# Regulatory Science for Evaluation of Medical Imaging Devices


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Division of Imaging, Diagnostics, and Software Reliability
Office of Science and Engineering Laboratories
Center for Devices and Radiological Health
U.S. Food and Drug Administration



**17th International Meeting on Fully Three-Dimensional Image Reconstruction in Radiology and Nuclear Medicine (Fully3D)** at Stony Brook -- July 19, 2023

# Outline

1. Introduction
2. AI/ML Image Processing Software regulatory Pathway and Considerations
3. Regulatory Science Research at FDA: Deep Learning Image Reconstruction and Denoising in CT
4. Considerations and Regulatory Science Research at FDA: Evaluating Imaging Systems with Photon Counting Detectors



**Most of this material is taken from other people.  Thanks to those people.**

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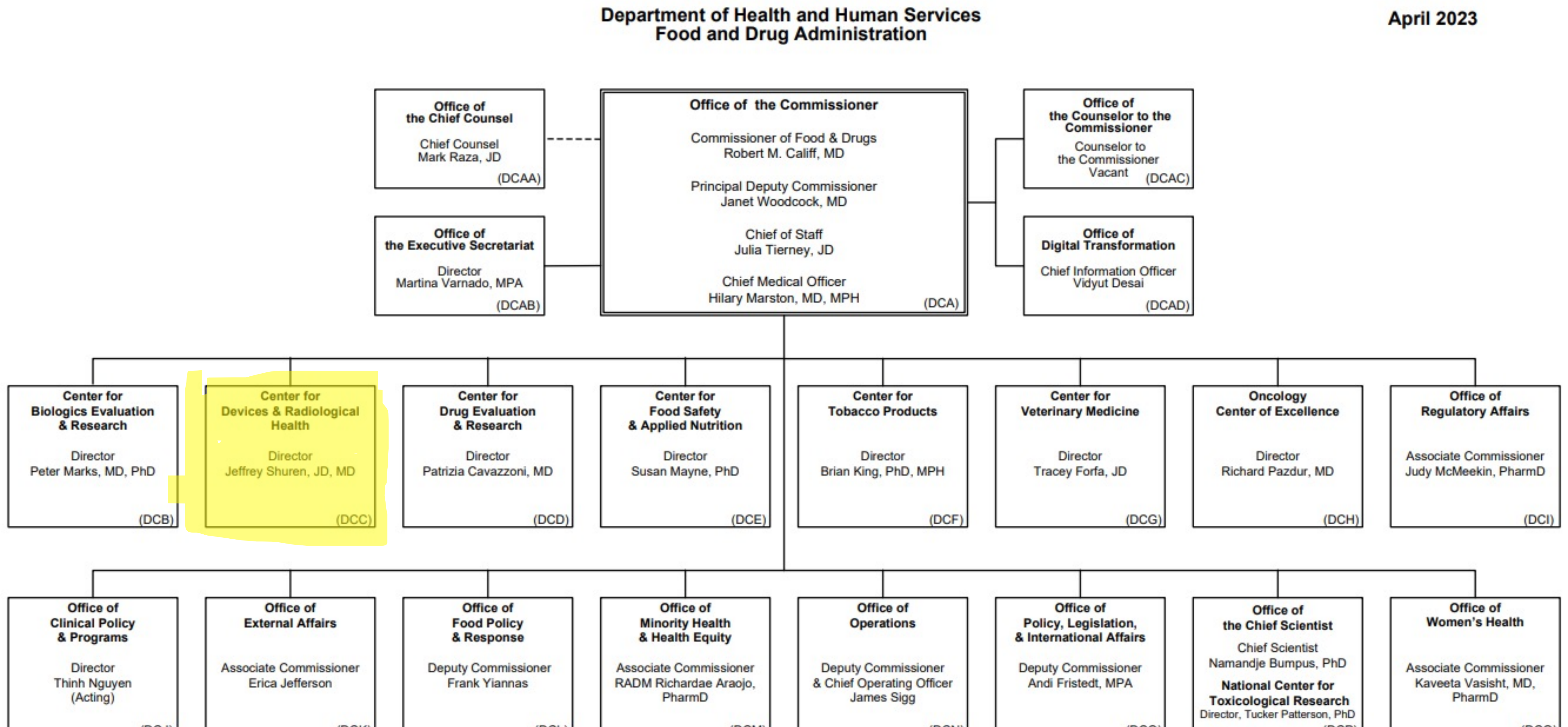
# Introduction

1. Brief overview of the Office of Science and Engineering Laboratories (OSEL)
2. Importance of regulatory science in medical imaging

# Regulatory science research at CDRH/OSEL/DIDSR




FDA
U.S. FOOD & DRUG
ADMINISTRATION
CENTER FOR DEVICES & RADIOLOGICAL HEALTH
OFFICE OF SCIENCE & ENGINEERING LABORATORIES
RESEARCH HAPPENS HERE

OSEL’s mission is to accelerate patient access to innovative, safe, and effective medical devices through best-in-the-world Regulatory Science.

OSEL’s vision is to transform the lives of patients by generating renowned and transparent Regulatory Science that streamlines the medical device review process.

OSEL Video

# Regulatory Science

*"**Regulatory Science** is an established discipline that entails the application of the scientific method to support regulatory and other policy objectives.*

***To assess benefits and risks, Regulatory Scientists develop new tools**, standards, and approaches to evaluate the effectiveness, safety, and quality of medical products."*

[Marble et al. J Pathol Inform 2020]

[Focus Areas of Regulatory Science Report]

# Office of Science and Engineering Laboratories (OSEL)

- Conduct laboratory-based regulatory research to facilitate development and innovation of safe and effective medical devices and radiation emitting products
- Provide scientific and engineering expertise, data, and analyses to support regulatory processes
- Collaborate with colleagues in academia, industry, government, and standards development organizations to develop, translate, and disseminate science and engineering-based information regarding regulated products
- https://www.fda.gov/about-fda/cdrh-offices/office-science-and-engineering-laboratories

# CDRH's Office of Science and Engineering Labs

**165**

FEDERAL EMPLOYEES
Up to 180 visiting scientists

**140 Research Projects**

In 20 Program Areas

**400/year**

Peer-reviewed presentations, articles, and other public disclosures

**> 3,000/year**

Premarket regulatory reviews

**75**

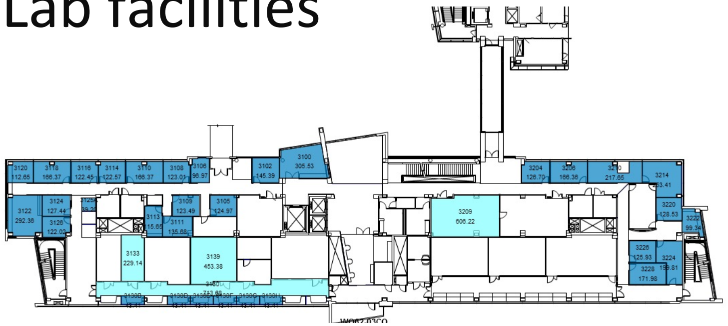
Standards and conformity assessment committees

**70%**

Staff with a graduate degree

**55,000 $ft^2$**

Lab facilities



# Division of Imaging, Diagnostics and Software Reliability (DIDSR)

FDA

- Develop least burdensome approaches for regulatory evaluation of imaging and big-data devices
- Develop measures of technical  effectiveness of imaging and big-data technologies
  - Phantoms, laboratory measurements, computational models

# DIDSR in Perspective

**50**
FEDERAL EMPLOYEES
40 Fellows/Students
Open Staff Positions

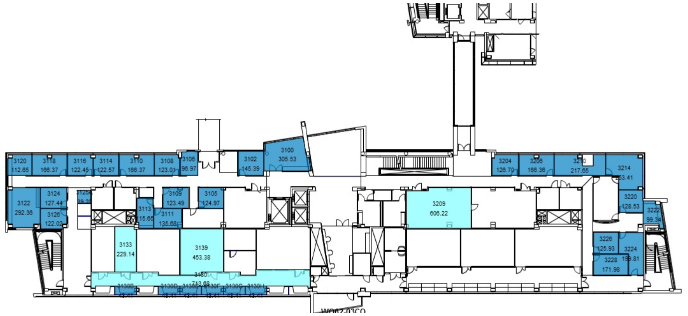
**100+/year**
Peer reviewed articles, code and presentations

**4 Program Areas**
- **AI/ML**
- **Medical Imaging and Diagnostics**
- **Medical Extended Reality**
- **Digital Pathology**

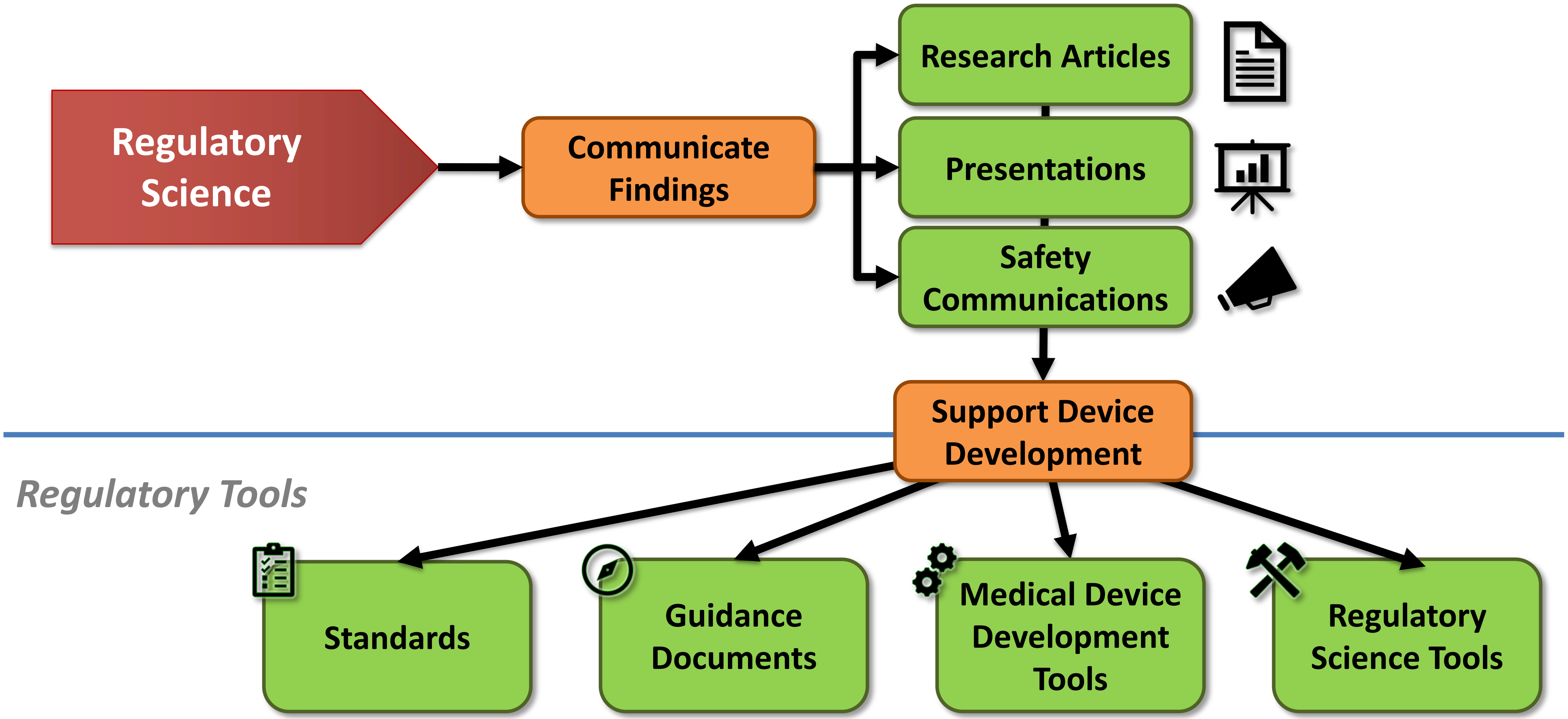
**350+/year**

Premarket
Regulatory consults

**~15,000 ft$^2$**
DIDSR Lab and facilities



# From Regulatory Science to Regulatory Tools



# OSEL Program Areas Advancing Regulatory Science Research and Tools

- Additive Manufacturing
- Advanced Patient Monitoring and Control
- AR/VR - extended reality (XR)
- **Artificial Intelligence (AI) / Machine Learning**
- Biocompatibility/Toxicology
- Cardiovascular
- Credibility Assessment in Modeling
- Digital Pathology
- Electromagnetic and Electrical Safety
- Emergency Preparedness
- Human Device Interaction
- Materials Chemistry and Mechanical Performance
- **Medical Imaging and Diagnostics**
- Microfluidics
- Nanotechnology
- Neurology
- Ophthalmology
- Orthopedic Devices
- Post Market Signal Response
- Sterility and Infection Control
- Therapeutic Ultrasound

- https://www.fda.gov/medical-devices/science-and-research-medical-devices/catalog-regulatory-science-tools-help-assess-new-medical-devices

# Evolution in Medical Imaging: A Personal Perspective

- AI/ML Enabled Devices - Artificial Intelligence and Machine Learning.
- AR/VR Technologies - Augmented and Virtual Reality
- Photon Counting Detectors in X-ray Imaging

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2. AI/ML Image Processing Software regulatory Pathway and Considerations
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**DISCLAIMER: The mention of commercial products herein is not to be construed as either an actual or implied endorsement of such products by the U.S. Department of Health and Human Services.**

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# AI/ML Image Processing Software Pathway and Considerations

FDA

1. Explanation of the regulatory pathway for evaluating AI/ML image processing software
2. Key considerations in regulatory science for AI/ML image processing software

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# Some AI/ML/CAD Devices Cleared/Approved by FDA

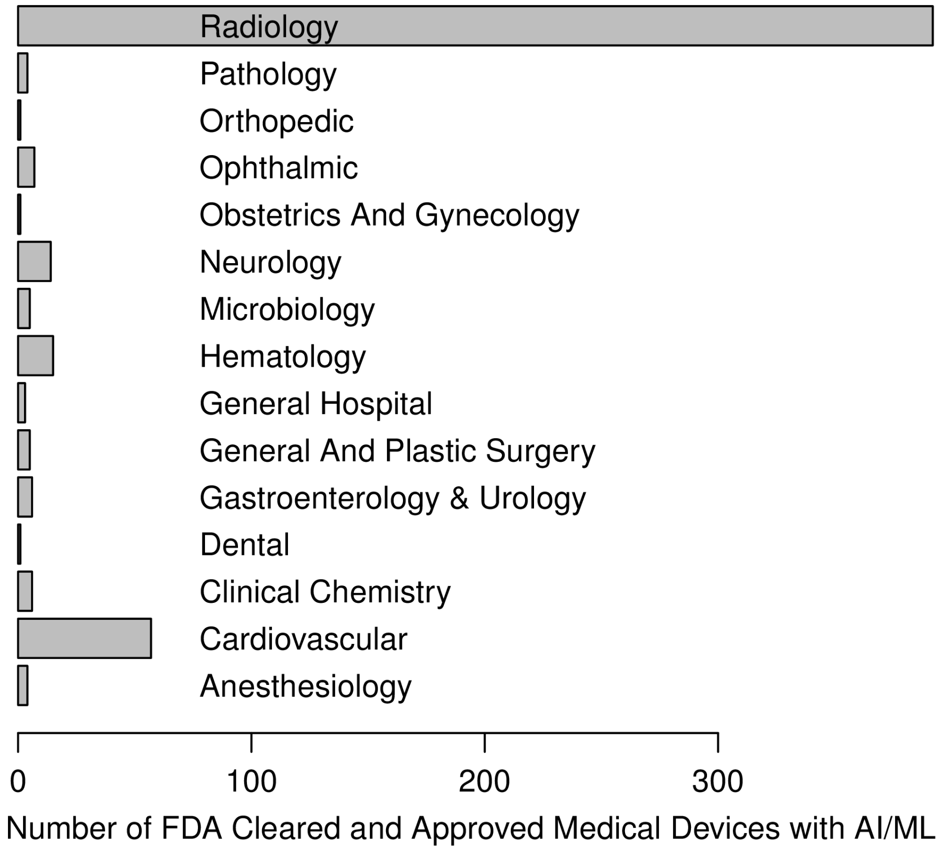
## AI/ML-Enabled Medical Devices

Devices are listed in reverse chronological order by Date of Final Decision. To change the sort order, click the arrows in the column headings.

Use the Submission Number link to display the approval, authorization, or clearance information for the device in the appropriate FDA database. The database page will include a link to the FDA's publicly available information.

