Introduction To AI Validation And Post-Market Monitoring

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Chief Medical Officer
ACR Data Science Institute
June 23, 2020

Advancing data science as core to clinically relevant, safe and effective radiologic care

No Commercial Conflicts Of Interest

Neither I, my immediate family nor the ACR DSI team have a financial relationship with a commercial organization that may have a direct or indirect interest in the ACR's role in data science

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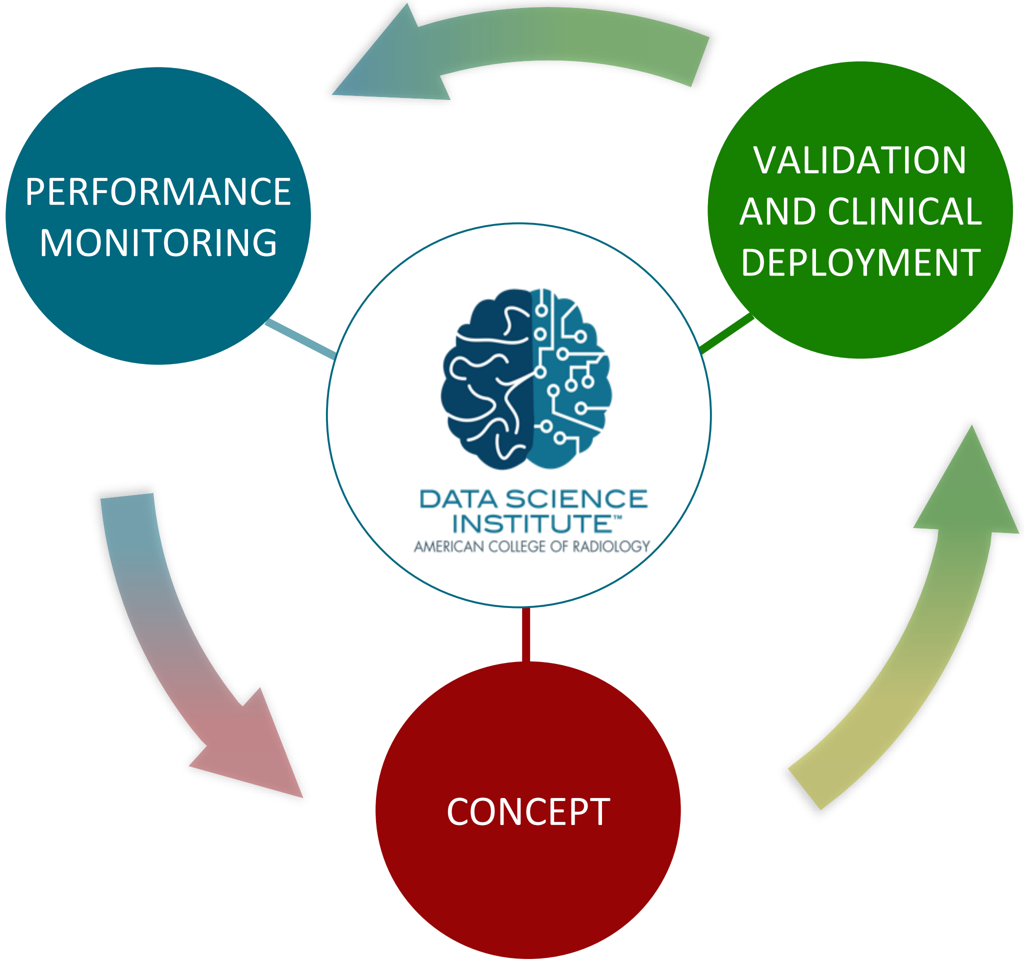
AI Effectiveness and Patient Safety Depend On Validation And Performance Monitoring

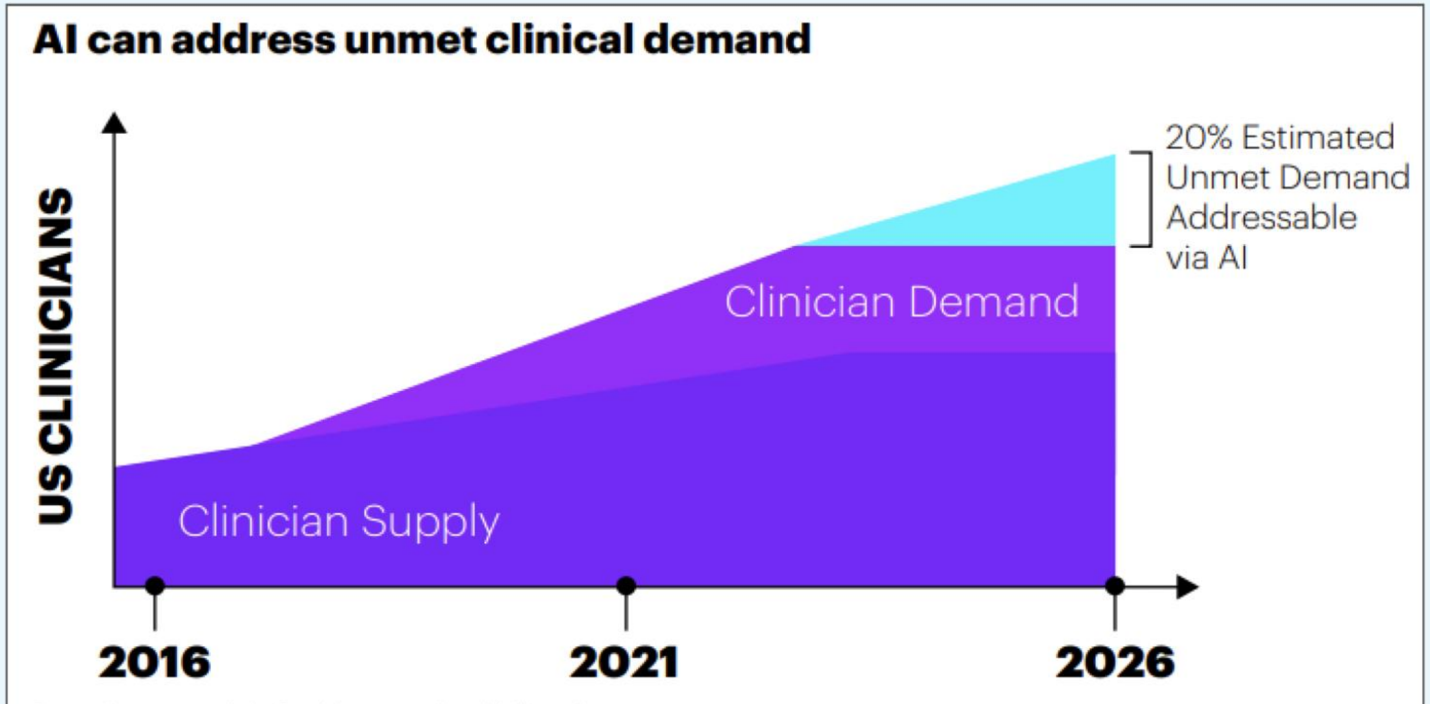
How Do We Make Sure AI Is Working In The Real World?



How Do We Validate AI Algorithms For Clinical Practice?

What Are The Most Important Clinical Tasks For AI?

The Promise of AI/ML in Healthcare



Source: Accenture analysis. Graph is not to scale and is illustrative.

