WORKSHOP REPORT

Evolving Role of Artificial Intelligence in Radiological Imaging

FEBRUARY 25 - 26, 2020

This Public Workshop Was Held
At NIH Main Campus, USA

Webcast link was available to participate online in this workshop.

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Artificial intelligence (AI), including machine learning technologies, has the potential to transform healthcare by deriving new and important insights from the vast amount of data generated during the delivery of health care every day. Radiological applications of AI-based technologies are numerous and expanding. These applications aim to automate and streamline tasks to improve efficiency, accuracy, and consistency. Early applications of AI in radiological imaging include computer aided-detection and diagnosis software (CADe and CADx). CADe and CADx software analyze radiological images to suggest clinically relevant findings and aid diagnostic decisions. Similarly, computer-aided triage (CADt) software analyzes images to prioritize the review of images for patients with potentially time-sensitive findings.

Large sets of widely available imaging data across imaging modalities have supported the development of AI-based algorithms for these devices. While historically the information provided by these algorithms has augmented the tasks performed by radiologists, software developments now can enable the devices to perform certain tasks autonomously. The potential for independent action by these devices to bypass human clinical review is an important factor in their benefit-risk profile, and it heightens expectations for the safety and effectiveness of these devices.

Another area of growth is the use of AI to provide prescriptive guidance for the operator to acquire optimal images. The image quality of ultrasound imaging can be greatly influenced by how the operator uses a handheld probe. Clinical AI applications may assist the acquisition of standardized images independent of the operator, guiding both sonographers and non-experts in sonography, potentially including lay, users, to acquire images with equivalent diagnostic quality. The addition of such clinical AI applications and the potential for new users of these devices, similarly affect the benefit-risk profiles for these devices and the expectations for the safety and effectiveness of these devices.

Through this workshop, the FDA is seeking to engage with stakeholders to explore the benefits and risks of these evolving applications of AI in radiology. As the benefit-risk profile changes, it is critical to adapt the methods used to evaluate and characterize their performance. In this workshop, the FDA is also seeking innovative and consistent ways to leverage existing methods and to develop new methods for validation of these AI-based algorithms and explore opportunities for stakeholder collaboration in these efforts.

This report provides an overview of the workshop, background information and Objectives, a summary of the presentations and conclusion.

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CONTENTS

EXECUTIVE SUMMARY

The Food and Drug Administration (FDA) was announcing a public workshop entitled "Evolving Role of Artificial Intelligence in Radiological Imaging." The intent of this public workshop was to discuss emerging applications of Artificial Intelligence (AI) in radiological imaging including AI devices intended to automate the diagnostic radiology workflow as well as guided image acquisition. The purpose of the workshop was to work with interested stakeholders to identify the benefits and risks associated with the use of AI in radiological imaging. They provided best practices for the validation of AI-automated radiological imaging software and image acquisition devices. Validation of device performance with respect to the intended use is critical to assess safety and effectiveness.

Discussion focused on fully autonomous AI systems and AI-guided image acquisition which offer many benefits and could:

- Change or challenge the standard of care.
- Introduce new questions of safety and effectiveness into an established radiological imaging workflow.
- New intended use including user and/or environment.
- Allows the agency to engage the public early to promote consistency and fairness.
- Develop approaches that ensure scientific integrity and data quality while allowing flexibility for algorithm change/ development.

Agenda for Day 1 and Day 2

- How and why do you bring an entire community including patients, healthcare providers, regulators, manufacturers, and advisors along in the decision-making process for novel, high-risk?

WORKSHOP OBJECTIVES

The primary objectives of the workshop were to bring Autonomous AI and AI-guided imaging with the radiological imaging together.

- **Day 1**: Software in which AI or ML is being used to automate some portion of the radiological imaging workflow.
- **Day 2**: Software used in conjunction with imaging hardware such that AI or ML driven real time feedback guides a non-expert user to acquire their own images to aid in or provide diagnostic or treatment decisions including in special environments.

