LUNG CANCER WORKSHOP

prevent cancer FOUNDATION

Executive Summary Workshop X: Application of High Resolution CT Imaging Data to Lung Cancer Drug Development: Measuring Progress

2013 EXECUTIVE SUMMARY

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The Tenth Lung Cancer Workshop, Application of Quantitative CT Imaging to Early Lung Cancer Management: Accelerating Progress, was held in Bethesda, MD on the May 2 and 3, 2013. The goals of the Workshops have been to convene a cross disciplinary assembly of professionals interested in advancing the use of computational imaging to enable better outcomes in the management of early lung cancer. This year's Workshop convened at a pivotal moment in time for public health decision-making on lung cancer screening. The United States Preventive Services Task Force (USPSTF) has underway its evidence review process to determine a new screening recommendation for lung cancer. In addition, this year's meetings again provided a multi-disciplinary forum for oncologists, pulmonologists and radiologists, along with representatives of federal agencies, the pharmaceutical and diagnostic imaging industries, and patient advocates, to explore the use of spiral CT scanning as a tool for evaluating response to new lung cancer therapies as well as for improved early lung cancer detection.

For lung cancer screening, low-dose CT (LDCT) is used both to detect suspicious lung nodules as well as to determine which nodules are growing at a rate consistent with the behavior of a clinically aggressive lung cancer. The latter application has led to the emergence of quantitative CT as a key tool for use in diagnostic work-up of suspicious lung nodules. A key topic of this workshop series is to determine how to integrate the accurate assessment of lung nodule volume change into the screening setting. These two challenges are complex and require a collaborative team of broad multi-disciplinary specialists to ensure that optimal processes are defined. The theme of ensuring quality and consistency in the quantitative aspects of lung cancer screening was introduced in the overview of the Workshop that was given by Dr. James Mulshine, but this topic was integral to many other subsequent workshop presentations. Dr. Mulshine reviewed the progress catalyzed by the efforts of previous workshops, including a number of publications, secondary meetings and establishment of a number of important database resources.

Of particular importance this year is the issue of lung cancer screening which is under review by the United States Preventive Services Task Force and involves the application of these computational imaging techniques. The Task Force will score the value of this cancer screening process and based on this score, the Center for Medicare and Medicaid Services (CMS) will determine if reimbursement for this service will be provided nationally. A question posed to the group in the Overview presentation was what would be the national response, if LDCT screening were given a favorable classification by the USPSTF? Would the nation be ready for LDCT implementation? What could be done to ensure a safer, more economical rollout?

In that regard, the recent report by Henschke and colleagues was topical. Their follow up of over 21, 000 screenees was recently published in which they looked retrospectively at the aggregate dataset after eight years of screening follow-up. With this approach, they analyzed diagnostic efficiency of screening work up as it related to the size of the detected pulmonary nodules. This report represents an early example of "rapid learning" as proposed by the Institute of Medicine, in which large datasets of care delivery are analyzed to devise approaches to improve health outcomes. In this case, restricting diagnostic work-up to individuals found to have non-calcified pulmonary nodules of 8mm in diameter and larger resulted in 75% fewer diagnostic work-ups than if invasive diagnostic work-ups were initiated in all individuals with suspicious nodules greater than 4mm.

In later sessions of the Workshop, experts addressed the progress with interpretation of coronary calcium for risk of cardiac death as well as assessment of pulmonary injury. In both cases, these analyses were done on the DICOM images obtained for lung cancer screening. A final vision shared with Workshop participants was: "In the post Accountable Care Act world of preventive directed care, LDCT will be an anchor of a periodic health evaluation tool in tobacco smoke-exposed populations." In this case, preventive care for major chronic diseases in this population would be anchored by dynamic changes in serial data provided by integrated quantitative assessment of periodic CT screening data. This periodic health encounter would bundle LDCT screening for early lung cancer, heart disease and COPD, and coaching on smoking cessation along with other health and wellness information for this high-risk cohort in an efficient ambulatory encounter.

LDCT and Public Policy

The plenary paper for the Workshop was given by Professor Cheryl Healton, the Chief Executive Office of Legacy Foundation. In this stirring presentation Professor Healton outlined her perspective from the intersection of a public health leader involved with the management of HIV / AIDS and her own strong family history of lung cancer. Further she reviewed the strong economic case for integrated smoking cessation and lung cancer screening in a practical and sustainable fashion. Prof Healton suggested that failure to provide federal support for lung cancer screening would be an issue of health equity that echoed her early experience in the area of HIV / AIDS care. She reminded the audience that proactive groups rallied public sentiment to provide comprehensive care for the disease and this approach has resulted in a great public health success. Prof Healton suggested that this experience offers a useful road map to those advocates supporting the implementation of LDCT screening.