Top 10 AI Applications

APPLICATION	VALUE*
Robot-Assisted Surgery**	$40B
Virtual Nursing Assistants	$20B
Administrative Workflow Assistance	$18B
Fraud Detection	$17B
Dosage Error Reduction	$16B
Connected Machines	$14B
Clinical Trial Participant Identifier	$13B
Preliminary Diagnosis	$5B
Automated Image Diagnosis	$3B
Cybersecurity	$2B
TOTAL	= ~$150B

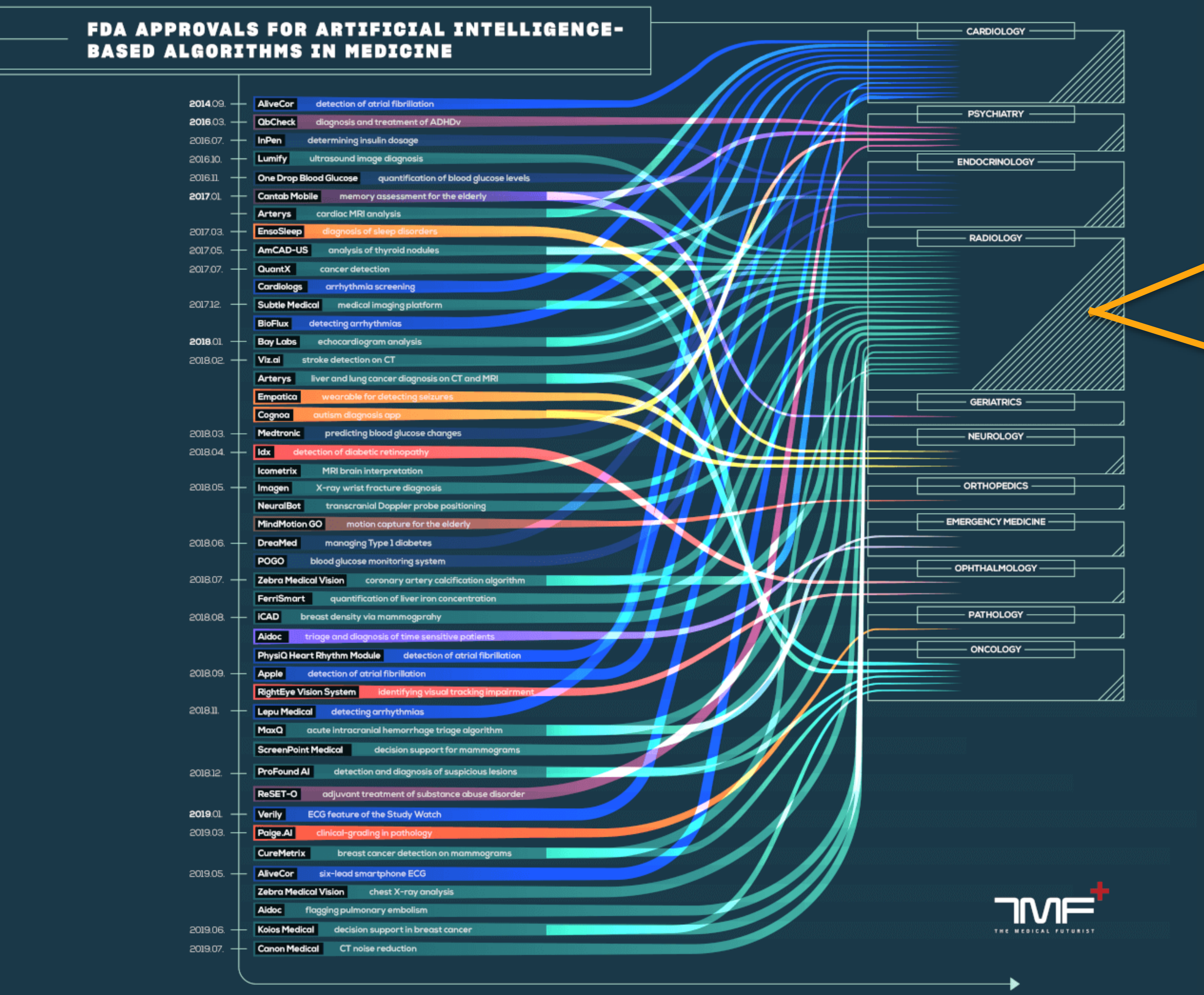
Source: Accenture analysis

* "Value" is the estimated potential annual benefits for each application by 2026.
** Orthopedic surgery specific

www.fda.gov/digitalhealth

Source: Bakul Patel, Director Digital Health, CDRH/FDA

FDA AI Market Assessment

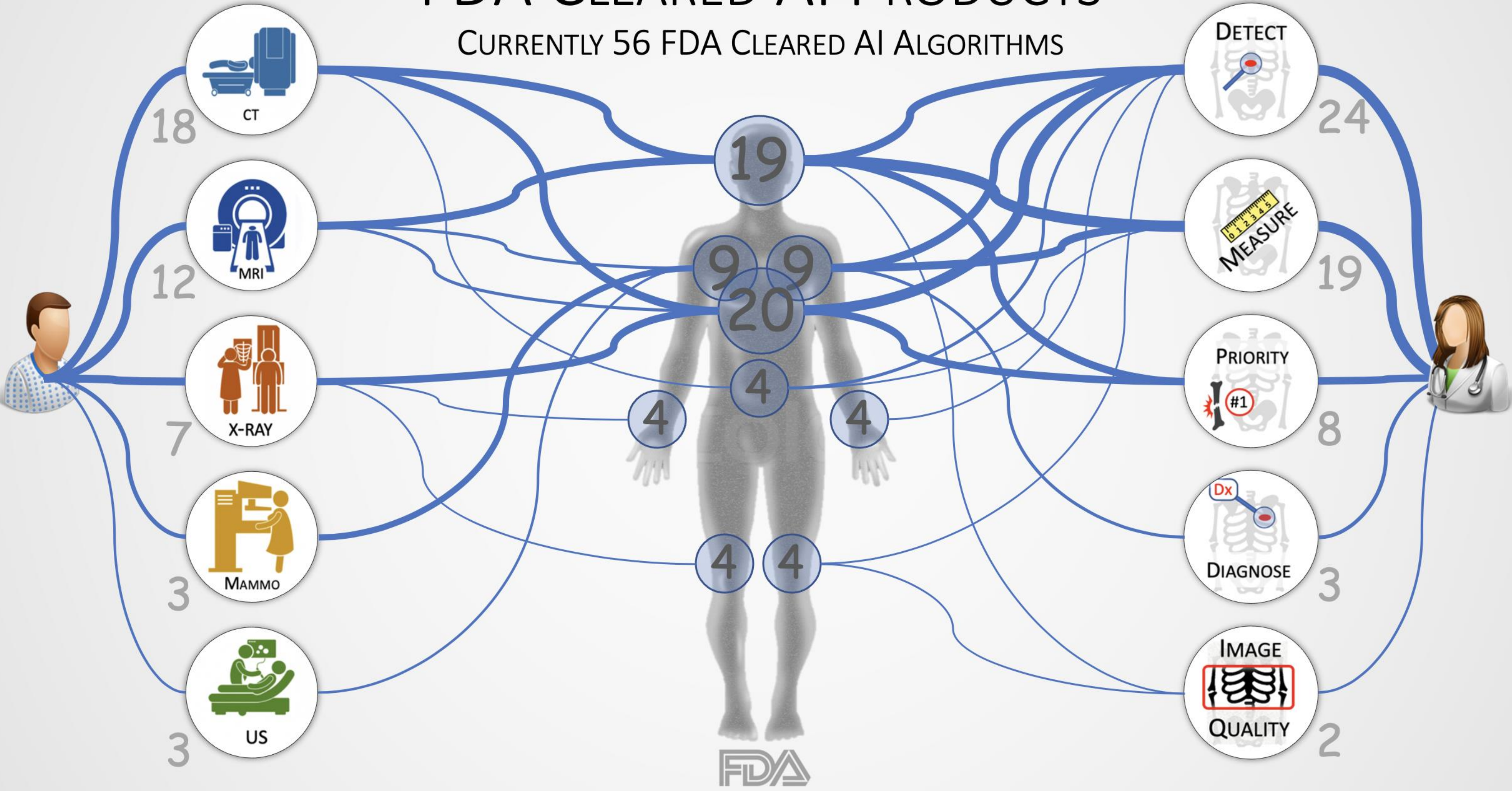


Radiology has the majority of FDA cleared healthcare AI

https://cdn.medicalfuturist.com/wp-content/uploads/2019/06/The-Medical-Futurist-FDA-approved-AI-algorithms-in-medicine-2019-09.png

FDA Cleared AI Products

Currently 56 FDA Cleared AI Algorithms



Five Excellence Principles Proposed

FDA

Patient Safety	Demonstration of a commitment to providing a **safe patient experience**, and to emphasizing patient safety as a critical factor in all decision-making processes.
Product Quality	Demonstration of a commitment to the development, testing, and maintenance necessary to deliver SaMD products at the **highest level of quality**.
Clinical Responsibility	Demonstration of a commitment to responsibly **conduct clinical evaluation and to ensure that patient-centric issues** including labeling and human factors are appropriately addressed.
Cybersecurity Responsibility	Demonstration of a **commitment to protect cybersecurity**, and to proactively address cybersecurity issues through active engagement with stakeholders and peers.
Proactive Culture	Demonstration of a commitment to a **proactive approach** to surveillance, assessment of user needs, and continuous learning.

