Comments by Steven E. Seltzer, MD, to Interagency Working Group on Medical Imaging

June 29, 2016

Ladies and Gentlemen:

My name is Steven Seltzer and I am the Chair of Radiology at Brigham and Women's Hospital in Boston. Thank you for allowing me to speak with you today on behalf of the Academy of Radiology Research.

Over the last 3 meetings of the Working Group, you have heard first, about the exceptional organizational infrastructure that supports the field of radiology and will permit us to design and execute a national medical imaging research investment plan. Second, you heard from our industry partners about their exceptional technologies that are giving us the tools for next great advances in radiology research, moving from a foundation of purely structural imaging into the complimentary arenas of functional and molecular imaging, image-guided therapy and informatics. Third, today, you've heard from our outstanding researchers who have the skills, creativity and drive to lead our research future, and I know you were tremendously impressed by their accomplishments.

A link to the presentations from the last 3 meetings is attached:

http://www.acadrad.org/information-on-the-iwgmi-meetings/
Password: IWGMI

You have not yet heard from the patient community, but I wanted to be certain you knew that the Academy of Radiology Research is affiliated with 100 patient advocacy groups! This staggering number is attributable to the fact that medical imaging touches almost every human disease. The Academy's leadership has energetically engaged these groups, and they help inform our comprehensive advocacy work for medical imaging research funding. <by the way, if you would like to connect with any of these patient groups the Academy could facilitate.>

I will take as a given that our **colleagues at NIH, particularly NCI and NIBIB, as well as academic scientists,** will continue to drive core research in physics, biology, biomarkers, engineering, informatics and other fields that are key to maintaining the pace of scientific advances in imaging, and that **our industry colleagues** will continue their development success translating scientific advances to create ever more powerful and precise imaging technologies, including higher field MRIs, CT and PET scanners that can do more with less radiation, biomarkers that definitively 'paint' pathology, and hybrid platforms that combine the strength of all of these technologies. I hope that each of the other Working Group agencies will explore cross-fertilization opportunities where your scientists may be able to propel radical or transformational leaps in technologies or approach.

So...My goal in these final minutes is to try to provide you with a framework that may help you organize and categorize all of the exciting information that you have heard over the past few months. I will use a reductive and simplifying approach to bring all these threads together. I want to facilitate your efforts to move on to the task of creating the white paper or road map that will help us combine the capabilities of many federal agencies to contribute their expertise in order to further the value that medical imaging can bring to improving the health of the American public as well as contributing to American economic activity and American competitiveness.

Sounds ambitious, but I suggest that we can approach these by grouping the information you have heard, into three cardinal, *clinical* categories, namely: ***Early Detection of Disease***, ***Precision Diagnosis***, and ***Image-Guided Interventions***. Simplifying our discussion by using these categories may help the Working Group chart a path forward that can help the country achieve our medical and economic goals for imaging AND catalyzes the use of the assets of each of the Federal agencies represented here, blasting apart the usual silos that separate them.

I'll try to explain what I mean.

Here is a very simplified version of the tasks imagers perform in each of these 3 clinical categories:

Early Detection of Disease	Precision Diagnosis	Image-Guided Intervention
Assess threats and conduct surveillance in populations	Characterize fully the nature of any abnormality in a specific patient	Use the precision diagnosis to develop an individualized, rational treatment plan and monitor its effectiveness
Use deep learning tools to calculate how findings on imaging tests in conjunction with other risk factors can calculate an individual patient's risk for developing a disease or its natural history.	Combine quantitative structural, functional and molecular imaging data with pathology, genomic, metabolic and clinical information to characterize a specific abnormality and understand its pathophysiology leading to a precision diagnosis	Use imaging modalities to guide tissue retrieval, resection or ablation.
Use non-invasive imaging tests to detect signs of pre-clinical disease. <Screening for cancer with mammography would be a prototype>	Use sophisticated information management tools to combine information from multiple sources as well as to 'learn' from experience	Select optimum medical therapy
Detect and locate pre-clinical disease in a patient with a positive liquid biopsy	Use imaging tests and specific biomarkers to precisely localize pathology when relevant (e.g., polyps), and plan therapy	Use imaging tests and other biomarkers to evaluate quantitatively the response to therapy

Interestingly, this 3 category classification scheme is highly analogous to the way we frame and solve other large-scale problems, which will be familiar to those of you from non-medical federal agencies.

For example, while it seems like a big stretch, I would argue that these 3 'clinical' categories apply to national security. The FBI, Homeland Security and the Department of Defense are first called upon to use all types of intelligence to assess threats and conduct surveillance of populations in order to detect suspicious targets (even when they are camouflaged). This is a problem of finding a small signal against a noisy background, similar to the problem confronting medicine. I suspect that your signal acquisition and analysis tools outperform those available in medicine. So first, the target is detected.