WORKSHOP SUMMARY

TUESDAY 25 FEBRUARY

Tailoring FDA's Regulatory Framework to Encourage Responsible Innovation in AI/ML:

- The promise of AI/ML in healthcare, Resulting challenges and opportunities
    - Data responsibility.
    - Learning bias data.
    - Augmenting healthcare data.
- Objectives for a tailored regulatory approach for emerging technology
    - Reasonable assurance of safety and effectiveness(RASE)
    - Improved time for patients to access high-quality software medical devices first in the world
    - Improved submission experience (Clarity, Predictability, Efficiency of review process)
    - Least burdensome.
- Five excellence principles proposed
    - Patient Safety
    - Product Quality
    - Clinical Responsibility
    - Proactive Culture
- A pathway towards practical regulation that promotes responsible innovation.
    - Allow for frequent iterations in alignment with the way AI work naturally.
    - Ensure that the performance of products improves over time while avoiding their degradation.
    - Advance the standard of care or create an environment with a better standard of care.

Artificial Intelligence in Radiology: Where Does It Stand and Where Is It Going?

- Opportunities
  - Integration of lab results, omics, medical record.
  - Routine automated quantitation.
  - Triage and critical result monitoring.
  - Prognosis prediction.
  - Global health.
  - Opportunistic screening (Detect things inside of images).
- Applications
  - Detection (Lung nodules, TB, Breast masses).
  - Segmentation (Organ and lesion volumetric).
  - Quantification and measurement (RECIST).
  - Workflow optimization (CXR and ICH triage).
  - Image reconstruction (Accelerated MRI).
  - NLP of reports.
  - Colitis detection.
  - Domain adaptation with adversarial network for Chest X-Ray.

New Challenges in Regulating Artificial Intelligence in Radiological Imaging

- General and Special Controls
  - General control applies to all medical devices (Registration, Listing).
  - Special control applies when general control is not sufficient (Performance testing, Labeling).
  - Special control provides consistency and transparency on expectations for validation of safety or effectiveness in future 510(k)s.

- Regulation of Radiological AI
  - Relied on experience and scientific knowledge to define special controls for risk mitigation.
  - Established the 510(k) regulatory pathway for more radiological AI device types through De Novos and reclassification.
- Challenging questions
  - What are approaches to establish an acceptable device performance?
  - What other risks are introduced for the radiological imaging workflow, patients, and healthcare providers?
  - What additional experience or knowledge do we need to develop sufficient risk mitigations?
  - Should real-world performance monitoring and QC be expected as AI becomes more autonomous?

Session 1: Emerging Trends in Radiological AI Software - Exploring Benefits and Risks

Advances in AI technology are leading to an expanding role for AI throughout the diagnostic clinical workflow. This session aim to identify scientific, clinical, and regulatory challenges for radiological AI software that is intended for increased automation of triage, detection, or diagnosis of disease based on the review of medical images

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Clinical Insights on Autonomous AI Implementation: A Radiologist's Perspective

- Autonomous AI image interpretation
- Risks
  - Performance of models in virtual setting does not translate to real world clinical practice.
  - Cancers are missed by AI model that would have been diagnosed by human reader.
  - Excellent AI tools developed in a specific population for a specific use are used inappropriately in “wrong use” cases.