www.fda.gov/digitalhealth

Source: Bakul Patel, Director Digital Health, CDRH/FDA

Research Needs to Advance AI in Clinical Practice

Radiology

ORIGINAL RESEARCH • SPECIAL REPORT

A Roadmap for Foundational Research on Artificial Intelligence in Medical Imaging: From the 2018 NIH/RSNA/ACR/The Academy Workshop

Curtis P. Langlotz, MD, PhD • Bibb Allen, MD • Bradley J. Erickson, MD, PhD • Jayashree Kalpathy-Cramer, PhD • Keith Bigelow, BA • Tessa S. Cook, MD, PhD • Adam E. Flanders, MD • Matthew P. Lungren, MD, MPH • David S. Mendelson, MD • Jeffrey D. Rudie, MD, PhD • Ge Wang, PhD • Krishna Kandarpa, MD, PhD

From the Department of Radiology, Stanford University, Stanford, CA 94305 (C.P.L., M.P.L.); Department of Radiology, Grandview Medical Center, Birmingham, Ala (B.A.); Department of Radiology, Mayo Clinic, Rochester, Minn (B.J.E.); Department of Radiology, Massachusetts General Hospital, Harvard Medical School, Boston, Mass (J.K.C.); GE Healthcare, Chicago, Ill (K.B.); Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, Pa (T.S.C., J.D.R.); Department of Radiology, Thomas Jefferson University Hospital, Philadelphia, Pa (A.E.F.); Department of Radiology, Icahn School of Medicine at Mount Sinai, New York, NY (D.S.M.); Biomedical Imaging Center, Rensselaer Polytechnic Institute, Troy, NY (G.W.); and National Institute of Biomedical Imaging and Bioengineering, National Institutes of Health, Washington, DC (K.K.). Received March 17, 2019; revision requested March 19; revision received March 24; accepted March 25. **Address correspondence to** C.P.L. (e-mail: *langlotz@stanford.edu*).

Conflicts of interest are listed at the end of this article.

Radiology 2019; 291:781–791 • https://doi.org/10.1148/radiol.2019190613 • Content code: IN

Imaging research laboratories are rapidly creating machine learning systems that achieve expert human performance using open-source methods and tools. These artificial intelligence systems are being developed to improve medical image reconstruction, noise reduction, quality assurance, triage, segmentation, computer-aided detection, computer-aided classification, and radiogenomics. In August 2018, a meeting was held in Bethesda, Maryland, at the National Institutes of Health to discuss the current state of the art and knowledge gaps and to develop a roadmap for future research initiatives. Key research priorities include: 1, new image reconstruction methods that efficiently produce images suitable for human interpretation from source data; 2, automated image labeling and annotation methods, including information extraction from the imaging report, electronic phenotyping, and prospective structured image reporting; 3, new machine learning methods for clinical imaging data, such as tailored, pretrained model architectures, and federated machine learning methods; 4, machine learning methods that can explain the advice they provide to human users (so-called explainable artificial intelligence); and 5, validated methods for image de-identification and data sharing to facilitate wide availability of clinical imaging data sets. This research roadmap is intended to identify and prioritize these needs for academic research laboratories, funding agencies, professional societies, and industry.

JACR Journal of the American College of Radiology

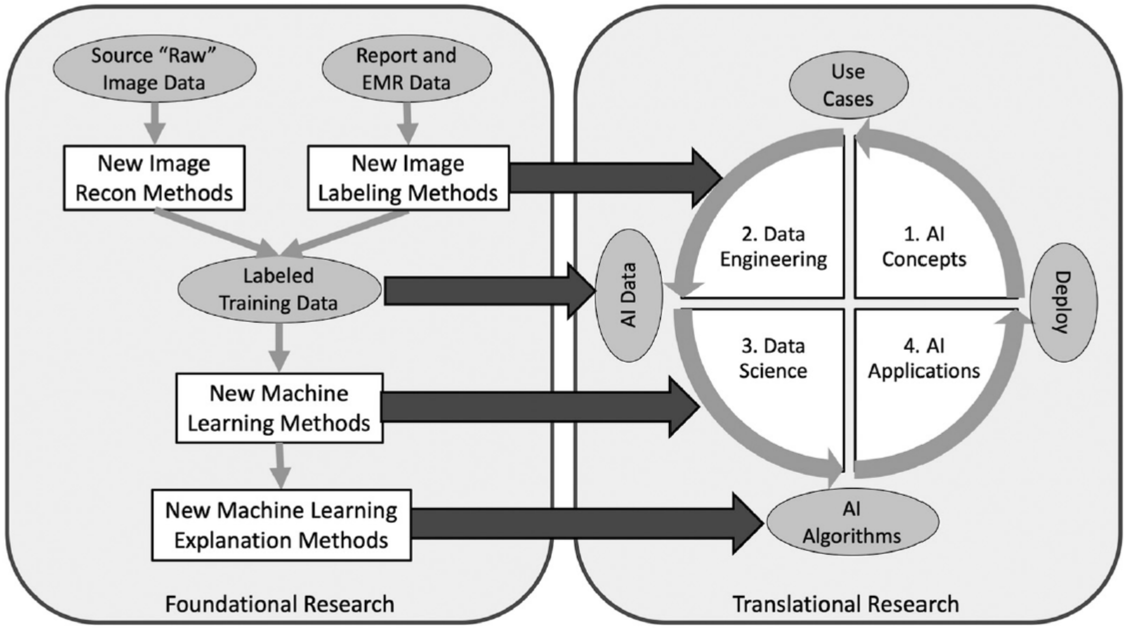
Health Services Research & Policy ▪ Clinical Practice Management ▪ Data Science ▪ Training & Education ▪ Leadership

A Road Map for Translational Research on Artificial Intelligence in Medical Imaging: From the 2018 National Institutes of Health/RSNA/ACR/The Academy Workshop

Bibb Allen Jr, MD[a], Steven E. Seltzer, MD[b,c], Curtis P. Langlotz, MD, PhD[d], Keith P. Dreyer, DO, PhD[e], Ronald M. Summers, MD, PhD[f], Nicholas Petrick, PhD[g], Danica Marinac-Dabic, MD, PhD, MMSC[h], Marisa Cruz, MD[i], Tarik K. Alkasab, MD, PhD[e], Robert J. Hanisch, PhD[j], Wendy J. Nilsen, PhD[k], Judy Burleson, BSW, MHSA[l], Kevin Lyman, BS[m], Krishna Kandarpa, MD, PhD[n]

Abstract

Advances in machine learning in medical imaging are occurring at a rapid pace in research laboratories both at academic institutions and in industry. Important artificial intelligence (AI) tools for diagnostic imaging include algorithms for disease detection and classification, image optimization, radiation reduction, and workflow enhancement. Although advances in foundational research are occurring rapidly, translation to routine clinical practice has been slower. In August 2018, the National Institutes of Health assembled multiple relevant stakeholders at a public meeting to discuss the current state of knowledge, infrastructure gaps, and challenges to wider implementation. The conclusions of that meeting are summarized in two publications that identify and prioritize initiatives to accelerate foundational and



AI DEVELOPMENT IN MEDICAL IMAGING

Fig 1. As in other industries, AI development in medical imaging includes both foundational and translational research activities. The foundational portion of the National Institutes of Health Workshop considered research priorities to accelerate and improve the development of AI algorithms for medical imaging [8]. The translational portion of the workshop considered medical imaging use cases for algorithm development and how these applications will be validated, deployed, and monitored in routine clinical practice. The diagram shows how foundational and translational research activities are connected. Foundational research leads to new image reconstruction and labeling methods, new machine learning algorithms, and new explanation methods, each of which enhance the data sets, data engineering, and data science that lead to the successful deployment of AI applications in medical imaging. AI = artificial intelligence; EMR = electronic medical record; Recon = reconstruction. The figure was developed by the authors for publication in both *Radiology* and *JACR*. This figure also published in reference 8.

