics of the biomarker under defined conditions.

In these efforts the FDA is principally focused on evaluating whether the imaging device, software or process is safe and effective. Based on extensive experience, the FDA has evolved to a process that is rigorously calibrated, considering the potential for threat to the public, so low-risk candidates would experience a low burden of proof compared to a high-risk proposal.

The primary responsibility for regulating medical imaging devices at the FDA is held by the Center for Devices and Radiological Health (CDRH), which has a complementary role in the review of imaging devices, software and imaging biomarkers. Dr. Nick Petrick from the Division of Imaging, Diagnostics and Software Reliability discussed how CDRH participates in the validation process for imaging biomarkers. To accomplish this, in 2017 the FDA developed the Medical Device Development Tool (MDDT) process.

The MDDT process outlines a flexibly-staged framework that involves specific interactions and formally defined terms. This is designed to allow for an efficient and productive dialogue with the Agency to advance relevant products to the marketplace responsibly. The MDDT process is used for the review of a method, material, or measurement used to assess effectiveness, safety, or performance of a medical device. A MDDT is scientifically validated and qualified for a specific Context of Use (COU) under carefully defined and specific conditions. After the review, if the FDA concludes that within the proposed COU that a MDDT has a specific interpretation and application in medical device development, the candidate is considered to be qualified for that measurement purpose. (https://www.fda.gov/medical-devices/science-and-research-medical-devices/medical-device-development-tools-mddt)

A specific example of a COU where a process has been defined to guide medical management is in the specific context of diagnostic work-up in the CT imaging of individuals at risk for lung cancer undergoing low-dose CT thoracic imaging. The imaging biomarker in this situation is a change in size in the suspicious pulmonary nodule. A process has been reported to use cloud-based phantom assessment to ensure that measurement of the pulmonary nodules in the relevant volume range from 6-10 mm in diameter is precisely characterized (Caroline McNeil. Low-Dose CT Lung Screening: New Developments Support Increased Quality, More Data, Deep Learning. ASCO Post December 25, 2018: https://www.ascopost.com/).

Investigators from QIBA have been funded by the Prevent Cancer Foundation to evaluate the international performance of CT scanners used for lung cancer screening. This involves a cloud-based quality evaluation at 65 screening sites around the world using the Quantitative Image Biomarker Alliance quality assessment outline in the Small Lung Nodule Profile conformance certification phantoms. (Radiological Society of North America. Quantitative imaging biomarkers alliance (QIBA). 2017; http://qibawiki.rsna.org/index.php/Main_Page. Accessed 5/3/17). This conformance certification process was discussed as an example of an interesting candidate for MDDT review by the FDA. In this fashion, the MDDT review will allow evaluation of the dynamic performance characteristics of the nodule volume measurement by low-dose CT under defined conditions. The expectation would be then to move forward to evaluation of the volume measurement of lung nodules in real world settings of CT-based lung cancer screening. The specific clinical context of use would be considered for FDA biomarker qualification to support clinical decision making for screening management.

SUCCESSES IN LUNG CANCER SCREENING PROGRAMS

The burden of lung cancer mortality is different across various settings; two particularly important high-risk groups are veterans of the armed services and economically disadvantaged urban populations. Dr. Claudia Henschke from

Mt. Sinai Medical Center reviewed progress in implementing a pilot study at a number of Veterans Hospitals in an exciting project underwritten by the Bristol Myers Squibb Foundation, called the Veterans Affairs (VA) Partnership to Increase Access to Lung Cancer Screening (VA-PALS). VA-PALS is adapting the International Early Lung Cancer Action Program (I-ELCAP) management system for integration with the existing VA electronic health record.

Dr. Mary Pasquinelli from the University of Illinois in Chicago reported on published outcomes with implementation of lung cancer screening in a federally qualified health center in Chicago. Dr. Andrea McKee presented the compilation of screening approaches implemented across the nation by a number of sites, organized by the American Lung Association. The resource outlines a wide range of solutions adapted across centers that have successfully implemented lung cancer screening in a fashion that meets the needs of their stakeholders.

BROADENING SCREENING IMPLEMENTATION: GLOBAL LESSONS

Chronic obstructive pulmonary disease is the most common of the inflammatory parenchymal diseases of the lung, but there are a number of other related conditions. A shared aspect of these diseases is that they are now frequently detected in the high-risk population undergoing thoracic CT for lung cancer detection.

An important topic that was discussed throughout the Workshop was the issue of the slow adoption of lung cancer screening. As observed with earlier introduction of cancer screening, such as for breast and colorectal cancer, percolation into the target population is a slow process. At the recent Workshop, we heard about the 10-year follow up of the major Dutch/Belgian Lung Cancer Screening study (NELSON Trial), which was presented at the World Conference on Lung Cancer and showed an overall lung cancer mortality reduction benefit of 26% in the CT screening arm compared to a 20% mortality reduction benefit reported with the United States National Lung Screening Trial. An Italian randomized trial reported the mortality reduction benefit from 5-10-year follow-up was a 58% reduction in lung cancer mortality.

In addition, national screening implementation pilot trials are now being launched in a number of countries. A challenge with this new trend is that the most efficient screening results have been reported with groups that use volumetric analysis to select large pulmonary nodules to trigger invasive diagnostic work-up for invasive lung cancer. Examples include the I-ELCAP group and NELSON group, as well as the pilot study from England (UKLS group). However, a validated tool that can perform nodule volume assessment in routine clinical workflows is not yet available. Therefore, the 2018 Quantitative Imaging Workshop centered on discussions about how to address this challenge with broadening screening implementation.

In conclusion, we are seeing great strides in advancing high quality lung cancer screening, but there are still gaps in making critical tools available for routine clinical support. A major focus for our next Workshop will be to explore mechanisms to advance tool development and validation through the development of a large image archive.

SPECIAL THANKS TO THE 2018 QUANTITATIVE IMAGING WORKSHOP SUPPORTERS!

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