Second, once a threat has been detected, it needs to be characterized and localized as precisely as possible. Again, signal processing and analysis, combination of data from disparate sources, advanced pattern recognition and quantitative prediction rules are used for this purpose. So, second, the target has been 'painted'.

Once a threat has been identified, characterized and localized, a rational intervention takes place. The type of intervention can vary enormously, but can certainly be guided by the same tools that detected, characterized and localized the threat. The effectiveness of the intervention is often confirmed by these same tools. So, third, a rational intervention has occurred.

Cutting across these 3 clinical categories is a fourth cardinal concept, namely that the underpinning of all of medical imaging's contributions is the optimum use of *data* (of all types). In fact, medical imaging has led the way in the recognition that medicine is entering an era in which all practitioners are in the data management business. A critical part of your report will be to identify priority areas for investments in deep learning and other bioinformatics efforts. As an editorial comment, I believe that it is critical that you specify that all data collection and analysis tools be based on uniform standards (e.g. DICOM or FHIR) and that relevant software be open source and freely available to all.

Here are simple examples of the way in which the collection, analysis, processing and mining of data from multiple sources contribute to the 3 clinical efforts:

Early Detection	Precision Diagnosis	Image-Guided Intervention
Sift through massive amounts of population data from imaging, genomics, pathology, behavioral factors and other sources to assess risk and predict disease	Digest and analyze an individual's data from all of these sources to precisely diagnosis that person's problem and chart the most effective course of treatment	Design, execute and monitor a treatment plan that maximizes benefits to the patient while minimizing pain, cost (days in hospital) and waste

Data from every activity in the 3 clinical categories provide the crucial inputs for the iterative processes that drive advances in imaging science and technology as well as our constant push to improve the quality, productivity and efficiency of medical imaging and healthcare in general. So harvesting, aggregating, mining and using data at every step of every process is vital to our collective future, and I hope this resonates with the vision for each of your agencies.

So even though I've chosen our security agencies in my case example, I would also argue that these same 3 clinical categories plus data management (I'll call it a 3 plus 1 classification system) help us start to frame an imaging research work plan that calls on the talent and technologies of each of your agencies.

Now focusing a bit more on how the 3 clinical categories open opportunities for collaboration among members of this Working Group that will help us meet our common strategic objectives, here are just a few more examples, not an exhaustive list:

Early Detection of Disease. This category cries out for the application of the science and skills that several of the agencies have developed to find the dimmest signal in a noisy universe. Just as your scientists can detect chiral molecules in interstellar space, or an ominous conversation among billions of mundane phone calls, (among many other examples), we need to tap into gigantic data sets to predict an individual's risk of developing disease and to intervene effectively to stop disease early when the outcomes are best and the costs are lowest. But first we need to build and validate the algorithms that will allow us to confidently predict and time individual risk. This may involve pooling data of disparate types (such as data from imaging, pathology, genomics, outcomes etc.) and from different sources (perhaps hundreds of health care systems), ensuring that the research database is properly anonymized to protect patient privacy, and then setting in motion the Deep Learning strategies that will help us make new discoveries in the treasure trove of data that is currently lying fallow in thousands of health system computers. It is easy to imagine the contributions that every one of your agencies could make toward this effort.

Precision Diagnosis. All of the data, signal and insights generated through Deep Learning would be immediately available to improve the health of individuals if we can create the tools and environment needed for an expert diagnostician to effectively tap into the data without being overwhelmed. We call this environment the "Diagnostic Cockpit" of the Future and you can think of the diagnostician of the future as a Pilot. This Pilot (who may need one or more Co-Pilots, at least until we adapt medical education sufficiently to embrace all of the required disciplines) will be called on to rapidly synthesize all of the data presented for an individual in order to precisely diagnosis a condition, discriminate among available treatments to select the most clinically effective for the particular patient, and work with the patient's care team to create a personalized care plan, and to execute and monitor that care plan.

Synthesis of multi-parametric data from imaging, pathology, genomics and other sources will be necessary. Using our current paradigms, this challenge would be beyond the abilities of any physician, as no one person can be expert in so many disciplines. But with your help, we will be able to apply computer power to help the human observe to perceive the subtle patterns in the data, connect the right dots, and work through the variables to make a confident, precise diagnosis. As with Early

Detection, I can envision roles for many of your agencies in the effort to make the Diagnostic Cockpit a reality.