Radiology AI Ecosystem

- Structured use cases
- Data access
- Patient safety
- Clinical integration

FDA Discussion Paper on Continuously Learning Algorithms and the FDA Software Precertification Program

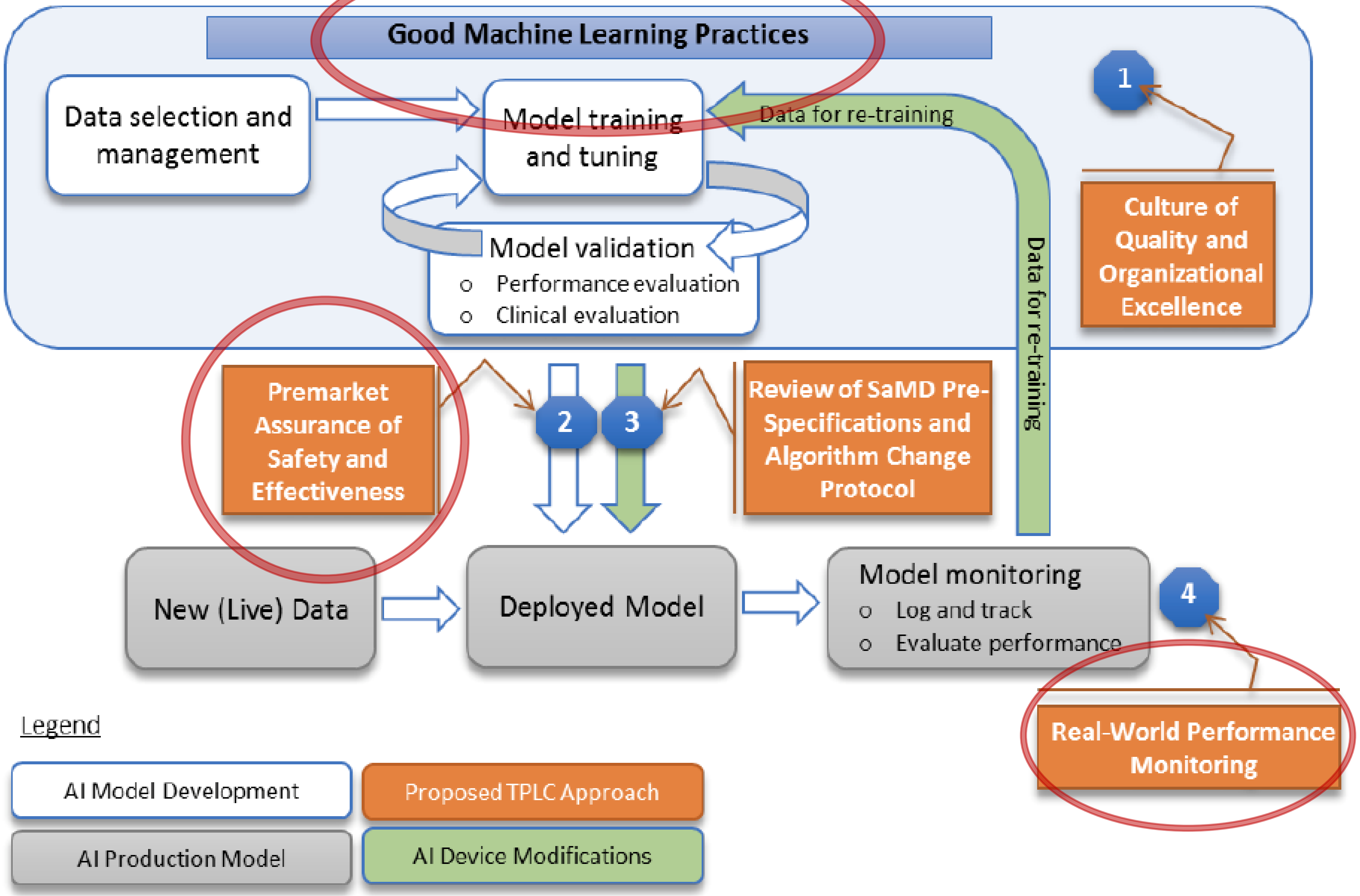


Figure 2: Overlay of FDA's TPLC approach on AI/ML workflow

"Good Machine Learning Practices"

Structured AI Use Cases

- Standardized inputs and outputs
- Common data elements
- Defined pathways for clinical integration

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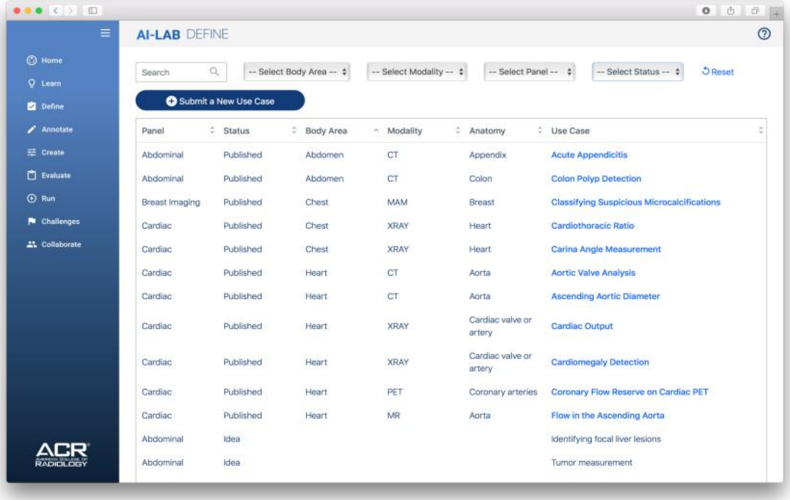
Define-AI



Panel	Status	Body Area	Modality	Anatomy	Use Case
Abdominal	Published	Abdomen	CT	Appendix	Acute Appendicitis
Abdominal	Published	Abdomen	CT	Colon	Colon Polyp Detection
Breast Imaging	Published	Chest	MAM	Breast	Classifying Suspicious Microcalcifications
Cardiac	Published	Chest	XRAY	Heart	Cardiothoracic Ratio
Cardiac	Published	Chest	XRAY	Heart	Carina Angle Measurement
Cardiac	Published	Heart	CT	Aorta	Aortic Valve Analysis
Cardiac	Published	Heart	CT	Aorta	Ascending Aortic Diameter
Cardiac	Published	Heart	XRAY	Cardiac valve or artery	Cardiac Output
Cardiac	Published	Heart	XRAY	Cardiac valve or artery	Cardiomegaly Detection
Cardiac	Published	Heart	PET	Coronary arteries	Coronary Flow Reserve on Cardiac PET
Cardiac	Published	Heart	MR	Aorta	Flow in the Ascending Aorta
Abdominal	Idea				Identifying focal liver lesions
Abdominal	Idea				Tumor measurement

"Premarket Assurance of Safety and Effectiveness"

Algorithm Validation

- Diverse validation data sets
  - Multiple institutions
  - Diverse patient demographics
  - Diverse imaging equipment
- Built according to the use case
- Reasonable costs for developers as compared to reader studies
- Access to diverse data for validation

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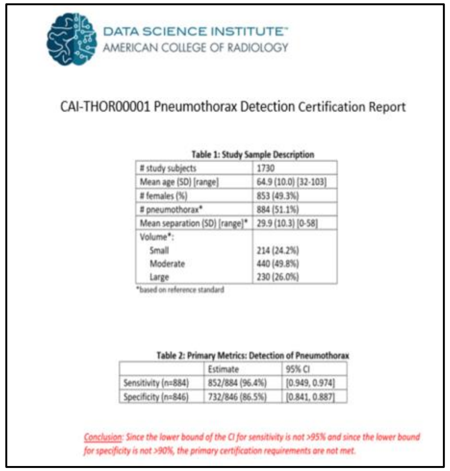
Certify-AI



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CAI-THOR00001 Pneumothorax Detection Certification Report

Table 1: Study Sample Description

# study subjects	1730
Mean age (SD) [range]	64.9 (10.0) [32-103]
# females (%)	853 (49.3%)
# pneumothorax*	884 (51.1%)
Mean separation (SD) [range]*	29.9 (10.3) [0-58]
Volume*:	
Small	214 (24.2%)
Moderate	440 (49.8%)
Large	230 (26.0%)

*based on reference standard

Table 2: Primary Metrics: Detection of Pneumothorax

	Estimate	95% CI
Sensitivity (n=884)	852/884 (96.4%)	[0.949, 0.974]
Specificity (n=846)	732/846 (86.5%)	[0.841, 0.887]

Conclusion: Since the lower bound of the CI for sensitivity is not >95% and since the lower bound for specificity is not >90%, the primary certification requirements are not met.