Artificial Intelligence in Breast Cancer Screening: Regulatory and Clinical Considerations

- Technical considerations and challenges
  - Generalizability of Data and access to the data to train the algorithm.
  - Transparency (How to explain the output of algorithm)
  - Validation of model(Performance requirement and standardized testing)
  - Workflow and integration
  - Changes in clinical reporting

- Clinical considerations and challenges

  - Performance.
  - Reimbursement.
  - Enhancing Quality using the inspection program(EQUIP)
  - Workflow and integration
  - Peer Review
  - Patient acceptance
  - Medical legal aspects

- Regulatory considerations and challenges

  - Risk benefit analysis
  - Regulatory pathway (Classification/Clinical Study/Modification).
  - Standards medical devices with respect to AI
  - Global Regulatory on AI
  - Mammography quality standards Act

Diagnostic rule-out: A path to confidence and efficacy for time-sensitive, life-threatening indications

- Potential Benefits
  - Increased Speed and diagnostic accuracy.
  - Expert level performance.
  - Increased clinical confidence
  - Optimized treatment.
- Diagnostic rule-out
  - Low-prevalence
  - High-Risk
  - Significant error rates
  - False Positive are risky

Session 2: Evaluation of AI Software for Radiological Applications

Stakeholders across the medical imaging community are working to develop effective methods for the validation of radiological AI software. This session will feature a discussion of ongoing efforts to develop methods and standards for the validation of these medical devices and different roles stakeholders can play.

Pre- and Post-Market Evaluation of Autonomous AI/ML: Lessons Learned from Prior CAD Devices

- Newest CAD devices
  - CADa/o : Computer aided acquisition and optimization
  - …
- CAD assessment framework
  - Clinical, Standalone, …
  - Verification and validation
  - labeling
  - …

Proposed Regulatory Framework for Modifications to Artificial Intelligence/ Machine Learning (AI/ML)- Based Software as a Medical Device (SaMD)

- Fundamentally transform the delivery of healthcare
  - Earlier disease detection
  - More accurate diagnosis
  - New insights into human physiology
  - Personalized diagnostics and therapeutics

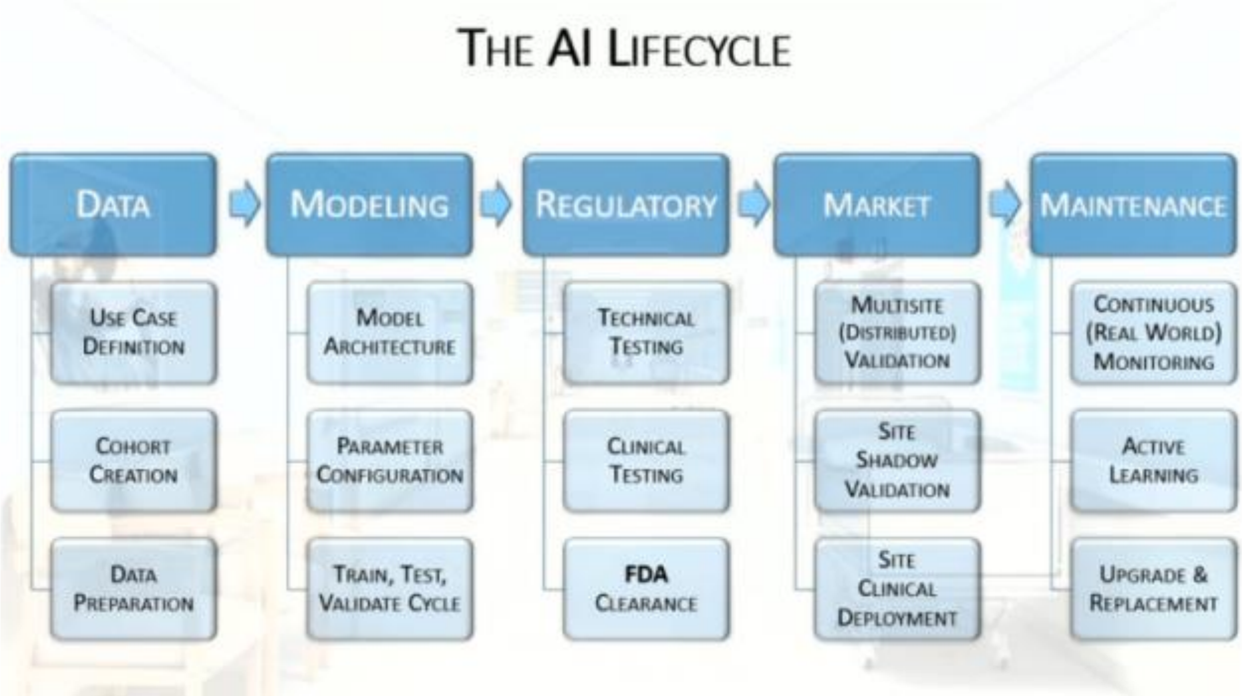
Evolving Paradigms of Radiology AI Software - Current and Future Trends