Export Excel Show 50 entries

| Date of Final Decision | Submission Number | Device | Company | Panel (Lead) | Primary Product Code |
|---|---|---|---|---|---|
| 07/29/2022 | K213760 | ABMD Software | HeartLung Corporation | Radiology | KGI |
| 07/29/2022 | K220961 | Deep Learning Image Reconstruction | GE Healthcare Japan Corporation | Radiology | JAK |
| 07/28/2022 | K213998 | cvi42 Auto Imaging Software Application | Circle Cardiovascular Imaging Inc | Radiology | QIH |
| 07/28/2022 | K221923 | Swoop Portable MR Imaging System | Hyperfine, Inc. | Radiology | LNH |
| 07/27/2022 | K210822 | DeepRhythmAI | Medicalgorithmics S.A. | Cardiovascular | DQK |
| 07/25/2022 | K220439 | Viz SDH | Viz.ai, Inc. | Radiology | QAS |
| 07/22/2022 | K220624 | AI4CMR v1.0 | AI4MedImaging Medical Solutions S.A. | Radiology | LLZ |
| 07/22/2022 | K220882 | Vivid E80, Vivid E90, Vivid E95 | GE Medical Systems Ultrasound and | Radiology | IYN |
| 07/22/2022 | K220940 | EchoPAC Software Only, EchoPAC Plug-in | GE Medical Systems Ultrasound and Primary Care Diagnostics, | Radiology | QIH |
| 07/20/2022 | K220956 | Libby Echo:Prio | Dyad Medical, Inc | Radiology | QIH |
| 07/19/2022 | K213357 | Study Watch with Irregular Pulse Monitor (Home), Study Watch with Irregular Pulse Monitor | Verily Life Sciences LLC | Cardiovascular | DXH |



# Regulatory evaluation of image processing software

FDA

**Qualifications** → **Classifications** → **Clinical evaluation**

Is your device a medical device?

Indication for use and associated risks

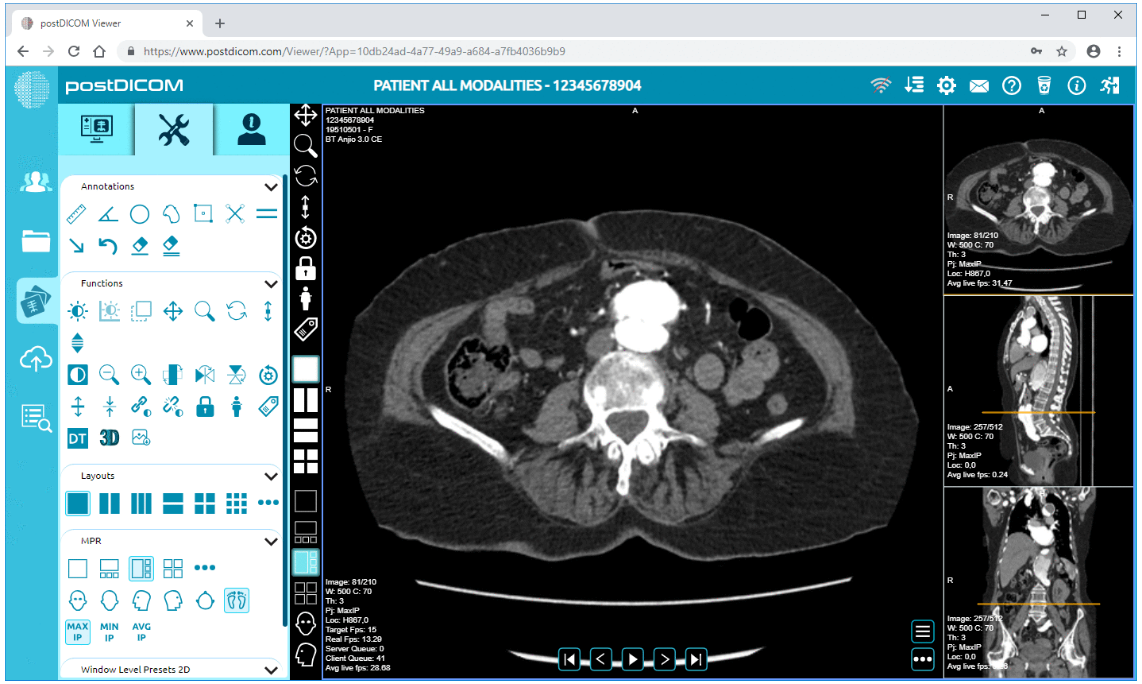
Demonstrate of safety and effectiveness

# Medical device classification

- FDA employs a risk-based classification paradigm for medical devices:
  - Medical devices are classified and regulated according to degree of risk to the public.

# Image processing software

Image processing and tomographic reconstruction software devices are typically classified as class II and cleared through 510(k) as substantially equivalent to a predicate device.



# CAD software has multiple regulations

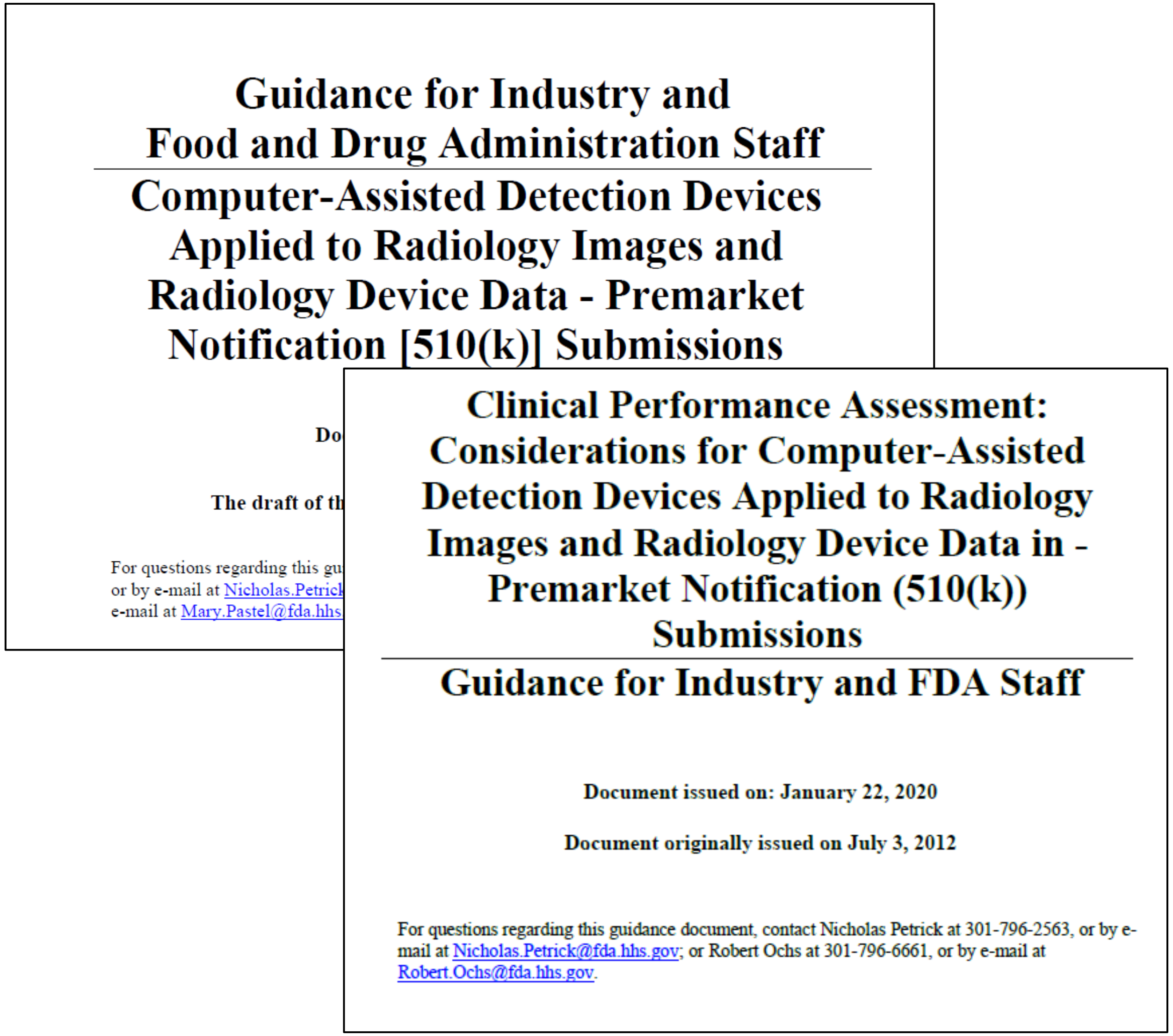
| | |
|---|---|
| Computer Aided Detection | • CADe: direct clinician's attention to aid the identification of potential disease; 510(k) under 21 CFR 892.2050 or 892.2070 |
| Computer Aided Diagnosis | • CADx: concurrent/sequential use to aid the classification of lesions suspicious of cancer; 510(k) under 21 CFR 892.2060 |
| Computer Aided Detection & Diagnosis | • CADe/x: combined systems that both detect and provide a classification of potential disease; 510(k) under 21 CFR 892.2090 |
| Computer Aided Triage & Notification | • CADt: notification of potentially time sensitive findings – not CADe/x; 510(k) under 21 CFR 892.2080 |
| Radiological Acquisition & Optimization Guidance | • CADa/o: aid the acquisition/optimization of images/diagnostic signals; 510(k) under 21 CFR 892.2100 |

[Slide provided by Jana Delfino]

# 3. Guidance for Assessment of Radiological AI/ML

- 510(k) guidance
  - Stand-alone device performance
  - Content of a 510(k) submission

- AI/ML enabled device:
  - Large representative validation dataset likely needed



**Guidance for Industry and Food and Drug Administration Staff**

**Computer-Assisted Detection Devices Applied to Radiology Images and Radiology Device Data - Premarket Notification [510(k)] Submissions**

**Do**

**The draft of th**

For questions regarding this gu
or by e-mail at Nicholas.Petrick
e-mail at Mary.Pastel@fda.hhs

**Clinical Performance Assessment: Considerations for Computer-Assisted Detection Devices Applied to Radiology Images and Radiology Device Data in - Premarket Notification (510(k)) Submissions**

**Guidance for Industry and FDA Staff**

**Document issued on: January 22, 2020**

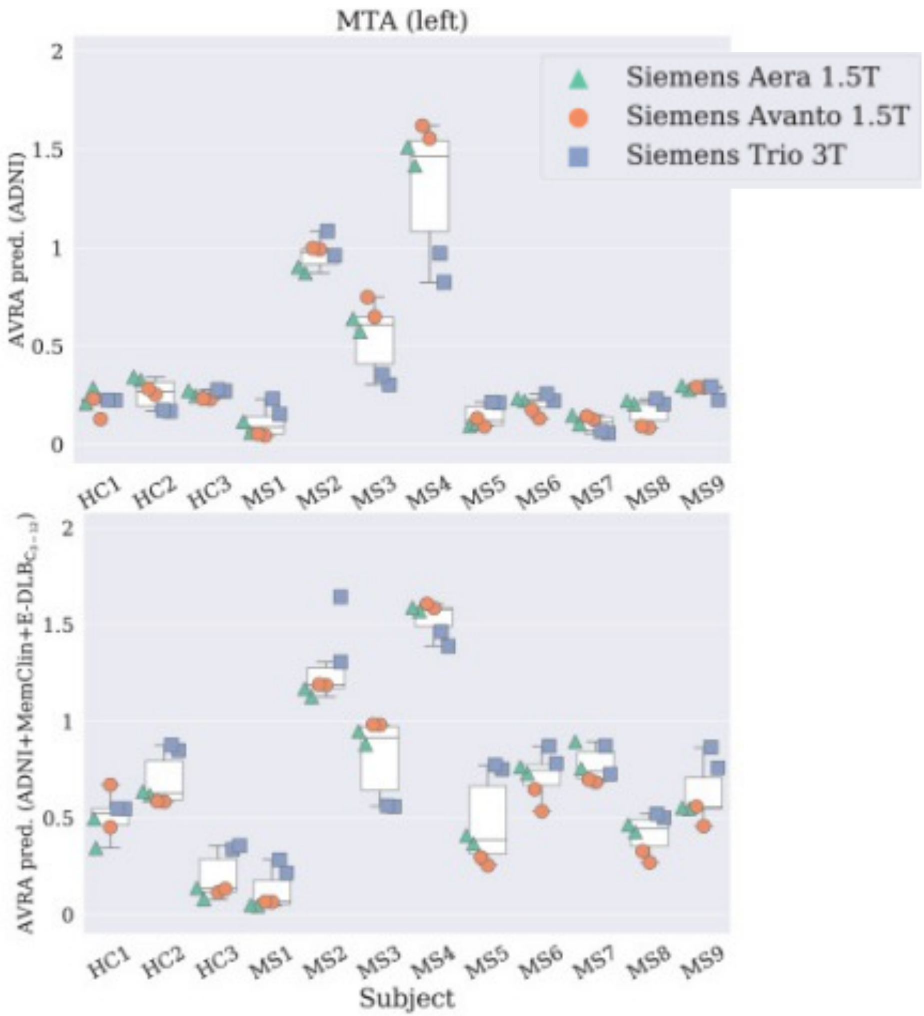
**Document originally issued on July 3, 2012**

For questions regarding this guidance document, contact Nicholas Petrick at 301-796-2563, or by e-mail at Nicholas.Petrick@fda.hhs.gov; or Robert Ochs at 301-796-6661, or by e-mail at Robert.Ochs@fda.hhs.gov.

# Opportunities and Challenges

The performance/outputs of an AI/ML software can change between sites or scanners.

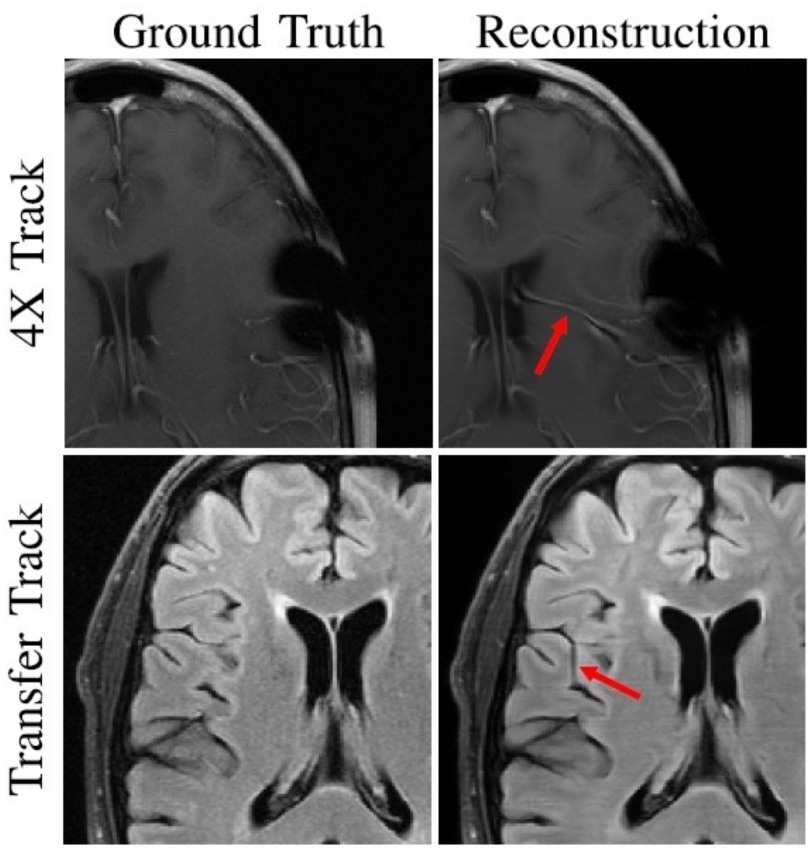
The outputs of the Medial Temporal Atrophy (MTA) scale are affected by the scanners and the training datasets used.