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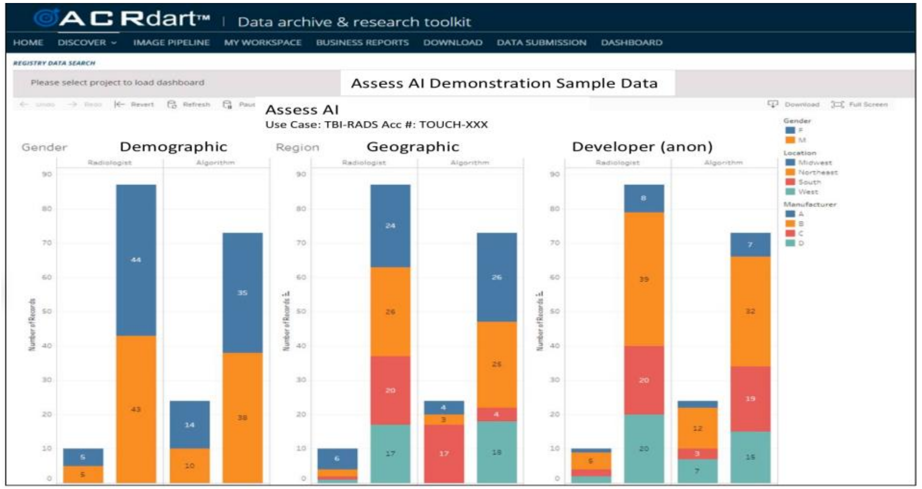
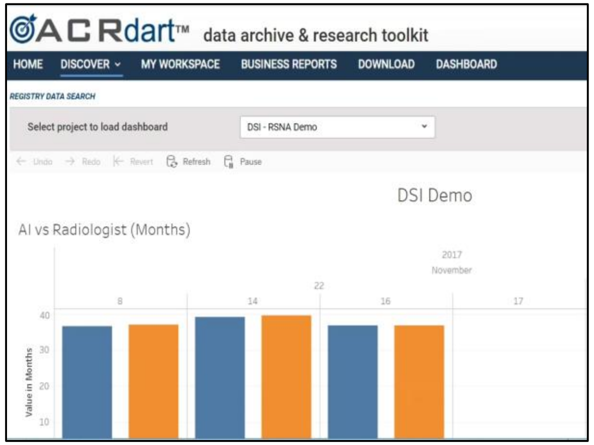
Assess-AI

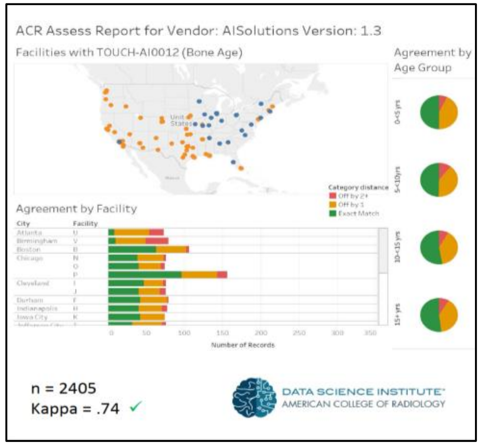
"Real World Performance Monitoring"

Algorithm Monitoring In Clinical Practice

- AI registries
- Capture algorithm performance from practicing radiologists
- Capture meta-data about the examination
- Feedback to developers / FDA
- Working with FDA to capture data







FDA Discussion Paper on Continuously Learning Algorithms and the FDA Software Precertification Program

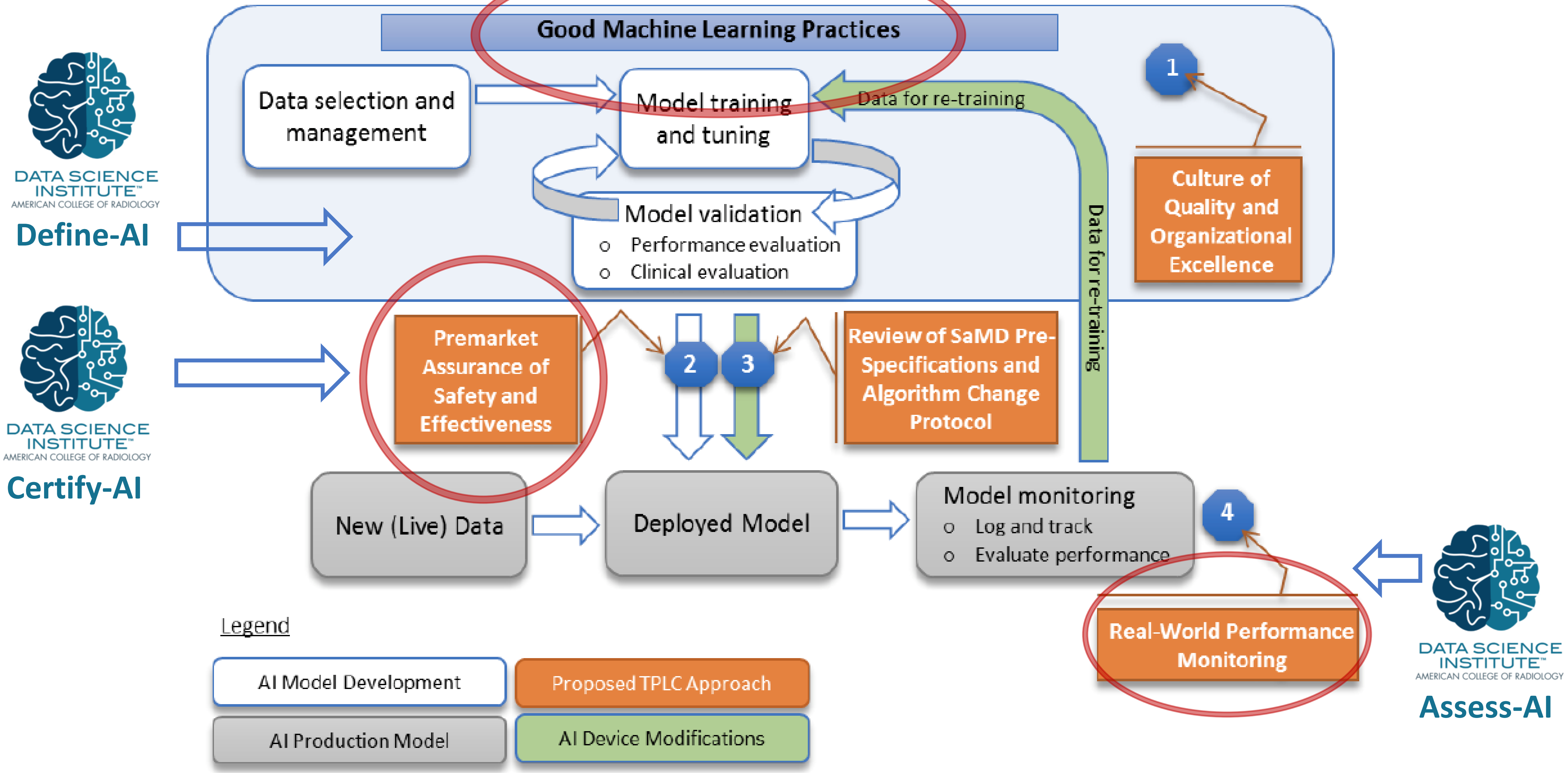
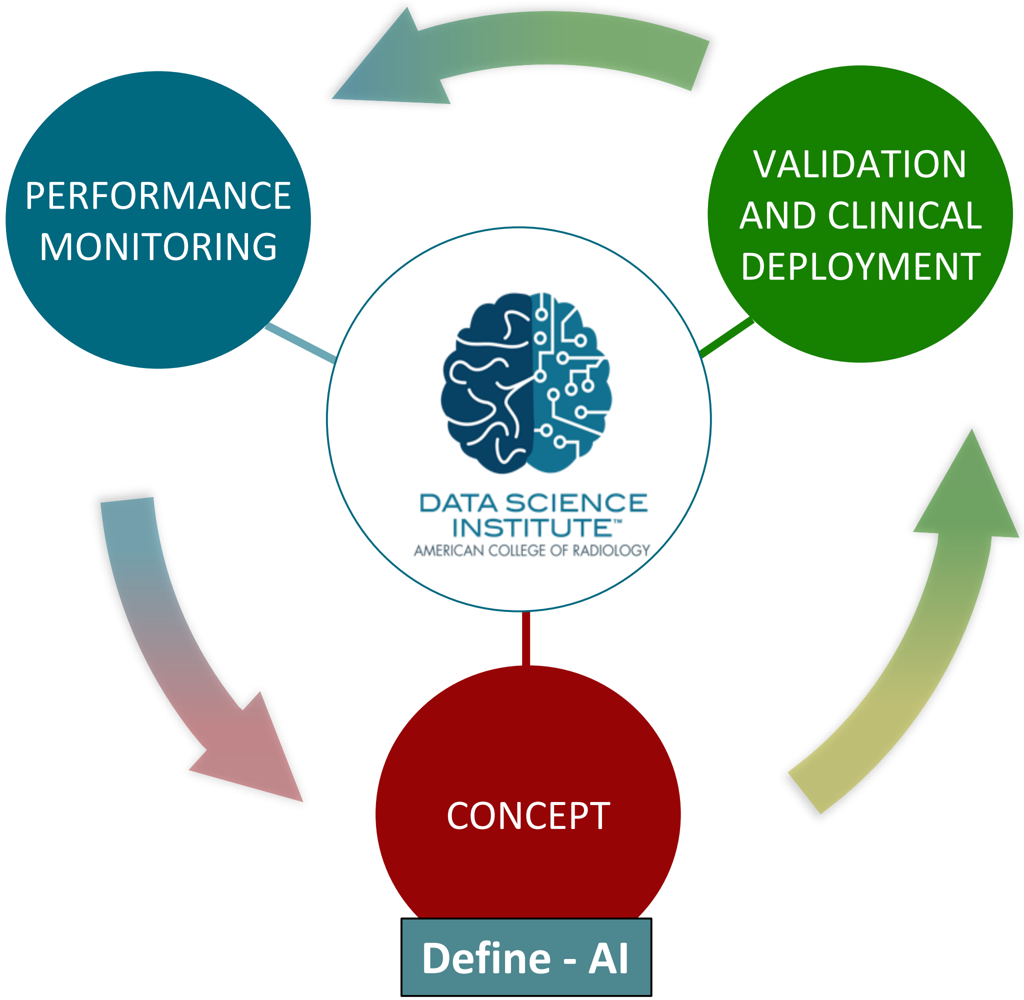