- Current trends
  - Triage and workflow(Worklist prioritization)
  - Quantification (Segmentation)
  - Image preprocessing (Deep learning MR reconstruction, Low dose imaging, Super-resolution)
- Future trends(Multisite training)
  - Data sharing bottlenecks(Cultural barriers, Technical challenges, Anonymization)

  Solutions
  - Continuous fine-tuning
  - Federated machine learning
  - Distributed deep learning

The Evaluation and Monitoring of AI Algorithms Pre and Post FDA Clearance

- The AI life cycle summary
  - Successful AI algorithms require many phase of validation and monitoring
  - Unlike other approved devices, AI algorithms' input data changes constantly
  - Methods for clearance and labeling are inconsistent and unclear to the public
- Rule-out algorithm
  - Require an extremely high negative predictive value
  - Tests for safety and effectiveness should be different than other CAD
  - Prevalence of radiologic findings for many diseases are often very low
  - Should continuously monitor for false negatives in the released product



Post-Market Surveillance Methods for AI in Radiology

- Problem
  Safety and efficacy of AI software in radiology cannot be ensured exclusively through pre-market testing
- Solution
  Post-market surveillance designed to empower intended users to determine whether AI medical devices actually work for them

WEDNESDAY 26 FEBRUARY

Opportunities and Challenges in AI-Enabled Healthcare:

- Advantages of ultrasound imaging
  - No ionizing radiation.
  - Low cost and widely accessible.
  - Real time imaging and real time feedback.
- Challenges linked with ultrasound image acquisition
  - Image quality
  - Variability across different manufacture
  - Many presets which would be very confusing for the new users.
  - Noise and artifacts during acquisition

Clinical AI applications may assist the acquisition of standardized images independent of the operator, guiding both sonographers and non-experts in sonography, potentially including lay users, to acquire images with equivalent diagnostic quality.

- Challenges with AI-guided image acquisition.
  - Device Error: Failure to provide guidance on acquiring diagnostic-quality images or signal.
  - User Error: Operator failure to follow the guidance provided by the device to acquire diagnostic-quality images or signals.

No-Human-in-the-Loop AI-enabled Healthcare: Risk, Rewards, and Regulation

- No-Human-in-the-Loop AI:
  - A human cannot practically be involved in the decision making(Image reconstruction).
  - No-Human-in-the-Loop AI will be ubiquitous.
  - The risk profile of No-Human-in-the-Loop AI is fundamentally different to conventionally engineered systems.
  - Post-market surveillance will be a key element of successful regulation.

- Application (Shear Wave Elastography assist)
  - Selection of appropriate imagery.
  - Discarding SWE images of poor quality.
  - Performing computational diagnostics using algorithms.
- Application (Hepatorenal index)
  - Automatically detecting liver and kidney.
  - Selecting appropriate regions of interest.
  - Comparing the echogenicity of the two organs.
- Intervention (Cath-AI)
  - Enhance image interpretation.
  - Provide procedure guidance.
  - Reduce need for specialized training.

Implications and Opportunities for AI Implementation in Diagnostic Medical Imaging

- Medical Imaging
  - Anatomical(functional).
  - Image-guided (Information guided information)
- Application (Refining Tissue Characteristics)
  - With Quantitative ultrasound (QUS) statistical information can be seen as a new source of tissue contrast, increases specificity and possibility of system and operator independence.
- Application (Reconstruction of 7T-like images from 3T MRI)
  - Improve anatomical details and tissue contrast.