*Mårtensson, Gustav, et al. "The reliability of a deep learning model in clinical out-of-distribution MRI data: a multicohort study." Medical Image Analysis (2020): 101714. [MRI brain imaging, site variability]*

# Opportunities and Challenges

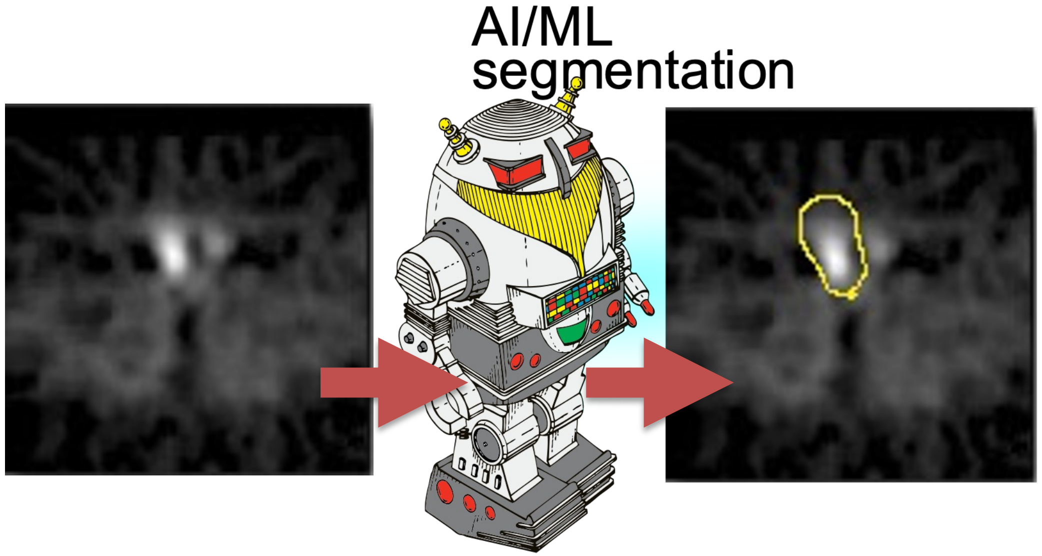
**Opinions of experts about device output may not be adequate.**




A schematic of hallucinations from DL-based reconstruction of a clinical pediatric MR brain image with training performed on adult brain images.

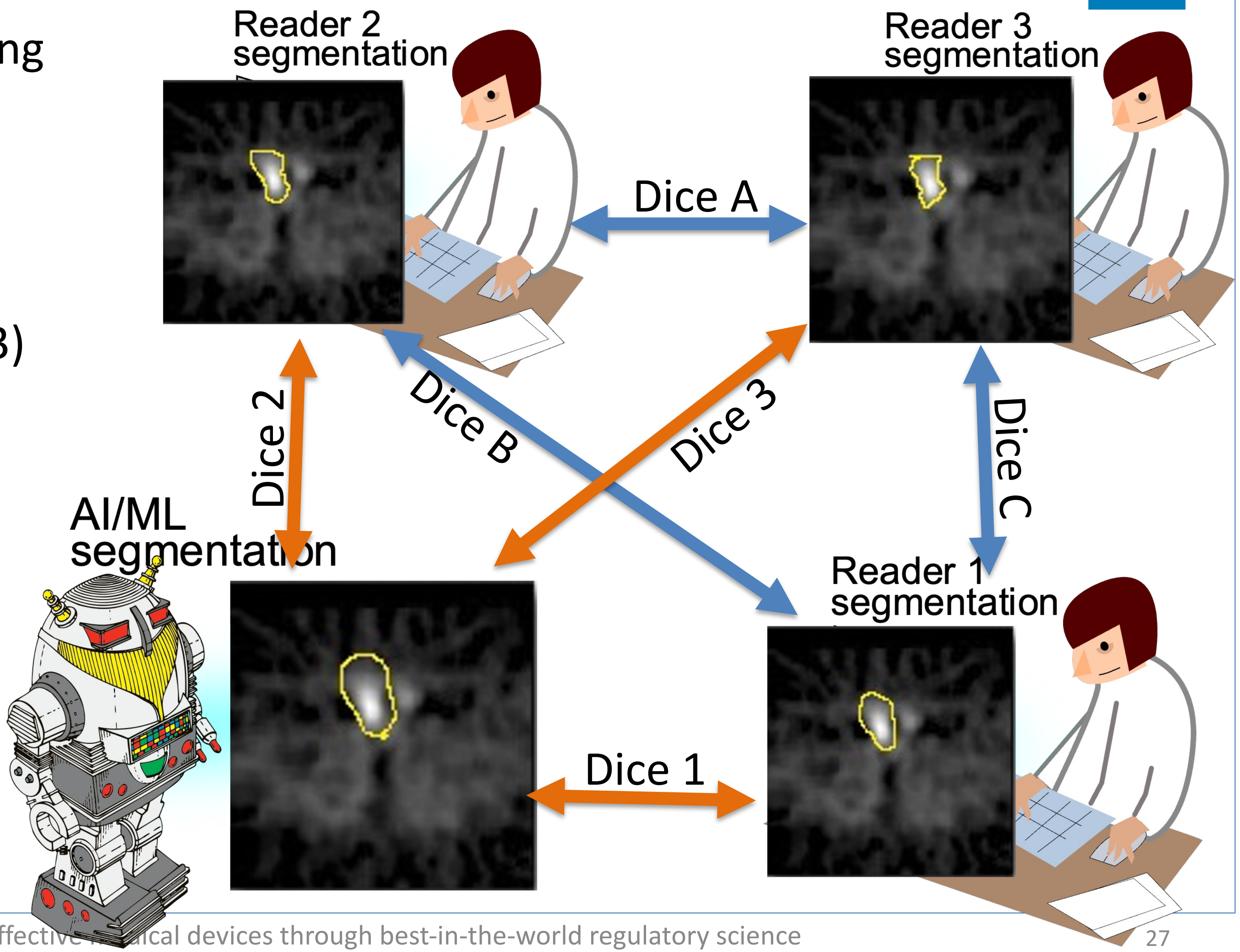
# AI/ML/CAD Segmentation Devices

- Claim: Software can automatically segment lesion
- Example evaluation study: Agreement study



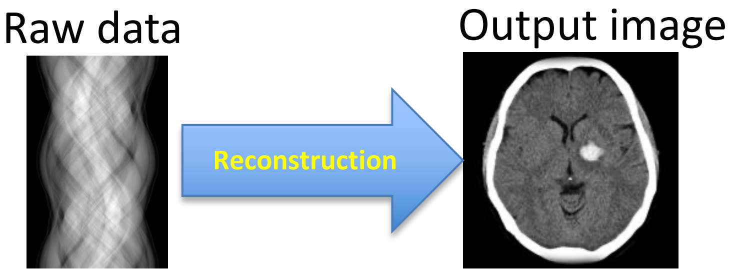
# AI/ML/CAD Agreement for Segmentation Devices

- Compare segmentations among readers using Dice or other measures (A,B,C).
- Compare segmentations between AI and readers (1,2,3)
- Are Dice 1,2,3 non-inferior to Dice A,B,C?
  - Then AI may be interchangeable with readers



# Deep Learning Image Reconstruction and Denoising Devices

# Generalizability Performance of Deep Learning Image Reconstruction and Denoising in CT




Generalizability test
Ensure clear labeling related to applications, limitations and cautions.

**Analytical methods**
Filtered back projection

1970s

- Linear
- Fourier Slice Theorem

**Iterative methods (IR)**
e.g., ASiR, Veo, SAFIRE, IMR, AiDR…

2008-2018

- Nonlinear
- Physics-based

**Deep learning-based methods (DLR)**
e.g., AiCE, TrueFidelity, HyperDLR…

2019-present

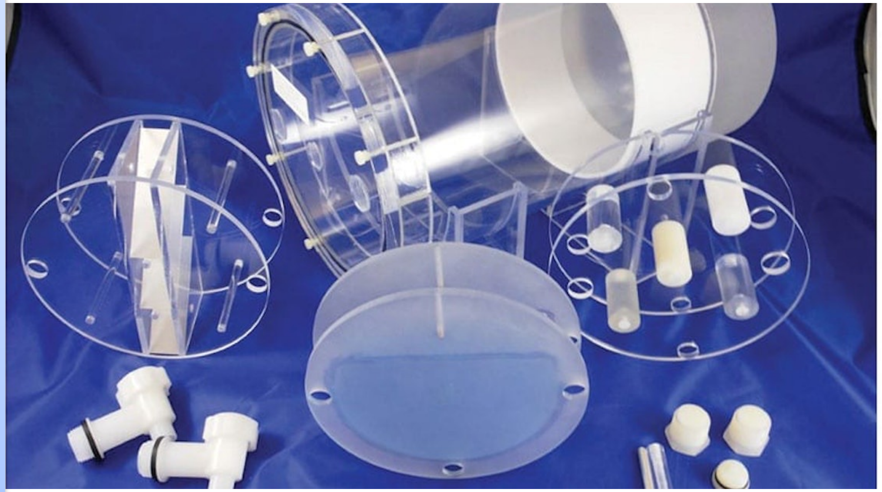
- Nonlinear
- Data-driven

# Reconstruction AI Devices

**Bench testing performance:**

- CT Number Accuracy
- Contrast-to-Noise Ratios (CNR)
- Uniformity
- Slice Sensitivity Profile (SSP)
- Modulation Transfer Function (MTF)
- Low contrast Resolution
- Standard Deviation of Noise (SD) in Midplane
- Standard Deviation of Noise (SD) along z-axis
- Noise Power Spectra (NPS)
- Visual inspection of image artifacts.
- Low Contrast Detectability (LCD) (dose claims)

. . .



# Reconstruction AI Devices

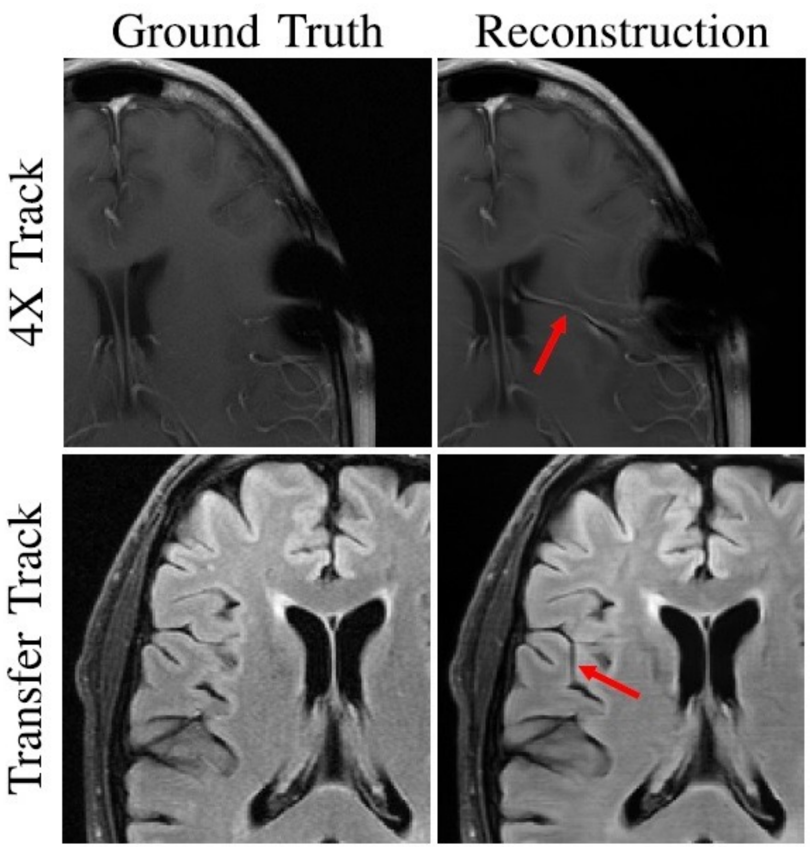
**Clinical Evaluation:**

Favor objective image quality evaluation through detection or estimation tasks.

Considerations:

- Engage certified radiologists.
- Employ side-by-side image comparison.
- Use actual patient images.
- Ensure data is representative, covering the IFU, patient population, anatomical variants, etc.

# Reconstruction AI Devices

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# Regulatory Science Research at FDA: Deep Learning Image Reconstruction and Denoising in CT

1. Generalizability in CT imaging
2. Generalizability in pediatric populations
3. Generalizability in testing backgrounds

# Generalizability Performance of Deep Learning Image Reconstruction and Denoising in CT

- Imaging aspect
  - CT systems
  - Acquisition parameters
  - Reconstruction parameters
- Patient aspect
  - Body parts
  - Patient populations
  - Pathological features

- What are the major impacting parameters?
- What is the underlying data distribution shift?

**Least Burdensome**

The **minimum** amount of information **necessary** to **adequately** address a relevant regulatory question or issue through the **most efficient** manner **at the right time**.

GUIDANCE DOCUMENT

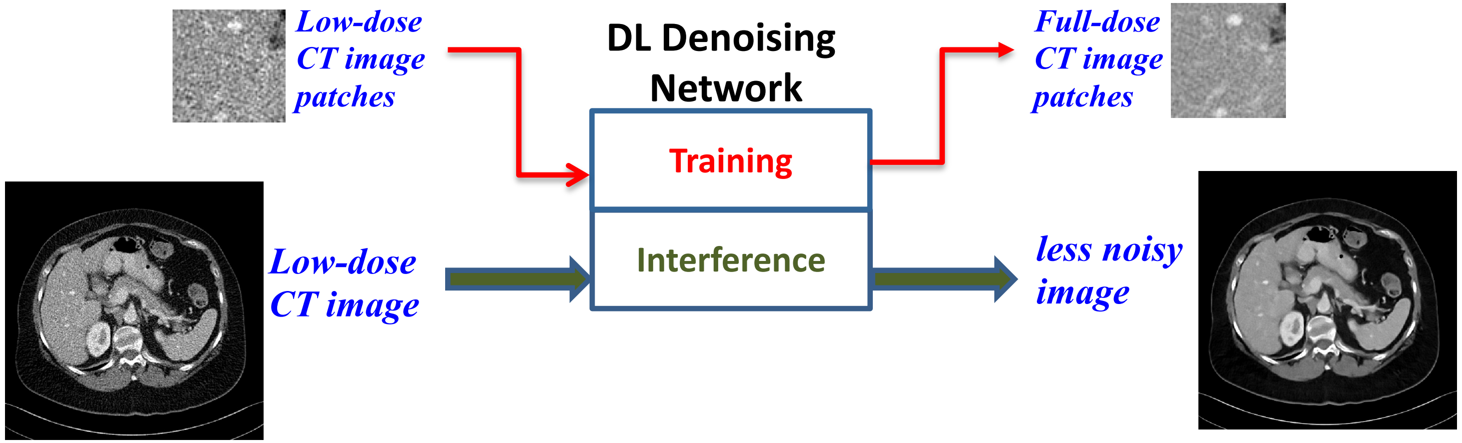
**The Least Burdensome Provisions: Concept and Principles**

*Guidance for Industry and FDA Staff*

FEBRUARY 2019

# 1. Generalizability in CT imaging parameters

Zeng et. al., MedPhys 2021: **Performance of a deep learning-based CT image denoising method: Generalizability over dose, reconstruction kernel and slice thickness**
Huber et. al., JCAT 2021: **Evaluating a Convolutional Neural Network Noise Reduction Method When Applied to CT Images Reconstructed Differently Than Training Data**




Slice thickness

Recon kernel

Dose levels

....