Figure 2: Overlay of FDA's TPLC approach on AI/ML workflow

How Do We Make Sure AI Is Working In The Real World?



How Do We Validate AI Algorithms For Clinical Practice?

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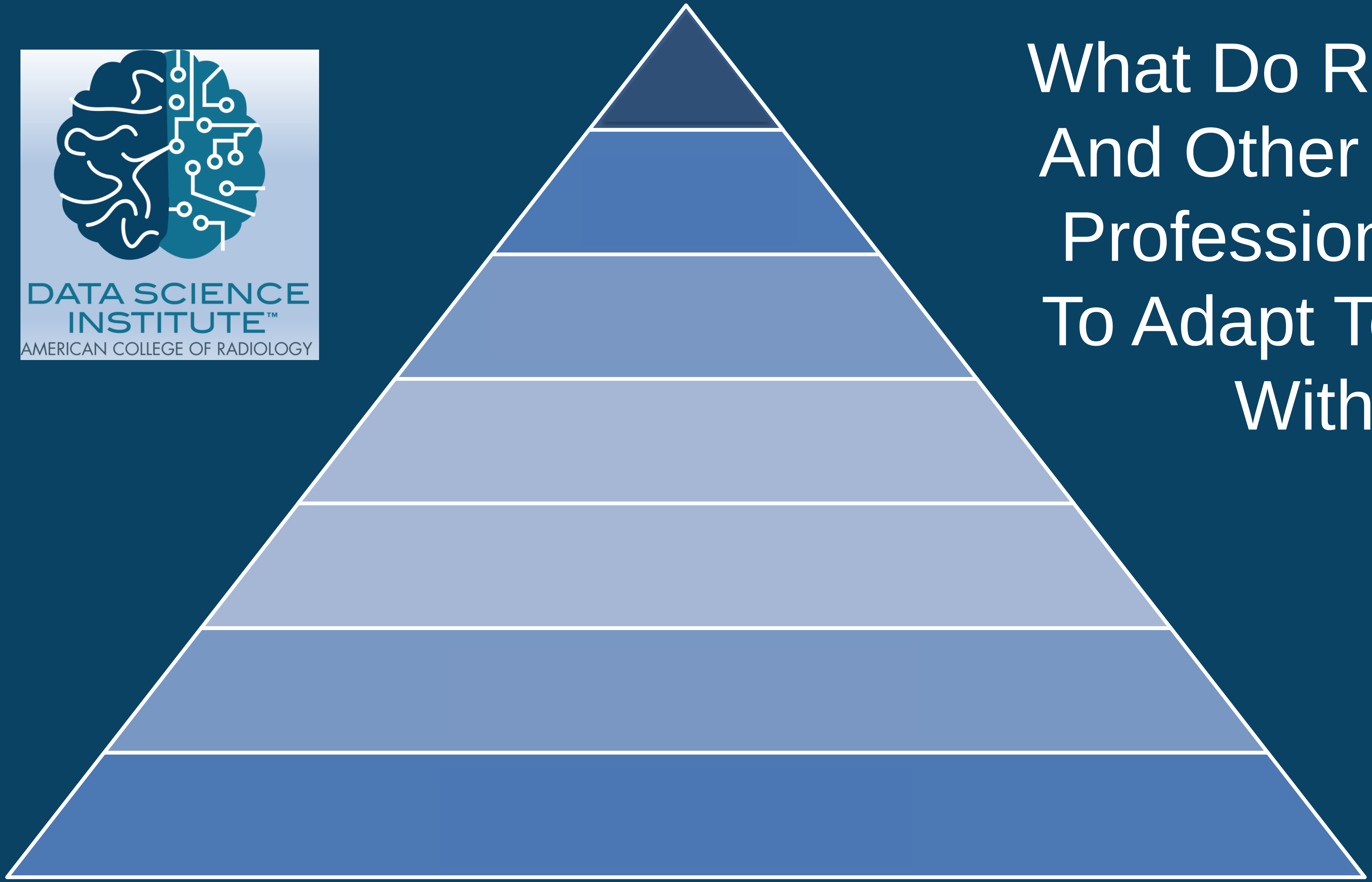
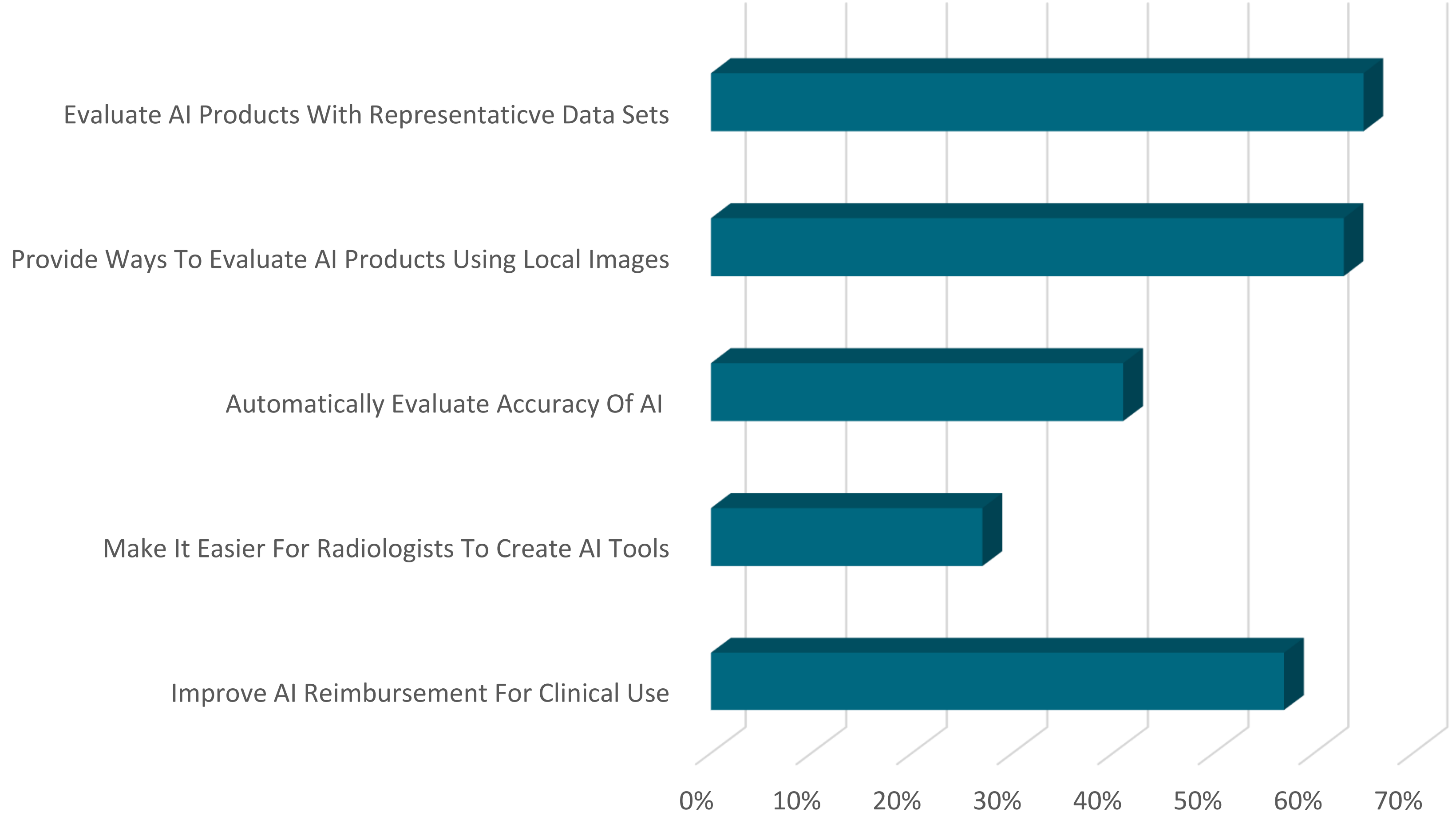
What Are The Most Important Clinical Tasks For AI?