Image-Guided Intervention. Many of the care plans developed under Precision Diagnosis will involve medicines and other therapies that do not require surgical or other invasive strategies. But in many cases, it will be important to retrieve tissue for pathology and genomic analysis, to remove or neutralize harmful tissue, or to address problems that are best treated with surgical or interventional techniques. In these cases, we need to continue to advance technologies that minimize the trauma of surgery or intervention and advanced image guidance will be a crucial part of these less invasive approaches. As you may know, image-guided, less invasive procedures typically allow much shorter recovery times, less time in the hospital, few complications and, therefore, lower costs to the health system. As our technologies become more advanced, such as through the use of intra-operative MRI and specialized biomarkers to confirm that the intervention has achieved its therapeutic goal, IGI will allow us to lower re-admission rates, repeat surgery rates and disease recurrence rates. This field is perfect for many of the technologies that your agencies have developed or sponsored, including robotics, spectroscopy, microscopy, precision guidance, advanced visualization and others.

As you can see, I've allowed my imagination to wander and paint a picture of the future that could be accelerated through a robust collaboration among the members of this Working Group. To make this a bit more concrete, I would like to suggest some specific goals that the Working Group consider as it drafts its white paper on medical imaging. Following directly on my prior comments, I propose that the Working Group white paper lay a foundation for three related initiatives:

1. Designing and creating a multi-disciplinary data repository capable of organizing data of all relevant types from many contributing sources, and initiating research efforts, such as those described as Deep Learning, to mine this repository as I have briefly described.
2. Designing and creating of an actual prototype Diagnostic Cockpit at the NIH Clinical Center in Bethesda where experts can begin the iterative process needed to allow human experts to use multi-source data. Building this prototype would be a strong proof of concept that this approach to precision diagnosis is feasible and effective.
3. Creating avenues to explore the application of the technologies developed by so many of your agencies to health and medical problems in early detection, precision diagnosis and image-guided interventions and therapies.

As a starting point for your consideration, I've taken the liberty of preparing a simple grid that illustrates some of the contributions that specific agencies could make to this effort. This grid, together with the presentations made to the task force by members of the medical imaging community and other relevant materials, have all been posted for your convenience on the website of the Academy of Radiology Research.

Relevance to other Federal Initiatives

Supports and can be a component of other initiatives, but is not subsumed nor supplanted by them.

Relevance to Cancer Moonshot
This approach to imaging covers just about every disease beyond cancer, including neurologic, cardiovascular, musculoskeletal, GI, GU, GYN

Relevance to Precision Medicine
More of an emphasis on imaging is needed than has been discussed up until now.

Thank you again for your time and I would welcome your questions.

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Potential Areas of Collaboration for Members of the Interagency Working Group on Medical Imaging

Comments of Steven E. Seltzer, M.D. to IWGMI June 29, 2016

	Early Detection	Precision Diagnosis	Image-Guided Intervention
NIH (NIBIB and NCI CIP)	Accelerate current and novel imaging science, imaging technologies, data research and new biomarkers to advance molecular and functional imaging. Collaborate with IWGMI agencies to tap into skills, technologies and programs.	Advance the development, testing and deployment of a Diagnostic Cockpit combining multi-parametric data from imaging, pathology, genomics, etc.	Advance current and novel IGI approaches and technologies
NIST	Promote standardized methods for data collection and analyze to set stage for Deep Learning	Promote standardized methods, tools and data across technologies, vendors, providers (supporting Diag. Cockpit)	Promote standardized methods, tools and data for IGI development, use and evaluation
NSF	Accelerate R&D in the physical sciences with links to imaging sciences and technologies	Help bridge advances in the physical sciences with imaging science to promote molecular and functional imaging	Support NIBIB and NCI with robotic and other technology programs/expertise
NASA	Apply remote sensing, data mining and advanced imaging processing/analysis tools to medical imaging	Suport the synthesis of data from imaging, genomics, pathology and other sources to inform Diagnostic Cockpit	Support NIBIB and NCI with robotic and other technology programs/expertise
DOD	Contribute tools to aid high fidelity data acquisition and processing/analysis tools to medical imaging	Suport the synthesis of data from imaging, genomics, pathology and other sources to inform Diagnostic Cockpit	Support NIBIB and NCI with robotic and other technology programs/expertise
DOE	Contribute to the development of biomarkers to facilitate disease detection	Advance biomarkers that will aid in precision diagnosis	Advance ablative technologies such as laser, heat, cryo, focused ultrasound and other energy related technologies
OSTP	Manage and coordinate interagency efforts, including project direction	Manage and coordinate interagency efforts, including project direction	Manage and coordinate interagency efforts, including project direction
FDA	Support and guide rapid regulatory pathways for novel imaging technologies and imaging biomarkers	Support and guide rapid regulatory pathways for Diagnostic Cockpit	Support and guide rapid regulatory pathways for novel IGI technologies
CMS	Contribute massive data to registries for Deep Learning	Facilitate planning for new, cost-effective care paradigms	Support Comparative Effectiveness Research (CER) and reimbursement for IGI