Slice thickness

Field of view (patient size)

# 1. Generalizability in CT imaging parameters

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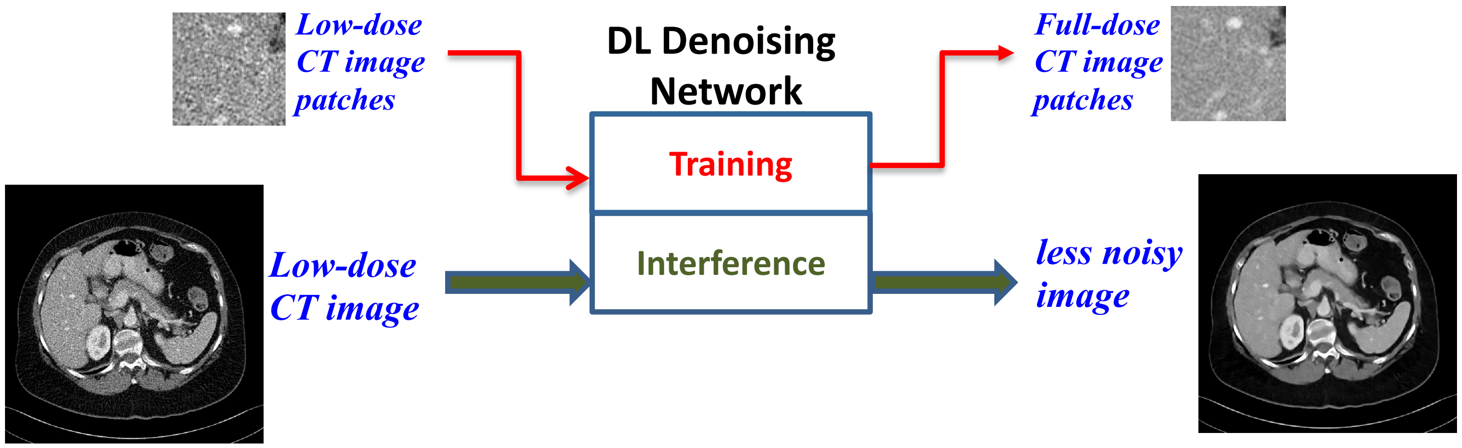
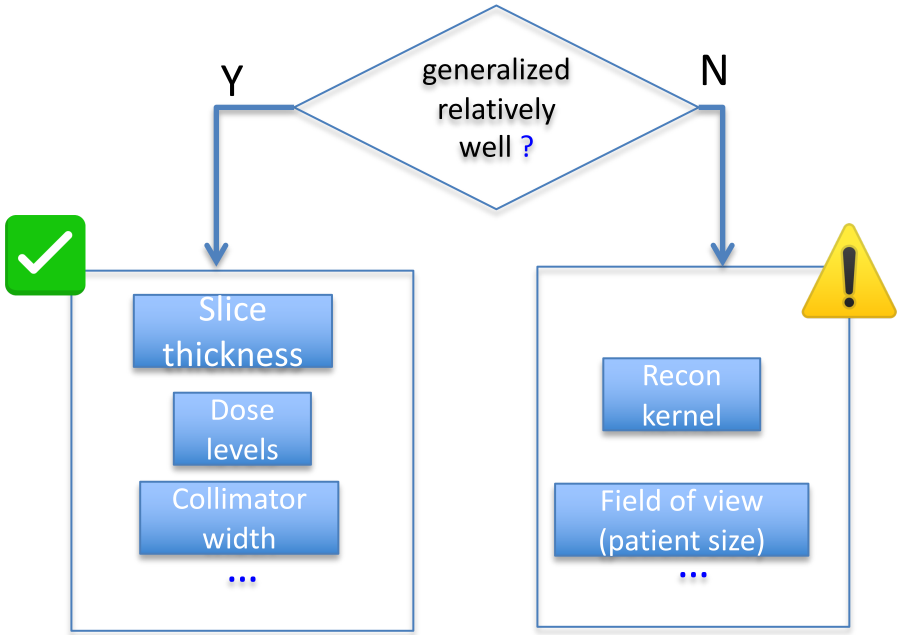
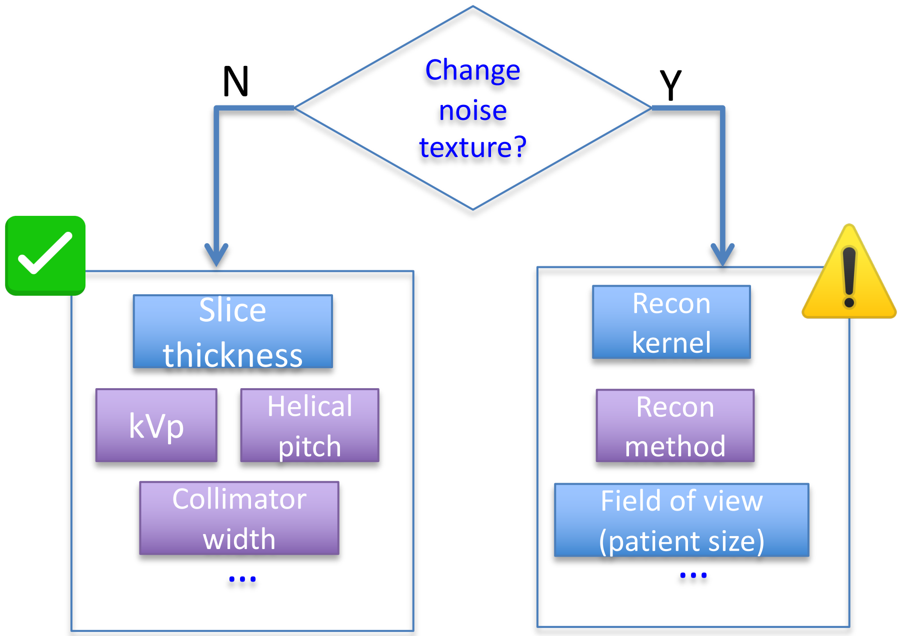


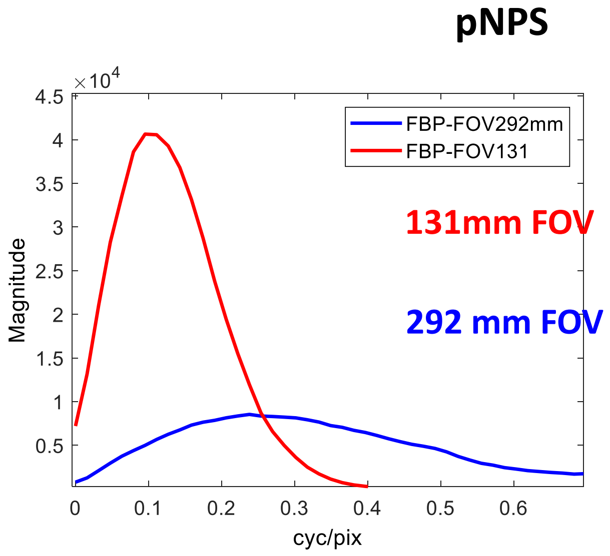
# Take-home message

- For a slice-based DL denoising network in low-dose CT
  - **Noise texture,** characterized by **pNPS**, of the input image is one underlying factor affecting its generalizability.
  - (**pNPS**: Pixel-wise noise power spectrum)



# 2. Generalizability in pediatric populations

- Does DLR benefit pediatric scans similarly as it does in adult scans?
  - DLR is mostly trained with adult CT scans.
  - CT images with smaller recon FOV have different noise texture, likely reducing the effectiveness of DLR.




1. **Brady et. al., Radiology 2021**: Improving Image Quality and Reducing Radiation Dose for Pediatric CT by Using Deep Learning Reconstruction

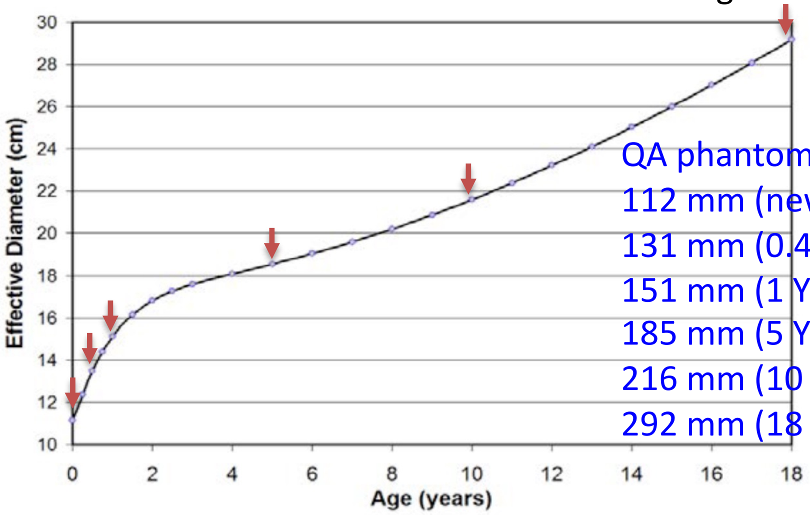
2. **Yoon et. al., BMC Med. Imag. 2021**: Image quality assessment of pediatric chest and abdomen CT by deep learning reconstruction

Great post-market studies!

Both studies concluded **Positive benefits** of using DLR in pediatric CT.

# Development of In silico methods for evaluating DLR performance in pediatric CT

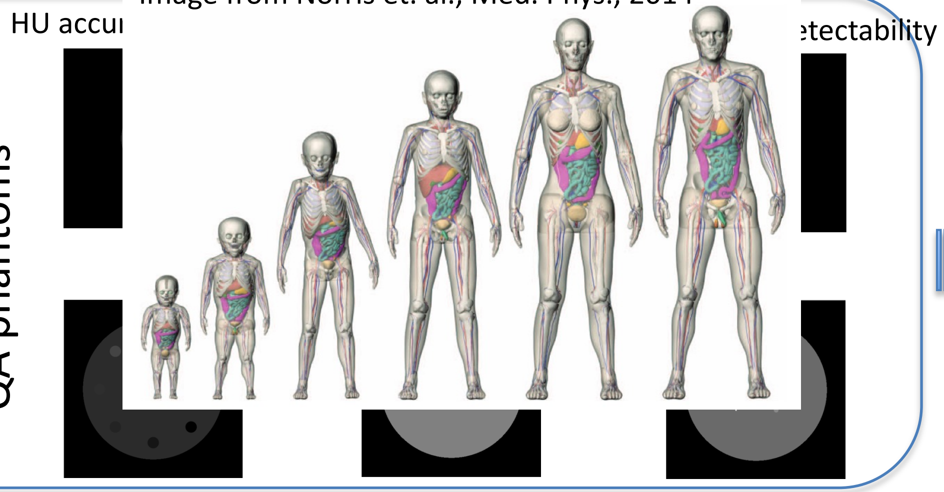
The effective diameter as a function of age[1]




QA phantom diameters
112 mm (newborn)
131 mm (0.4 Yr),
151 mm (1 Yr),
185 mm (5 Yr)
216 mm (10 Yr)
292 mm (18 Yr)

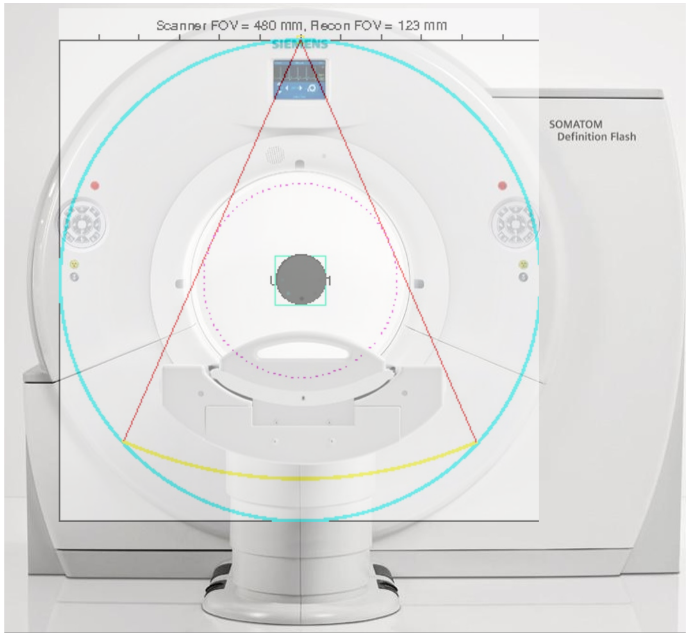
Image from Norris et. al., Med. Phys., 2014

Pediatric-size QA phantoms




- Geometry, recon kernel matching with the training data
- Adjusted pediatric scan parameters (dose, FOV=1.1D)

Virtual CT Scanner




<u>DL denoiser</u>: **REDCNN**
<u>Training data</u>: adult patient scans of **FOV 340-420 mm** [2]

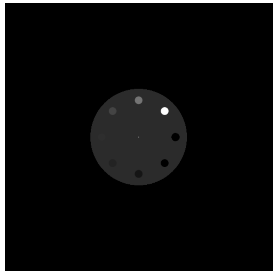
- FBP
- DL denoiser

1. AAPM TG204 report: Size specific dose estimates for pediatric and adult body CT examinations, 2011
2. LDCT Grand Challenge: https://www.aapm.org/GrandChallenge/LowDoseCT/

# Results

Image Sharpness | HU Accuracy | Noise | Low Contrast Detectability

112mm → 292mm



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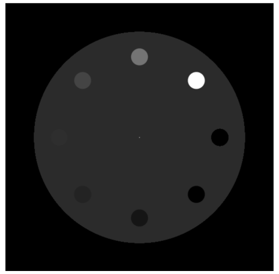