What Do Radiologists And Other Radiology Professionals Need To Adapt To A Future With AI?

What Should The ACR Do For Radiologists To Advance The Use Of AI In Clinical Practice



FDA U.S. FOOD & DRUG ADMINISTRATION

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Home / Medical Devices / News & Events (Medical Devices) / Workshops & Conferences (Medical Devices) / Public Workshop - Evolving Role of Artificial Intelligence in Radiological Imaging - 02/25/2020 - 02/26/2020

WORKSHOP

Public Workshop - Evolving Role of Artificial Intelligence in Radiological Imaging

FEBRUARY 25 - 26, 2020

9:15 – 10:15 AM	**Emerging Trends in Radiological AI Software - Exploring Benefits and Risks** Moderator: Jessica Lamb, PhD, Assistant Director (Acting), Mammography, Ultrasound, and Imaging Software Team, Division of Radiological Health (FDA) *Advances in AI technology are leading to an expanding role for AI throughout the diagnostic clinical workflow. In this session, we 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.* *Presentations will discuss the impact of radiological AI software on standard of care, clinical benefit, and risk.*

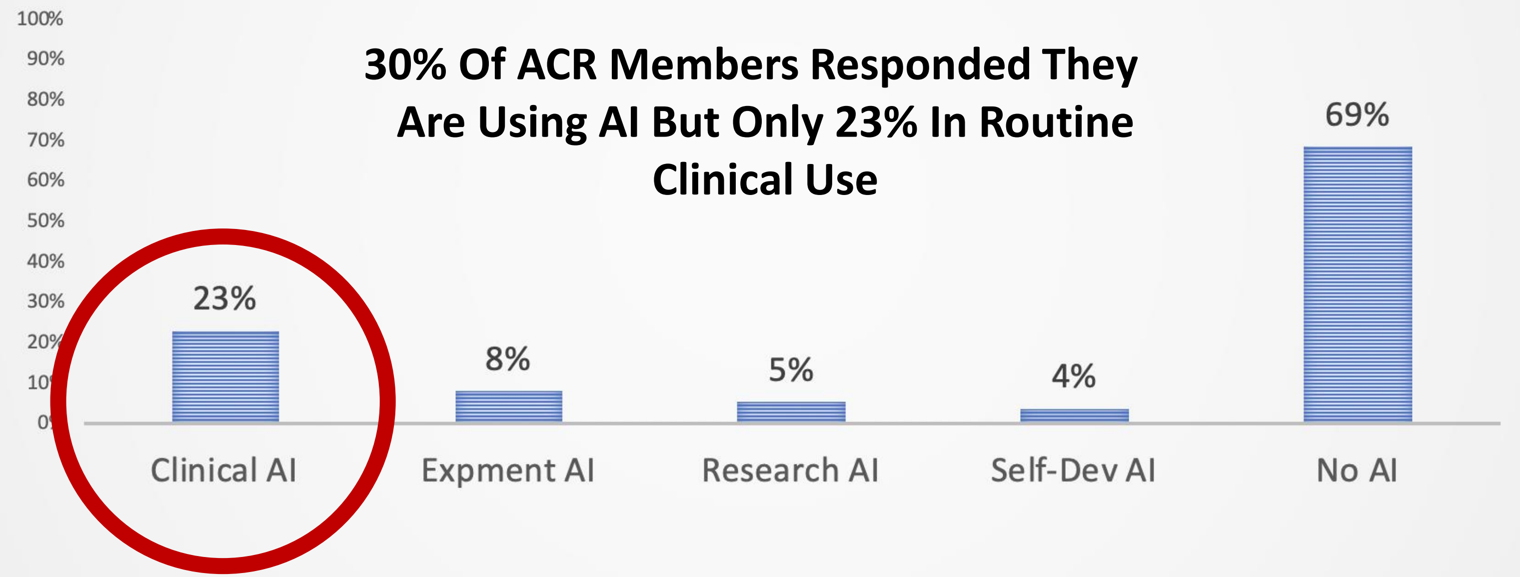
Autonomous AI In Clinical Practice

- **Device:** AI intended to identify a patient's condition as stable from images, without a radiologist's review to confirm
- **Benefits include**: Potential reduction in radiologists' workload allowing them to focus on more critical cases
- **Risks include**: Potential for false negatives and missing secondary findings the algorithm was not trained to identify
- **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?

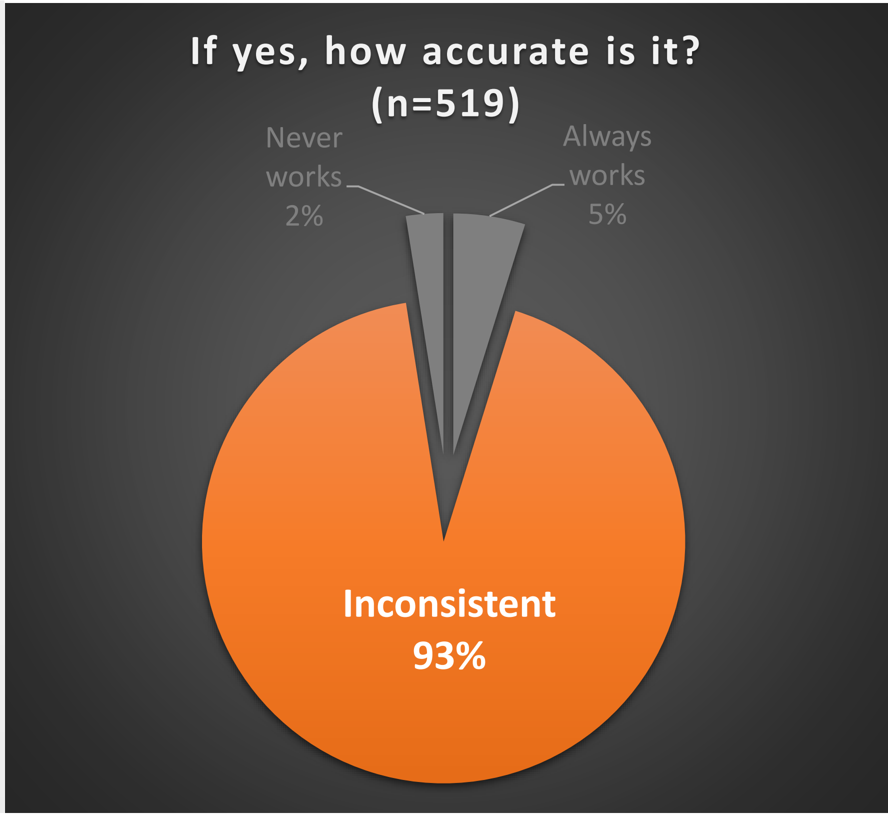
Source: Robert Ochs Deputy Director of Radiological Health / CDRH / FDA – FDA Workshop Presentation