This topic was further explored by Professor Robert Winn, Associate Vice President for Health Equity at the University of Illinois. Prof Winn is a pulmonary physician who has conducted a lung cancer screening trial in Colorado. He outlined that smoking is a habit that disproportionately affects economically- and socially-disadvantaged populations. The decision not to provide reimbursement for LDCT would mean that many of those who may benefit from LDCT screening would not have access to this service and that would be an extremely unfortunate new example of health care disparity.

Presentations ranged from progress on reducing variance of quantitative assessment with lung CT from the work of the Quantitative Imaging Biomarker Consortium, to further efforts to integrate combined lung cancer and COPD assessments using spiral CT, to efforts of patient advocates to catalyze cooperation in implementing a framework of excellence in approaching the national implementation of lung cancer screening. This topic of screening implementation was carried forward as a Workshop Breakout Group topic. The group explored the timeline for expecting a revision to the United States Preventive Services Task Force recommendation on lung cancer screening. The group also discussed what scientific evidence was strong enough to warrant the highest level of recommendation by the USPSTF for those at risk. This recommendation will be made against the backdrop of the National Lung Screening Trial (NLST), a two hundred and fifty million dollar study involving 53,000 randomized subjects, that achieved the threshold for significance, i.e. a 20% lung cancer mortality reduction benefit that was agreed to by consensus prior to study initiation as representing a convincing body of evidence.

David Yankelevitz pointed out how the results of the NLST are now being misrepresented to mean that only 20% of screen-detected lung cancers will be cured, when actually the NLST results suggest that a much higher proportion are cured. Certain guideline organizations have mistaken the mortality rate reduction found in the NLST to represent the fatality result, which is probably much greater. This point underscores the importance of continuing to assemble more data to allow the full benefit of lung cancer screening to be more clearly defined.

The second Breakout Group focused on technical issues with LDCT imaging, such as with understanding and controlling sources of variance in the screening setting. Important sources of acquisition variation include the larger number of scanner types and acquisition parameters. For purposes of controlling this variable in clinical trials evaluating drug effect, the dominant strategy to address this confounding factor is to limit the number of scanner types used in a particular clinical trial, i.e. use a small number of scanners in a controlled setting (n<=5). To further minimize variance in clinical settings, key parameters must be standardized including slice thickness, dose, reconstruction kernel and use of iterative reconstruction approaches. From a research perspective, the reference data available to study such imaging issues is often limited or non-existent, such as with public databases of small lung cancers DICOM images from longitudinal scanning experiences. Moreover, the need for better models to characterize the specific imaging process is key to devising methods that reduce variability and standardize the measurements across brands.
The group consensus was that there was good progress in better understanding sources of acquisition variation with LDCT. However it is also apparent given the complexity of evolving CT scans for lung cancer that there is also a need for machine-driven image acquisition to reduce the opportunity for operator variability. More specifically, future CT scanners that are being designed today should be engineered to achieve the high levels of imaging accuracy needed for quantitative imaging - unlike older scanners where subjective radiological viewing was the main goal. Due in part to this historical context, performance is not currently well defined for the CT scanners deployed throughout the world today. In light of this challenge, the group agreed that improved quantitative imaging acquisition standards are needed to allow for more consistent image quality for quantitative imaging tasks. Toward this goal it was recommended that an image quality report is one day available for each CT patient scan, similar to the reports on radiation dose that are now routinely available. Further contributions from all sources are needed but institutions such as NIST may have a critical role in bringing the rigor of measurement science to the field of clinical applications of quantitative lung imaging. Existing opportunities include developing software methods that allow a more systematic integration of useful algorithms and other related methods. An exciting new opportunity is to catalyze the field of automated image acquisitions so that the results of quantitative imaging might be more routinely applied for clinical care with low levels of measurement variability.

Another important consensus recommendation from the second breakout group addressed the largely unmet need to develop large and continuously updated open image archives for lung cancer imaging research. While several archives are now available for archiving large collections of data, obtaining large number of high quality lung cancer imaging datasets continues to be a major obstacle. Thus the meeting participants arrived at a new approach to this longstanding issue by recommended that a wide scale community-based effort is applied to obtain buy-in for contributing a percentage of cases (e.g., 10% to 20%) from many of the newly starting lung cancer clinical trials. Obtaining commitments from numerous studies to submit datasets has the potential to significantly improve the availability of open lung cancer imaging datasets.

This year's meeting concluded with by summarizing the large number of important new recommendations, spanning both policy opportunities as well as areas for technical innovation improvements. Over the coming year these major recommendations and opportunities will be addressed and pursued.