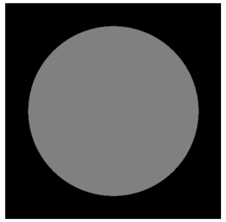
# Results

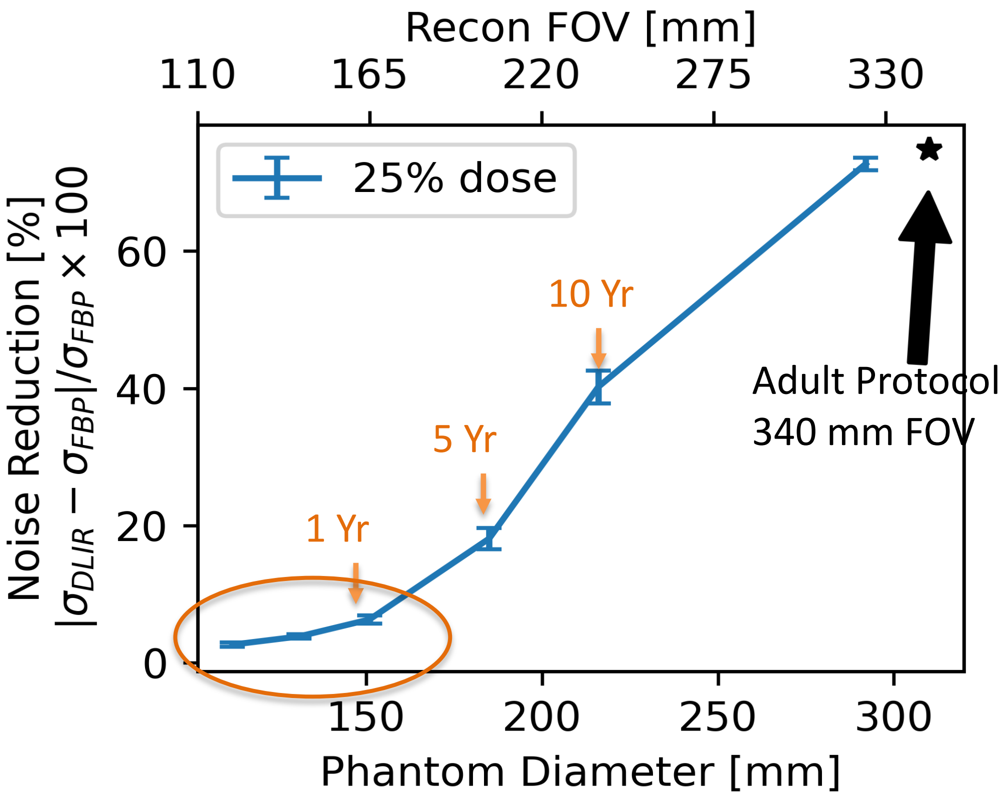
Image Sharpness

HU Accuracy

Noise

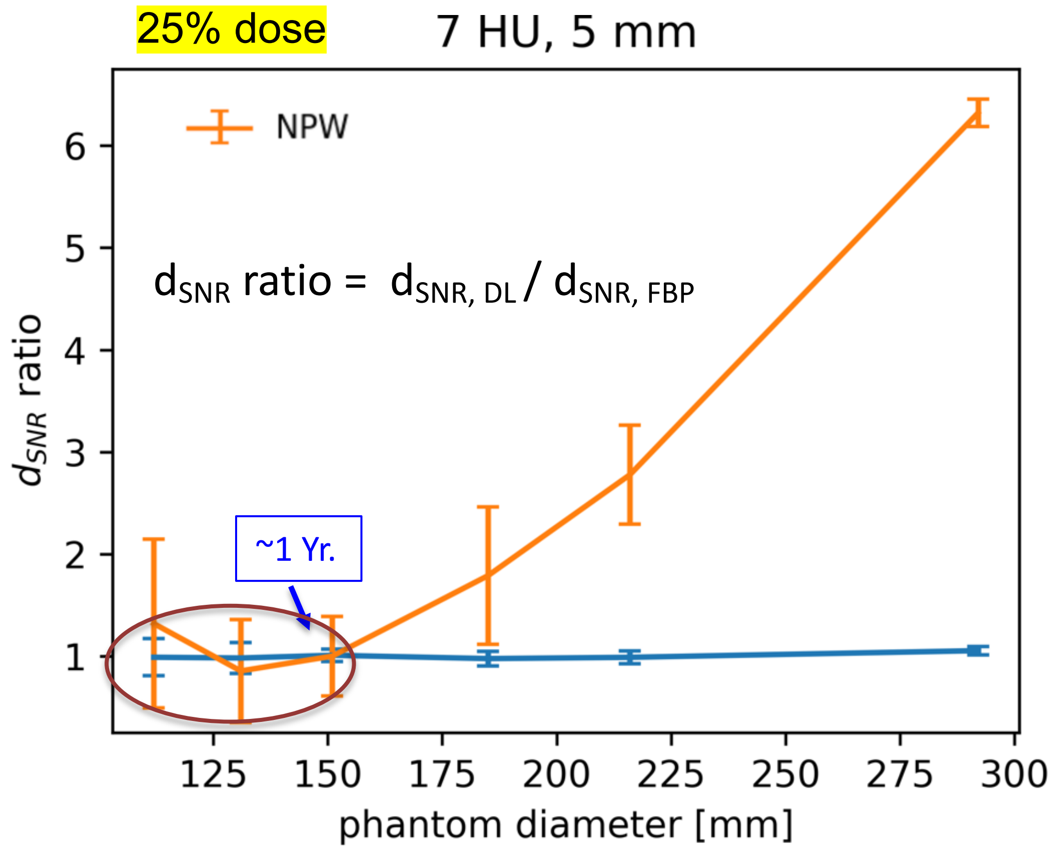
Low Contrast Detectability

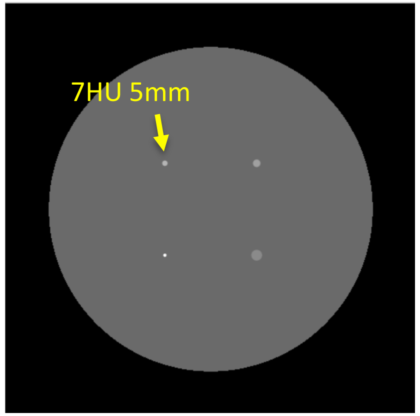




# Preliminary results

Image Sharpness ✓ | HU Accuracy ✓ | Noise ✗ | Low Contrast Detectability ✗



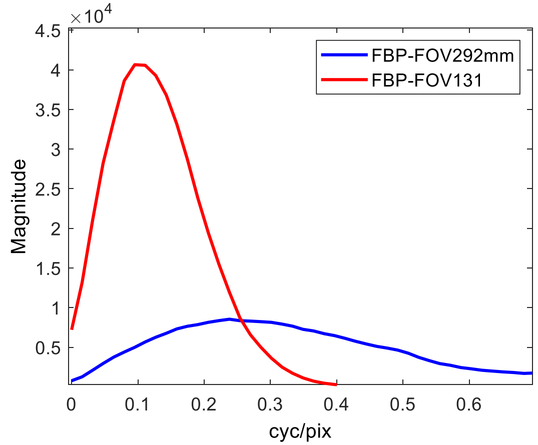



# Take-home message

Image Sharpness ✓ | HU Accuracy ✓ | Noise ✗ | Low Contrast Detectability ✗

- DLR, if trained exclusively with adult patient data, may lose benefit on CT scans of small pediatric patients (1 yr and under).
  - Noise texture substantially changes with a very small reconstruction FOV.
  - Data augmentation to include small-FOV noise features in training, or separately trained model for small-FOV scans.

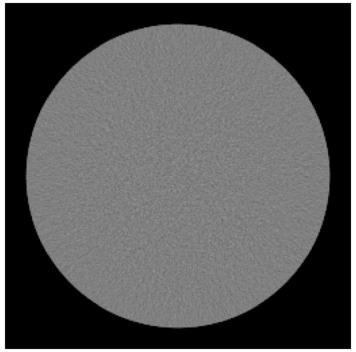
pNPS of FBP images of 292 and 131 mm FOV



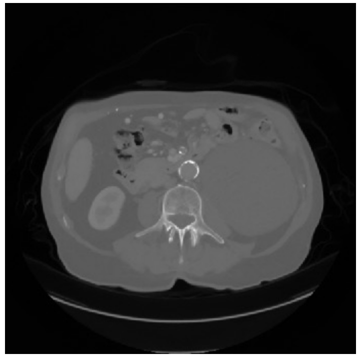
# 3. Generalizability in testing backgrounds

- The problem:
  - DLR is usually not trained with QA phantom images.
  - Do image quality (IQ) performances measured using the QA phantoms generalize well in patient images?
- Methods
  - Two types of image backgrounds
  - IQ measures: noise, edge-based MTF..
- Preliminary findings
  - MTF performance was similar between the two backgrounds
  - Noise performance could be quite different between the two backgrounds for some DL denoising models.

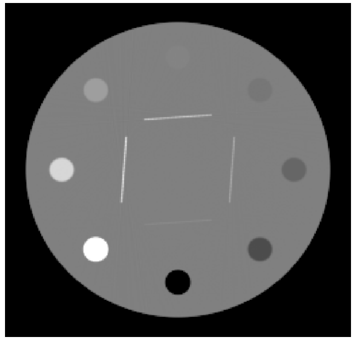
Uniform Bkg.



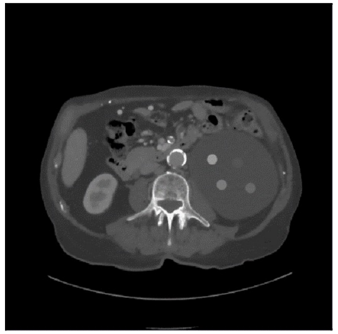
Anatomical Bkg.

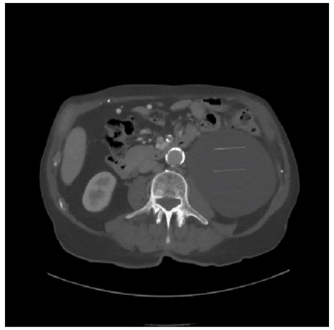


Test Objects in Uniform Bkg.



Test Objects in Anatomical Bkg.





Conference Presentation

**Bench testing performance of deep learning-based CT image denoising methods: influence of object background on image sharpness and noise texture**

Rongping Zeng, Prabhat KC, Brandon Nelson

23 February 2023 • 2:50 PM - 3:10 PM PST | Town & Country A | Part of SPIE Medical Imaging

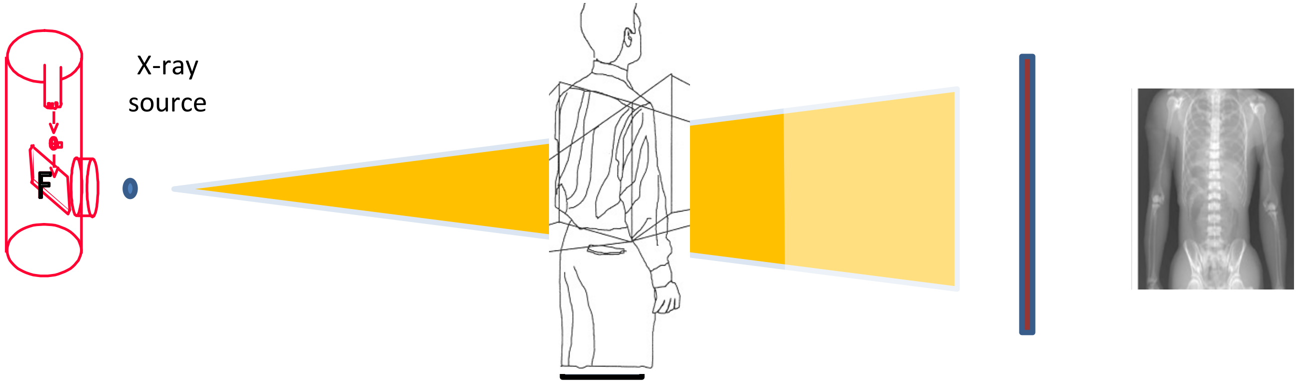
# Outline

1. Introduction
2. AI/ML Image Processing Software regulatory Pathway and Considerations
3. Regulatory Science Research at FDA: Deep Learning Image Reconstruction and Denoising in CT
4. **Considerations and Regulatory Science Research at FDA: Evaluating Imaging Systems with Photon Counting Detectors**

# Energy integrated X-ray detectors

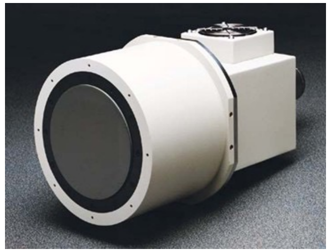
2- The energy fluence or exposition (J/mm²)

$$W = \int_{E_{min}}^{E_{max}} N(E)EdE$$




Photographic films


Imaging plates

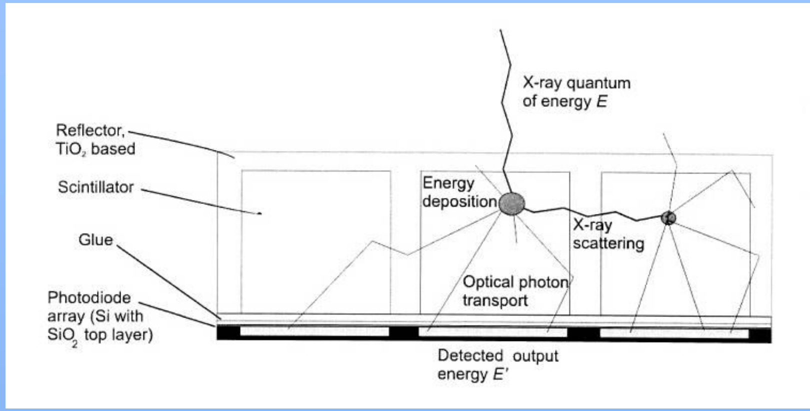


CCDs

Flat panel detector

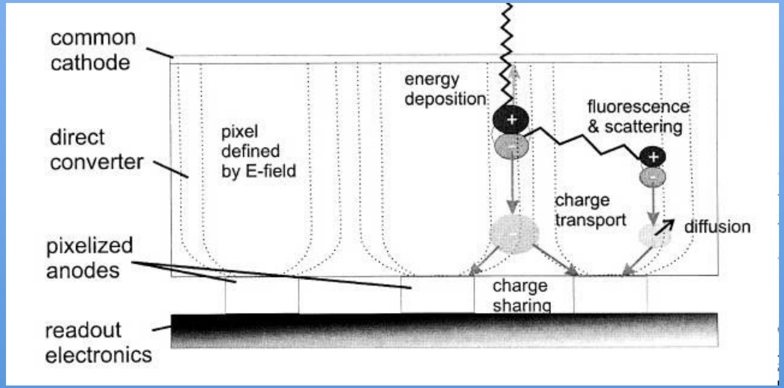
Electronically readable detectors

# X-Ray Energy Integrating Detector




Energy Integrating Detector


# X-Ray Photon Counting Detector

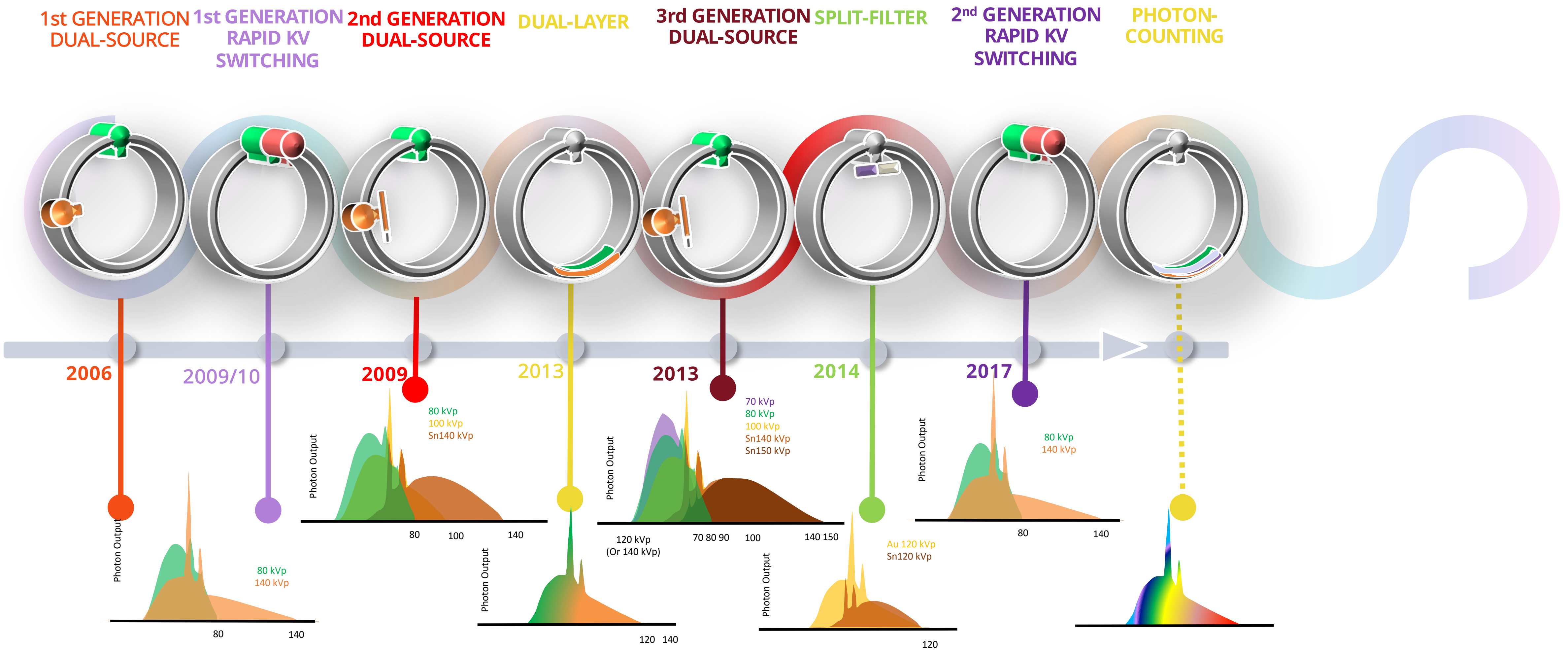



Photon Counting Detector


$$d_i = \sum_{j=\tau_{i-1}+1}^{\tau_i} r_{j,} \quad \text{for } i = 1,....N, \text{ and where } \{\tau_i$$

Acknowledgement: Jennifer Xu

# Spectral x-ray imaging Techniques




**Improved IQ, Workflow and Material discrimination capabilities**

**Dushyant V Sahani, CERN 2022**

# Spectral x-ray imaging Techniques

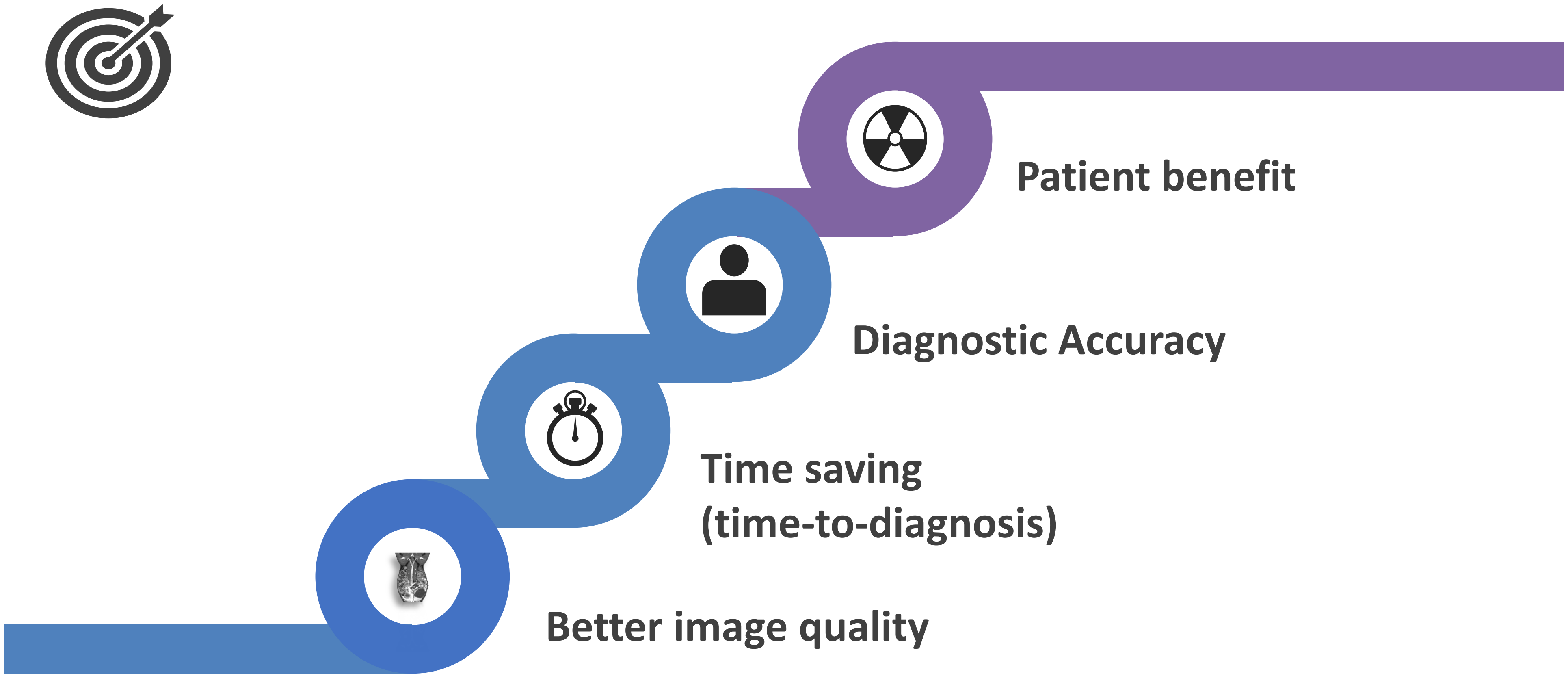
Techniques with photon counting detector

- No electronic noise
- Better spatial resolution
- Better SNR
- Shorter acquisition + Lower dose to the patient
- More than three Material-specific imaging can be generated

Dual-energy limitations:

- Spatial Resolution and Dose similar to conventional CT
- Very low contribution of low energy X-rays that contain most of the contrast information.
- Electronic noise can have a significant contribution to the total signal at low doses or in high attenuation
- body areas.