Session 1: Innovation in AI-Guided Image Acquisition

Artificial intelligence may be applied in imaging to provide guidance for the operator to acquire optimal images and signals. The clinical applications include assisting sonography experts for standardization of image quality, helping non-experts in sonography for acquiring images with quality equivalent to those obtained by expert, and guiding novices, such as home users, for collecting images of diagnostic quality and value. This session aims to identify scientific, clinical, and regulatory challenges for AI-Guided Image/Signal Acquisition systems.

Development and Validation of a Breakthrough AI-Guided Echocardiography System

- Medical imaging is the gateway to detection and diagnosis.
- Ultrasound is effective with many advantages.
  - Images most organ.
  - Low risk.
  - Images in real-time.
  - Small and low-cost devices.
- Ultrasound is hard to use
  - Unnatural hand-eye coordination.
  - Unintuitive images.
  - Everyone has different shapes of art.
- AI-ultrasound navigation system
  - Recognize all ultrasound imaging.
  - Providing the guidance.
  - Capturing expertise of ultrasound's experts.
- Application (AI-based heart ultrasound guidance)
  - Predicts the deviation of the current transducer positioning from the ideal positioning in real time.
  - Provides the user instructions to efficiently minimize the deviation.

Deep Learning-enabled Ultrasound Imaging – Opportunities, Risks, and Challenges

- Benefits of using Deep learning in Ultrasound Imaging

  Engineering
  - Offer higher flexibility in development.
  - More computationally efficient and robust.
  - Replicate complex algorithm calculations in much shorter time.
  - Minimal to none handcrafted feature extraction.

  Clinical
  - Faster and easier image acquisition without sacrificing image quality.
  - Emulate complex and expensive hardware with simpler and cheaper hardware.
  - More streamlined workflow.
  - More sophisticated applications.

- Technological Challenges
    - Data quality and governance.
    - Image quality evaluation.
    - Bias detection and correction.

Can machine learning tools bring diagnostic imaging to the home with safety and efficacy?

- Time Matters (2/3 of diagnostic Dilemma can be solved with simple imaging).
- Safety and efficacy threshold for imaging in the home
    - Consumer level interface.
    - Exam is easy to perform.
    - Reproducible results.
    - Accuracy that matches professional.
    - Guidelines for Physician Notification.
- Value proposition of machine learning
    - Image interpretation.
    - Image Guidance.

AI-guided ultrasound image acquisition; GE perspective

- Goals of AI in medical imaging
    - Improve outcomes (Effectiveness).
    - Efficiency.
    - Patient experience.
    - Clinician experience.
- AI-assisted guidance in medical imaging
    - Real-time CAD to highlight potential pathology while scanning.
    - Real-time anatomical identification and segmentation.
    - Guide probe movement by recognizing anatomy relative to the targeted view.
- Application (Volume acquisition supporting AI-based view selection)

    User performs a fetal head volume scan,

    Tool Automatically,
    - Extract 3 standard planes.
    - Performs 5 automatic measurements (BPD, HC, CM, CB, VP).

What's Real About Artificial Intelligence: A Clinician's Perspective

- Real AI needs,
    - Precise acquisition is imperative.
    - Clinical relevance and context.
    - Marked biological variability (Data augmentation).
    - Awareness of biases (Unconscious, generalizability…).
    - Access for everyone.

Artificial Intelligence (AI) and the Art of Sonography

- Current problem with AI application (Sonographer view)
  - Variety of images.
  - Inaccurate measurements.
- AI needs to help with acquisition of input images, not just analysis (Sonographer view).
  - The acquisition of an image (Classification, Segmentation, Optimization/Detection).
- AI is needed in sonography.
- Not just for analysis of images but for optimal acquisition.
- Acquisition requires assessment of image quality throughout.
- Mimicking sonography imaging methods may provide a roadmap for AI acquisition.