ACR DSI AI Survey

AI Penetrance In Clinical Practice And Accuracy

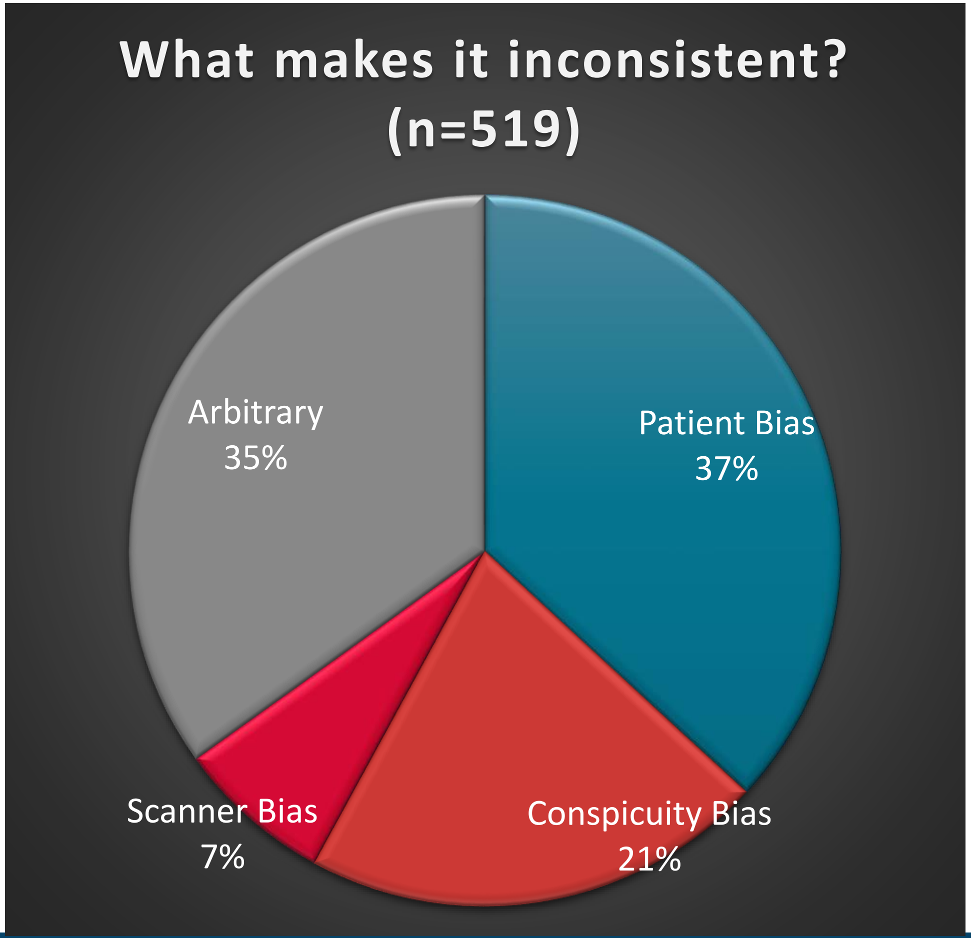


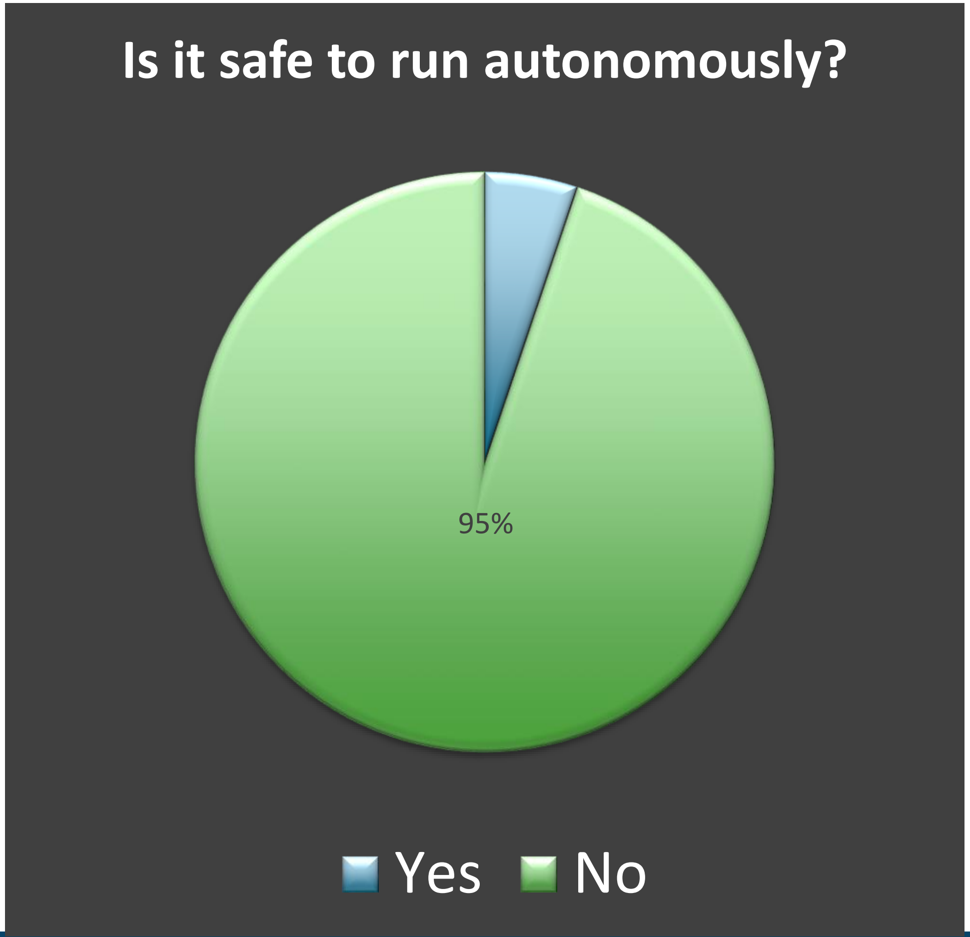
Survey Stats			Use AI	Clinical AI	Expment AI	Research AI	Self-Dev AI	No AI
Radiologists Surveyed	1,001	Responses	315	231	80	54	38	686
% of all US Radiologists	4%	% Surveyed	31%	23%	8%	5%	4%	69%
Est* of US Radiologists	28,000	Proj* Rads	8,811	6,462	2,238	1,510	1,063	19,189



ACR DSI AI Survey

AI Penetrance In Clinical Practice And Accuracy





ACR Will Submit Public Comments

Featured Result - Docket ID: FDA-2019-N-5592

Open Docket Folder

Public Workshop - Evolving Role of Artificial Intelligence in Radiological Imaging

Agency: Food and Drug Administration (FDA)

Instructions for Submitting Comments

Other by **FDA** on **12/02/2019** **ID:** FDA-2019-N-5592-0001

Comment Now!

Due Jun 30, 2020 11:59 PM ET

Open Docket Folder

Instructions for Submitting Comments

Other by **FDA** on **03/23/2020** **ID:** FDA-2019-N-5592-0008

Comment Period Closed

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PUBLIC WORKSHOP - EVOLVING ROLE OF ARTIFICIAL INTELLIGENCE IN RADIOLOGICAL IMAGING DAY 2 FINAL (003)

Other by **FDA** on **03/26/2020** **ID:** FDA-2019-N-5592-0010

Comment Period Closed

Open Docket Folder

PUBLIC WORKSHOP - EVOLVING ROLE OF ARTIFICIAL INTELLIGENCE IN RADIOLOGICAL IMAGING Day 1 FINAL (002)

Other by **FDA** on **03/26/2020** **ID:** FDA-2019-N-5592-0009

Comment Period Closed

Open Docket Folder

The ACR strongly believes that it is too soon for the FDA to consider clearance of algorithms that are designed to provide autonomous image interpretation, which are essentially rendering medical care without physician supervision. Without comprehensive research into the requirements for ensuring algorithms are generalizable to the heterogeneity in typical patient populations as well as the broad heterogeneity in imaging equipment and image acquisition protocols as well as a definable mechanism to ensure the longitudinal performance of the algorithm, we believe autonomously functioning algorithms would pose a significant risk to patient safety.

- Identification of normal examinations (e.g. screening mammography)
  - Continuous monitoring of large numbers of studies to account for the low prevalence of breast cancer
  - Must detect begin disease that could mimic breast cancer
  - Is there analogy to PAP smears (10% over-read in population with 6.8% positive)?

- Rule out examinations (e.g. pulmonary embolus)
  - Makes sense for work list prioritization but not for final interpretations
  - What about other disease processes – aortic dissection, pneumothorax?

Potential Use Cases For Early Use Of "Autonomous AI"

- Population health management
  - Osteoporosis, hepatic steatosis, emphysema, coronary calcification
  - Identify "missed care" opportunities that can be transmitted to patients EHR or referring physician outside of the standard imaging report

- Opportunities
  - Can be used without affecting existing services
  - Can test autonomous AI in an environment where treatment is not dictated by the algorithm
  - Puts radiologists at forefront of population health management

Trusted Relationships
Public Private Partnerships

OPEN DISCUSSION

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Physicians Technologists Industry Data Scientists Informaticists Health Care Execs

Patients