# PCD-CT potential value



# Current Photon-counting CT Projects Targeted Toward Full-Body Clinical CT

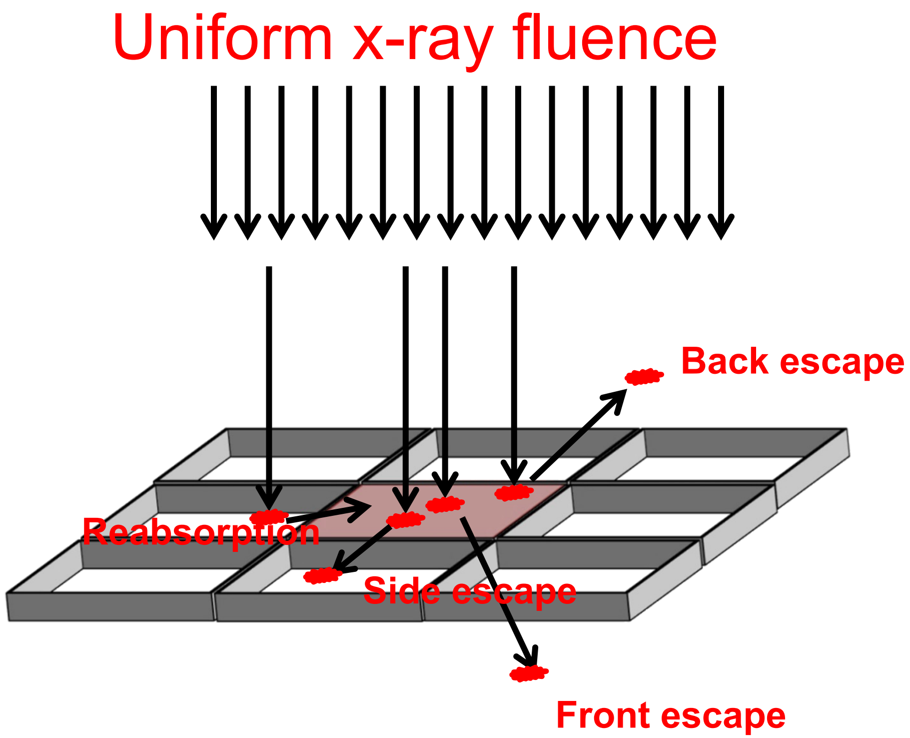
| Company | Detector Material | Detector element size () |
|---|---|---|
| Samsung or Neurologica: OmniTom Elite platform portable PCD CT system | CdTe | 1.25 mm and 0.625 mm |
| Canon Aquilion ONE ViSION (PCCT prototype) | CdZnTe | ? |
| GE Healthcare, Spectral photon-counting CT | CdZnTe | 0.5 x 0.5 $mm^2$ |
| Medipix (CERN, Switzerland) and MARS Bioimaging (Christchurch, New Zealand) Spectral photon-counting CT | CdZnTe | 0.11 x 0.11 $mm^2$ |
| Philips Healthcare, spectral photon-counting CT | CdZnTe | 0.5 x 0.5 $mm^2$ |
| Siemens (USA), Spectral CT, NAEOTOM Alpha | CdTe | 0.6 x 0.6 $mm^2$ |
| Siemens (USA), Spectral mammography System, Micro Dose | Silicon strip | 50 µm |
| GE Healthcare + KTH Royal Institute of Technology and Prismatic Sensors (Sweden) Spectral CT | Silicon strip | 0.5 x 0.4 $mm^2$ |
| Advanced-Breast-CT, AB-CT (Germany) | CdTe | 100 µm |

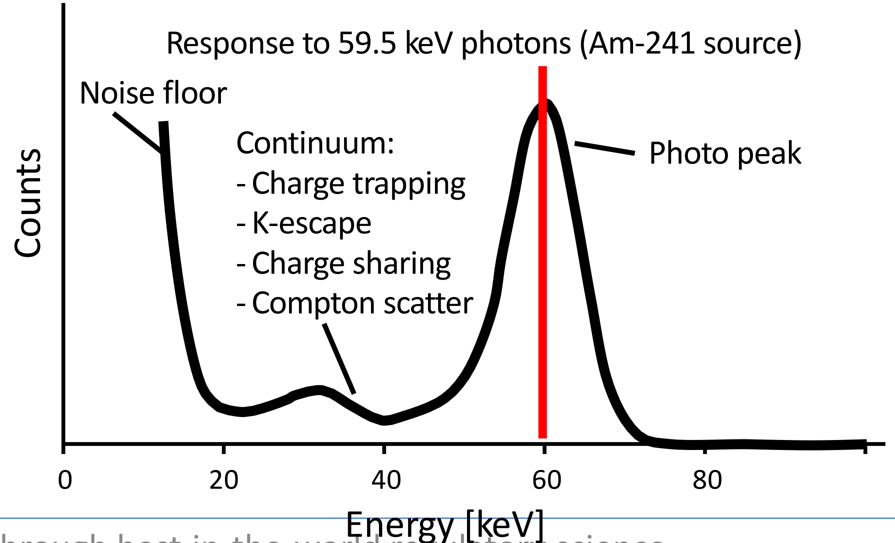
List Derived from Public Sources

# Photon counting detector: spectral and spatial distortions

Sources of distortions:

- X-ray fluorescence (Escape)
- X-ray fluorescence (Re-absorption)
- Charge trapping
- Pulse-pileup
- Transmission without interacting
- Compton scattering effects
- Image inhomogeneities & non-counting pixels



# Photon counting detector: spectral and spatial distortions

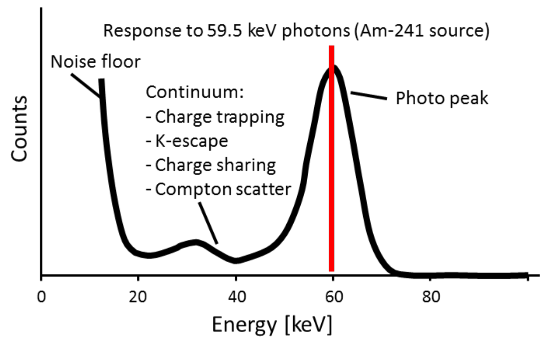
Sources of spectral distortions:

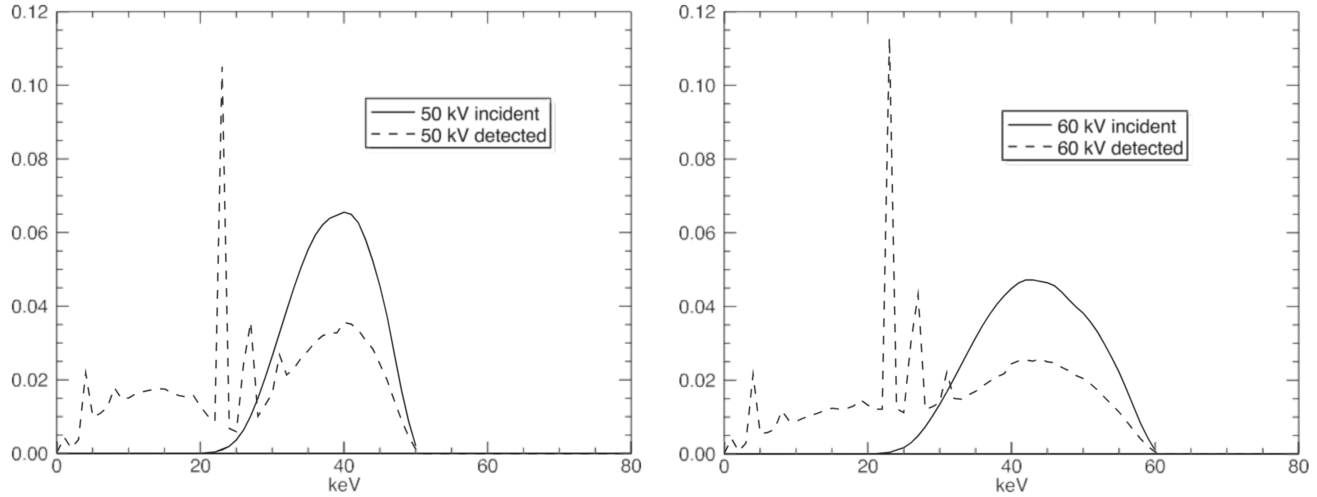
- X-ray fluorescence (Escape)
- X-ray fluorescence (Re-absorption)
- Charge trapping
- Pulse-pileup
- Transmission without interacting
- Compton scattering effects
- Image inhomogeneities & non-counting pixels

## Challenges

- Spectral response
- Large, gapless areas
- Sensor temporal stability
- Cost

# Photon counting detector: spectral and spatial distortions



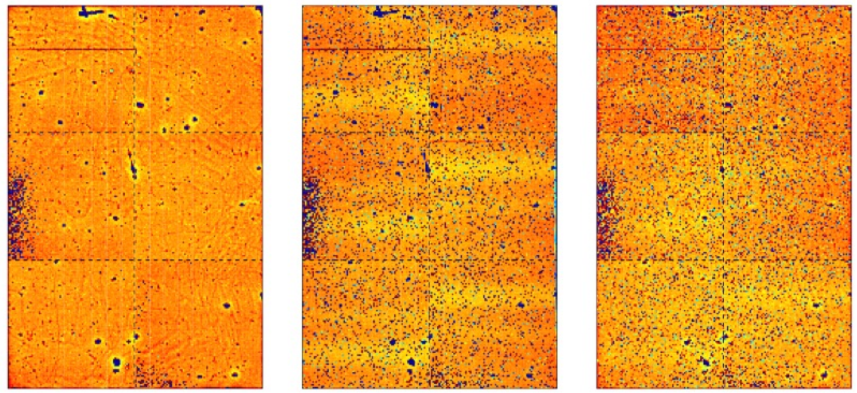



**Image inhomogeneity at different thresholds** **=> hard to modelled**

# Photon counting detector: spectral and spatial distortions

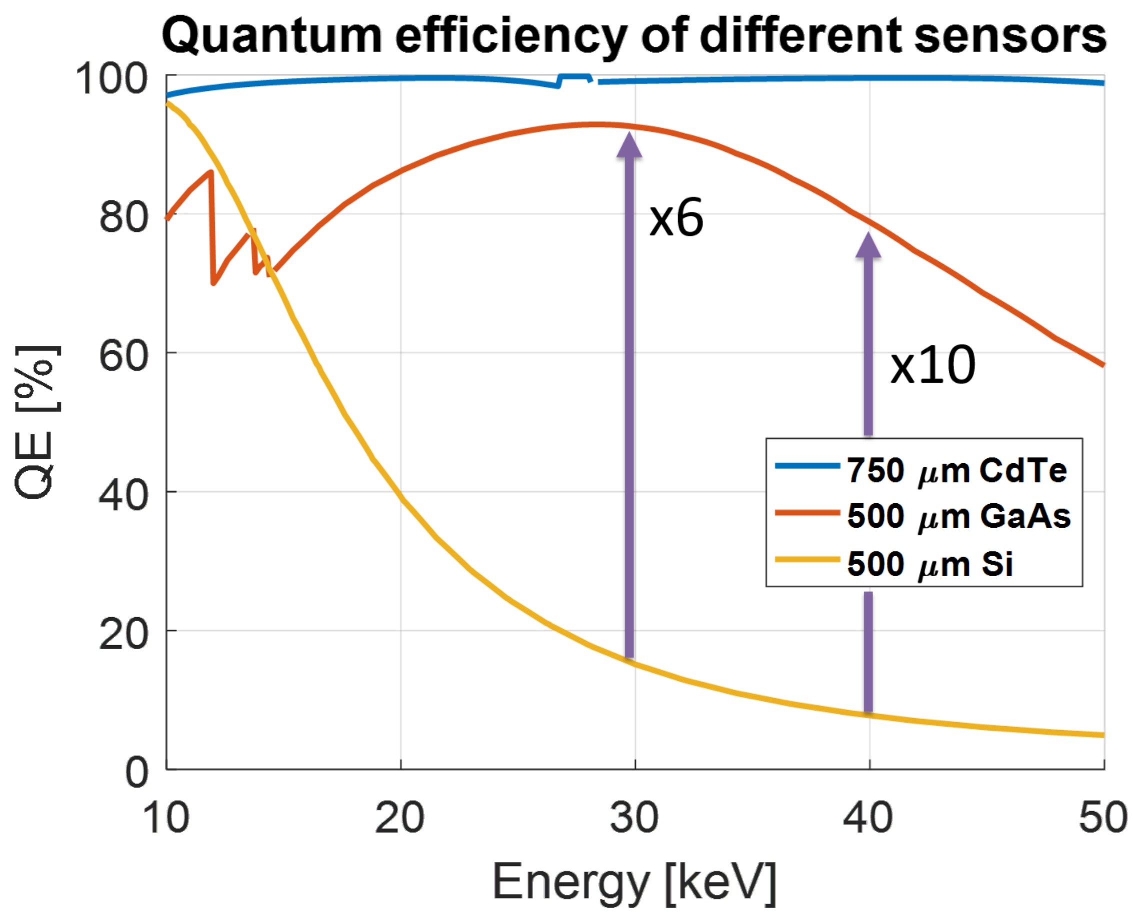
Photon Counting Detectors (PCD) - Unique Considerations:

Energy-Dependent Performance: The performance of PCDs can vary in several ways due to energy dependency.

- Pixel Variation within the same acquired image.
- Patient Variation
- Irradiation Condition Variation (kVp, filtration, and mAs).

Performance Test Adjustment:
to adapt standard performance tests traditionally used for conventional systems to assess the effectiveness of PCDs appropriately.

# Quantum efficiency (QE)




- **Silicon (Z=14)**
  - ✓ Very mature technology
  - x Relatively low Z
- **Gallium Arsenide (Z=31,33)**
  - ✓ Good charge collection properties
  - ✓ Fluorescence around 10 keV
  - x Crystal not widely available
  - x Crystal thickness (<0.5 mm) => low Quantum efficiency (>50 keV)
- **Cadmium Telluride (Z=48,52)**
  - ✓ High absorption efficiency <100 keV
  - ▪ Crystal quality is improving, but it is available only in small wafers
  - x Polarization issues at high photon fluxes (improving over the last years)
  - x Fluorescence at 23 and 27 keV

# Performance evaluation of Photon counting detector

**Fundamental properties of photon-counting detector should be provided and include:**

1. Detector resolution, Noise property: MTF, DQE
2. Count rate Vs current curve
3. Pulse pileup or maximum count rate
4. Lag or residual signal level from prior exposures that can be caused by polarization effects
5. Stability with time across the day and room temperature because CT scans can create a lot of heat
6. Spectral resolution
7. Bad pixel map

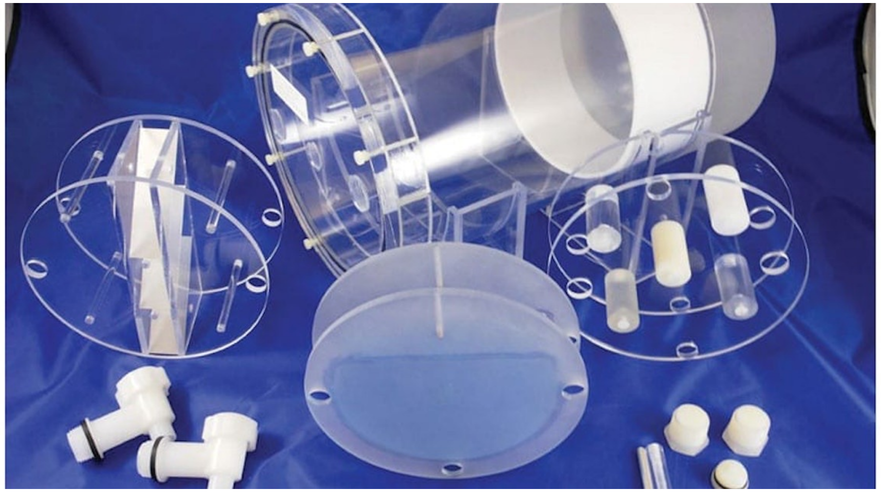
. . .