Session 2: Regulation of Imaging Devices Containing AI Software

This session features a discussion of regulatory evaluation of AI-Guided Image Acquisition systems. Ongoing efforts to develop methods and standards for the verification and validation of AI-Guided Image Acquisition systems was discussed. Some emphasis was placed on use of these devices by non-expert clinicians and patients as well as use of image acquisition systems in extreme environments.

Regulatory Considerations for AI-Guided Image Acquisition and Optimization

- Benefits of AI-guided image acquisition
  - Improved access to clinical care: location and time.
  - Improved performance.
  - Patient convenience: location and time.
- Risks of AI-guided image acquisition
  - Low image and signal quality.
  - Delayed clinical care.
  - Clinical care gap.

Achieving the Quadruple Aim with AI-Guided Ultrasound Systems in Clinical Settings Using the Current Ultrasound Premarket Guidance - Benefits and Challenges

- How will AI impact imaging Modalities?
  - Non-ionizing radiation.
  - Real-time image capture and display.
  - Safety through image guidance.
  - Eliminating risks associate with invasive procedures.
- Conventional algorithms are currently used in Ultrasound machines
  - The pathway for regulatory clearance is no different.
  - The submission elements are consistent.

- Key Takeaways
  - Existing marketing authorization pathways for medical devices and manufacturers are clear, effective and predictable while continuing to ensure safety and effectiveness.
  - The medical imaging industry has already started to develop standards for AI technologies to support public health.
  - Development of consensus standards, (such as DICOM, ISO, IEC…) through private-public partnerships has already proven effective.
  - Continued development and access to AI algorithms by clinicians will provide them with devices needed to achieve the Quadruple AIM.

Validation of AI Algorithms in Guided Imaging Applications

- Performance Testing

  Non-Clinical (Characterize the technical performance of the AI system for guided image Acquisition)
  - Interaction between the AI system and the user in the intended manner is not necessary.
  - Can be component-by-component (AI system maybe such that there are multiple components stack together- One component estimates the image quality and the other component inform user how to move the probe to obtain better quality images)

  Clinical (Evaluate diagnostic utility of the device when representative users use the device on a representative patient population)
  - Truly testing in clinic.
  - Accepted virtual or physical systems designed to capture clinical variability.
  - Comparison to closely related device with established clinical performance.

Human Factors and Usability Engineering for AI-guided Acquisitions

- Human Factors use knowledge of human abilities and limitation to design systems.
- Many concerns over AI applications seems to be human factors related.
  - The user interface should make sense to the user.
  - Understanding the user need and leveraging the design guidelines.
  - Repeating the human factors validation study will not save a flawed design.
  - The goal is to ensure that the device user interface has been optimized to support safe and effective use.

Practical AI Experience from Imaging Industry

- AI can Raise the standard of care.
- AI can improve components of the quadruple aim.
  - Reduced setup time.
  - Reduced variation.
  - Improved follow-up.
  - Faster.
  - More consistent.
- Adoptive Algorithm: Software independently learns, and changes based on reward mechanism.

- Challenges with Adaptative algorithms.
  - Repeatability and reliability (Same patient will measure done same day by the same machine at two different slightly location gets how many different diagnosis).
  - Validation, Maintainability, Traceability challenges.
  - Unintended consequences (Direction, Bias …).

Key Messages

- Most adaptive algorithms should be managed as discrete adaptive.
- Non-expert users create additional risks that must be managed.
- Existing regulatory framework should be updated inline with recent proposals.

Conclusions

In this workshop, the medical practitioners pinpointed a number of reasonable concerns, about standardize and improve measurements and image acquisition and diagnosis that results from those. One of the important things we heard in this workshop was the potential benefits of experts' accessibility to patients in the home.

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