# Quantitative image quality evaluation for photon counting CT through phantom studies

**Bench testing performance:**

- CT Number Accuracy at different mAs and kVp (Spectral resolution can be affected by fluence)
- Contrast-to-Noise Ratios (CNR)
- Uniformity
- Slice Sensitivity Profile (SSP)
- Modulation Transfer Function (MTF)
- Low contrast Resolution
- Standard Deviation of Noise (SD) in Midplane
- Standard Deviation of Noise (SD) along z-axis
- Noise Power Spectra (NPS)
- Visual inspection of image artifacts.
- Low Contrast Detectability (LCD) (dose claims)

. . .



# Quantitative image quality evaluation for photon counting CT through phantom studies

**Quantitative measurements should be provided under the following conditions:**

- Different concentrations must be tested.
- Measurements must be taken at different realizations.
- Measurements must be taken using different phantom sizes acquired with different kVps (body rings).
- Different inserts' locations or distances from the center of the phantom must be tested.
- Measurements at different mAs must also be provided.
- A calibration process should be described in detail to ensure that the tests are representative and were not part of the algorithm development.

# Regulatory Science Research at FDA: Evaluating Imaging Systems with Photon Counting Detectors

FDA

1. DIDSR photon counting x-ray imaging laboratory capabilities.
2. Characterization of a GaAs photon counting detector for mammography – Collaboration with Dectris Ltd
3. Advancements in using computational modeling for device evaluation: PcTK updates
4. Assessing Spectral Efficiency in Quantitative Contrast-Enhanced Breast CT Using a CdTe Photon-Counting Detector

# Available Commercial Photon Counting Detectors

| Available Commercial Photon Counting Detectors | | | | | | |
|---|---|---|---|---|---|---|
| Company | ASiC | Pixel Size (µm) | FOV size | Sensors | Thresholds | Price |
| Dectris - IBEX | custom | 75/150 | 19.2 mm | CdTe/GaAs | 2/4 | |
| X-Spectrum | Medipix 3XR | 55/110 | 14.1 mm | CdTe/GaAs | Up to 8 | |
| XIE | Medipix 3XR | 55/110 | 14.1 mm | CdTe/GaAs | Up to 8 | |
| DxRay | custom | 1.1 x 1.4 mm | 70.4 x 5.6 mm | CdTe | | |
| DxRay (edge-on Si) | custom | 100 | 0.1 mm x 25.6 mm<br>0.1 mm x 10.24 mm | Si | | |
| Varex | Xcounter<br>Xthor | 100 | 206mm x 6mm<br>350mm x 6mm<br>510mm x 6mm<br>80mm x 12.8mm<br>80mm x 25.6mm<br>100mm x 12.8mm<br>100mm x 25.6mm<br>13mm x 26mm<br>26mm x 26mm<br>39mm x 26mm<br>52mm x 26mm | CdTe | 2 | |
| HEXITEC | HEXITEC ASIC | 250 | 2 x2 cm | CdTe | MCA | |

# Available Commercial Photon Counting Detectors

| Available Commercial Photon Counting Detectors | | | | | | |
|---|---|---|---|---|---|---|
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| **HEXITEC** | **HEXITEC ASIC** | **250** | **2 x2 cm** | **CdTe** | **MCA** | |

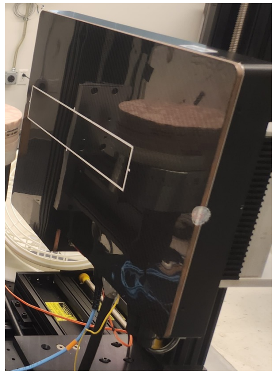
***Available in DIDSR***

# Available PCDs in DIDSR


1 pixel 3x3x1 mm³ Cadmium Telluride (CdTe) based detector (Amptek)


1 pixel 5x5x1 mm³ Silicon based detector (Amptek)

1 pixel High-purity Germanium (HPGe) one pixel Detectors



2D planner 30 x 5cm²) CdTe based detector with 100 µm pixel size (Xcounter)

2D planner (1.4 x 1.4 cm²) GaAs based detector with 52 µm pixel size (Medipix 3XR )


| Sensor | CdTe |
|---|---|
| Thickness | 500 µm |
| Pixels size | 100 µm |
| Size | 30 x 5 cm² |
| Max counts rate | 3.5 x10⁸ counts/mm²/s |

| Sensor | GaAs |
|---|---|
| Thickness | 500 µm |
| Pixels size | 55 µm |
| No of pixels | 256x256 |
| Max counts rate | 2.5 x10⁶ counts/mm²/s |

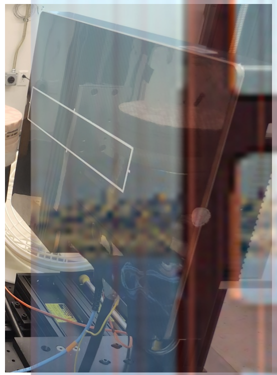
| Sensor | CdTe |
|---|---|
| Thickness | 1000 µm |
| Pixels size | 250 µm |
| No of pixels | 80x80 |
| Max counts rate | …….counts/mm²/s |

# Available PCDs in DIDSR


1 pixel 3x3x1 mm³ Cadmium Telluride (CdTe) based detector (Amptek)


1 pixel 5x5x1 mm³ Silicon based detector (Amptek)

1 pixel High-purity Germanium (HPGe) one pixel Detectors



2D planner 30 x 5cm²) CdTe based detector with 100 μm pixel size (Xcounter)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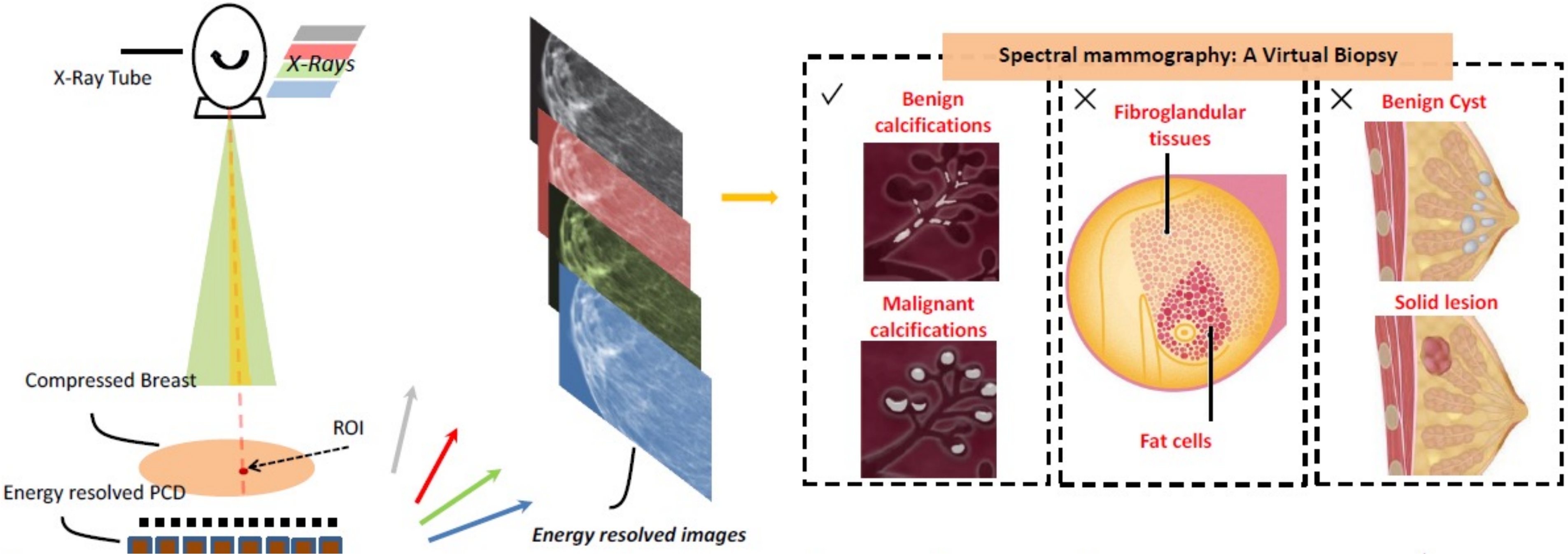
|---|---|
| Thickness | 1000 μm |
| Pixels size | 250 μm |
| No of pixels | 80x80 |
| Max counts rate | …….counts/mm²/s |

# Imaging of the Breast with Photon-Counting Detectors



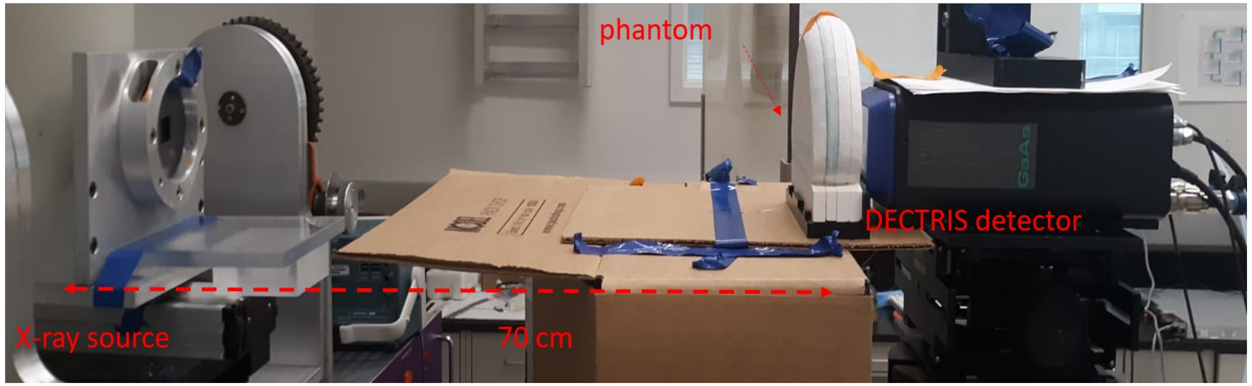

- To improve image contrast, noise, spatial resolution[2] and for dose reduction.
- To differentiate between malignant vs benign microcalcification clusters. Accurate quantitative estimation of breast density.
- Quantitative analysis of contrast-enhanced spectral mammography.
- To differentiate between solid lesion masses vs fat-filled cysts[3].

⇒ Will reduce unnecessary breast biopsies and provide improved patient risk stratification.


1 Glick, S. J. & Ghammraoui, B. in. Chap. Imaging of the Breast with Photon-Counting Detectors (CRC Press, 2020).
2 Van Eeden D, D. P. F. Multi-Energy Computed Tomography Breast Imaging with Monte Carlo Simulations: Contrast-to-Noise-Based Image Weighting. *Medical Physics* **44,** 106–112 (2019).
3 Erhard, K. *et al.* Characterization of Cystic Lesions by Spectra Mammography Results of a Clinical Pilot Study. *Invest. Radiol.* **51,** 340–347 (2016).

# Collaboration with DECTRIS

- Study 1: Characterization of a GaAs photon counting detector for mammography
- Study 2: Contrast-enhanced spectral mammography with GaAs photon counting detector
- Study 3: Classification of breast microcalcifications with GaAs photon-counting spectral mammography using an inverse problem approach




*[1] Investigating the feasibility of classifying breast microcalcifications using GaAs photon-counting spectral mammography B Ghammraoui, S Bader, T Thuering, SJ Glick - Medical Imaging 2022: Physics of Medical Imaging, 2022*
*[2] Classification of breast microcalcifications with GaAs photon-counting spectral mammography using an inverse problem approach B Ghammraoui, S Bader, T Thuering, SJ Glick Biomedical Physics & Engineering Express, 2023*

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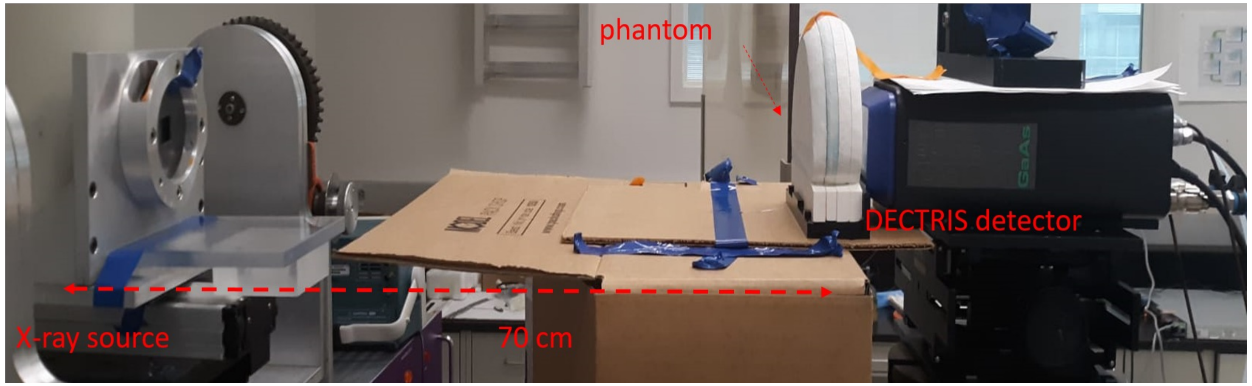


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# GaAs sensor for PCD breast imaging: Previous experimental studies

## Study 1: Characterization of a GaAs photon counting detector for mammography

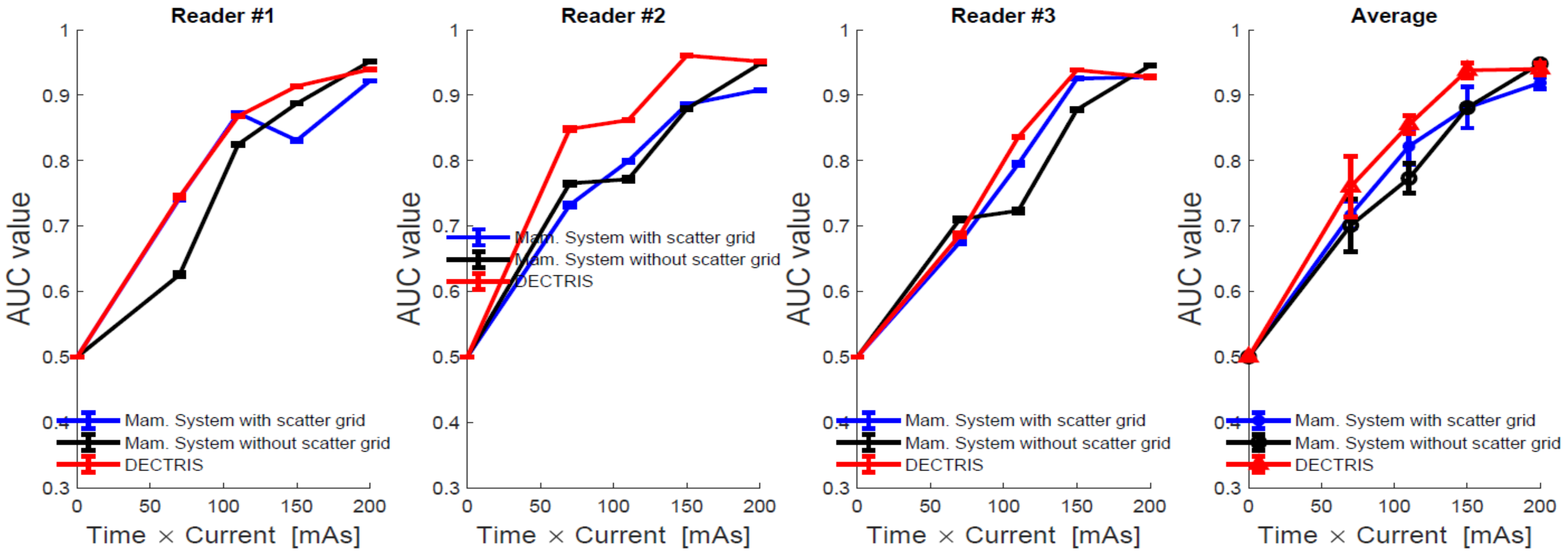
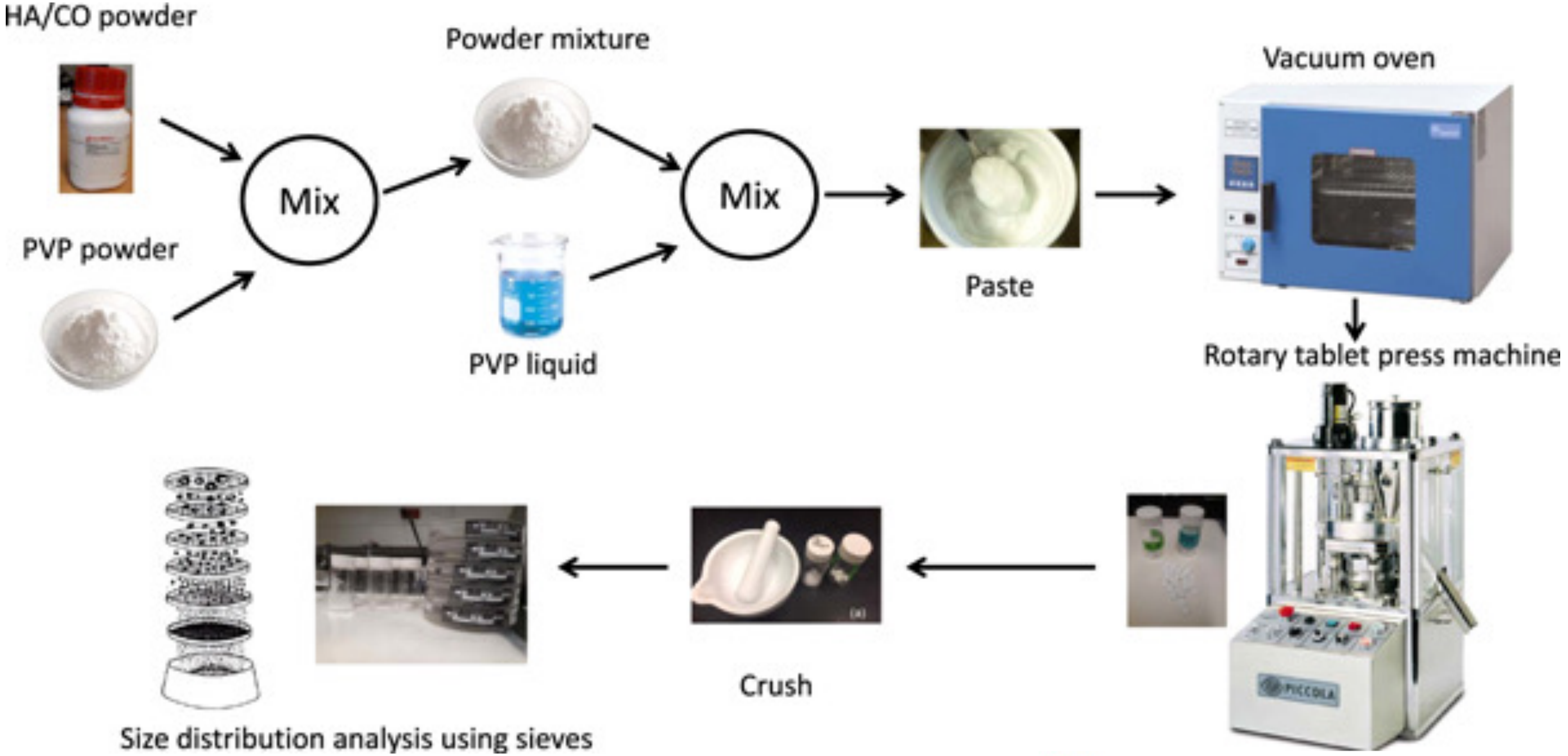



Figure: Microcalcification detectability: The area under ROC curves for the commercial digital mammography system and the mammography system with GaAs PCD.

In this study, GaAs spectral mammography demonstrated slightly improved or equivalent performance versus commercial mammography systems.

# Regulatory science tool: Method for Fabrication of microcalcifications for insertion into phantoms used to evaluate x-ray breast imaging systems.

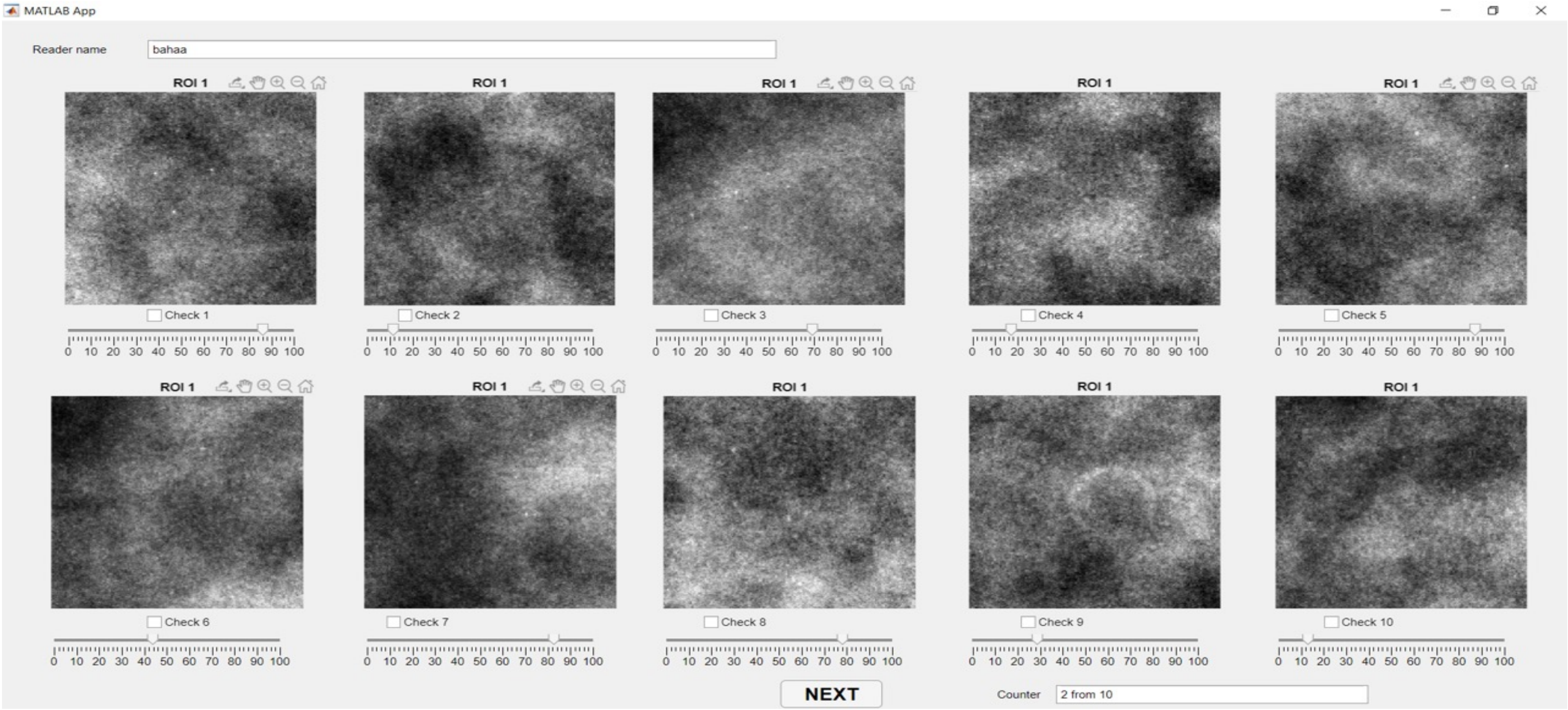



PAPER

Fabrication of microcalcifications for insertion into phantoms used to evaluate x-ray breast imaging systems

Bahaa Ghammraoui[1], Ahmed Zidan[2], Alaadin Alayoubi[2], Aser Zidan[2,3] and Stephen J Glick[1]

# Example deliverables: A GUI for human observer study with receiver operating characteristic (ROC) analysis.




Observers are asked to rate images using a continuous scale from 0 to 100, indicating their confidence that microcalcifications were in the image

# Collaboration with Johns Hopkins University

- Study 1: Inclusion of a GaAs detector model in the Photon Counting Toolkit software for the study of breast imaging systems
- Study 2: Theoretical comparison and optimization of cadmium telluride and gallium arsenide photon-counting detectors for contrast-enhanced spectral mammography

| Number of modules | 1 module with 1 GaAs sensor |
|---|---|
| Sensor | GaAs |
| Thickness | 500 µm |
| Quantum efficiency | 75% at 40 keV |
| Readout chip | Medipix3 |
| Pixel size | 55 × 55 µm |
| Count rate per pixel | 200,000 counts/pixel/s (with count rate correction)<br>800, 000 counts /pixel/s (without count rate correction) |
| Energy range | 5 keV – 80 keV |
| Energy resolution | 1 keV |
| Max framing rate | 2000 Hs (12 bit mode) |

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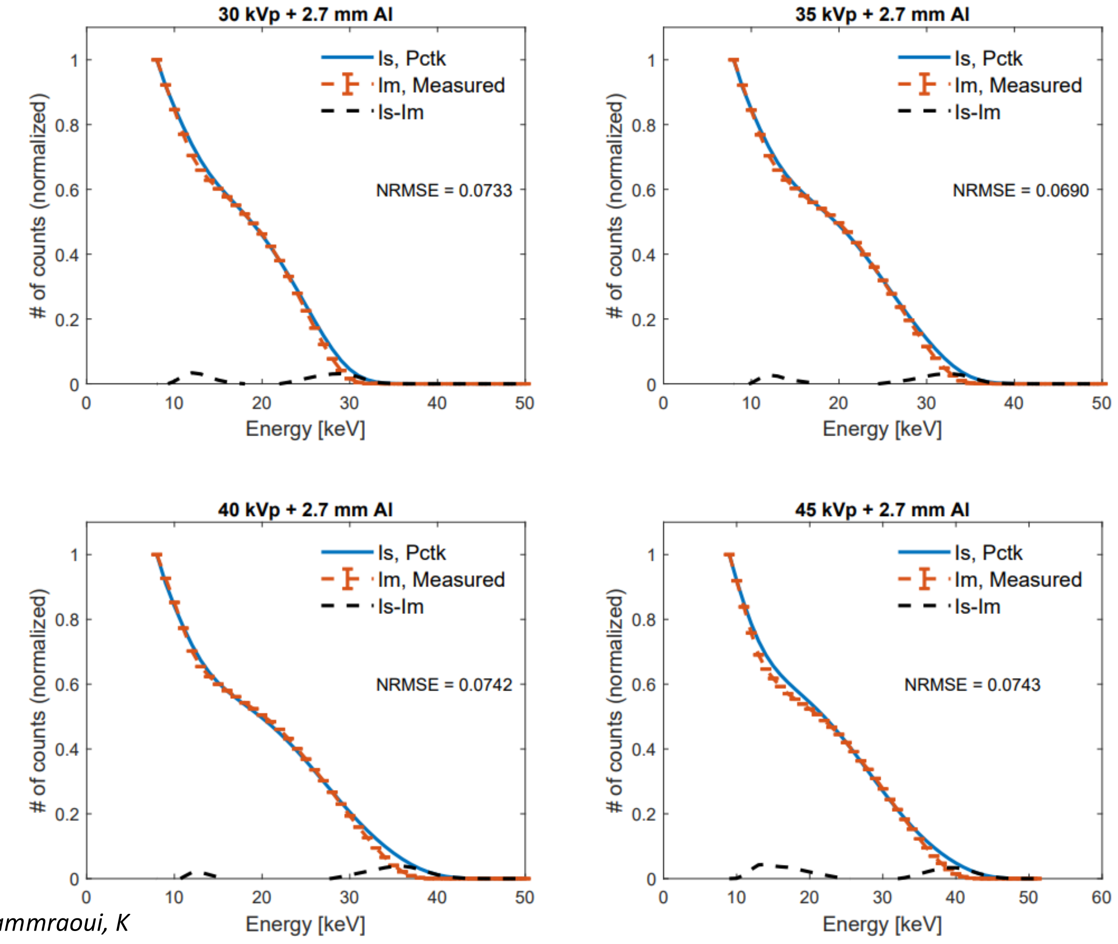
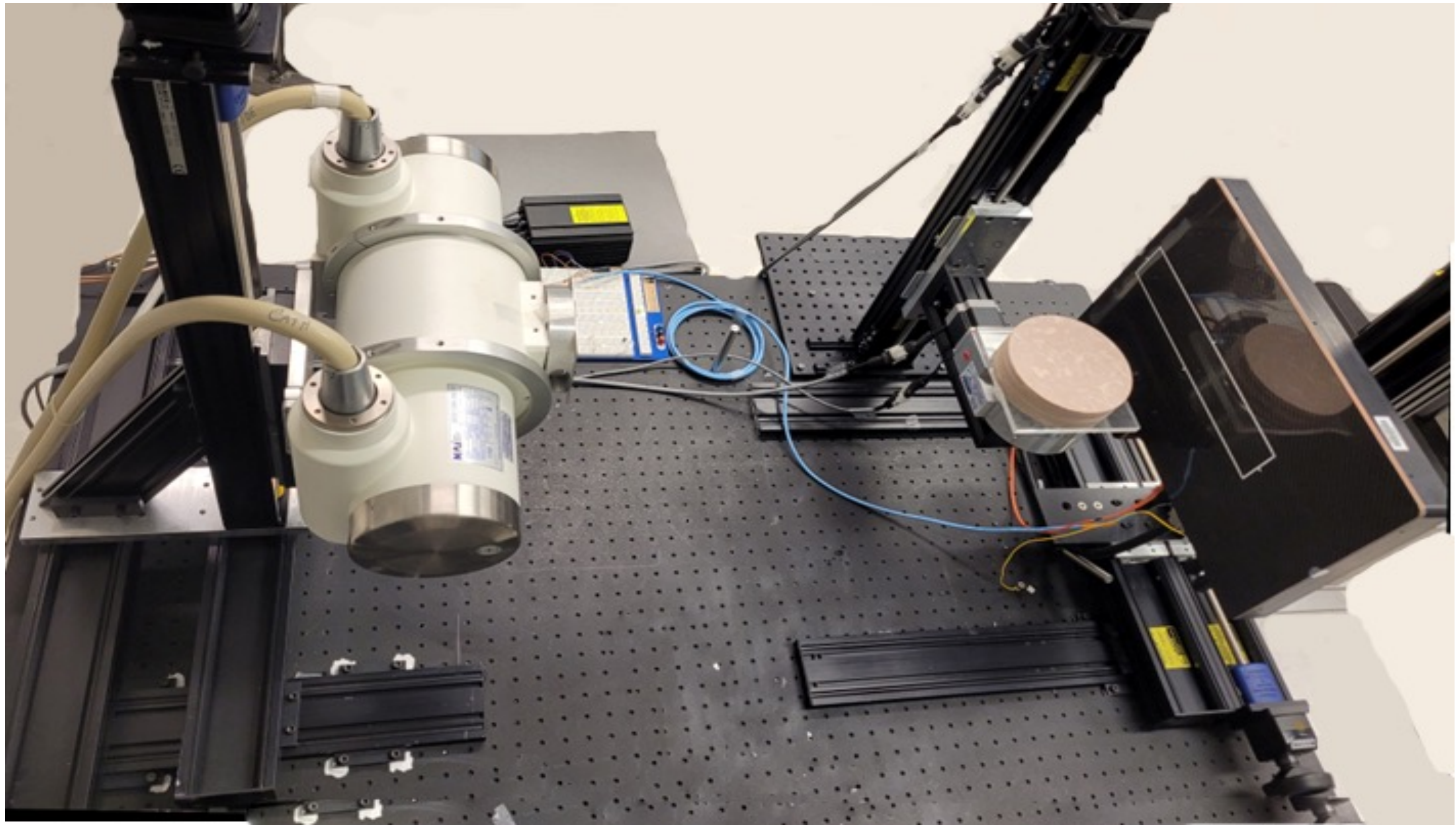



*[1] Inclusion of a GaAs detector model in the Photon Counting Toolkit software for the study of breast imaging systems B Ghammraoui, K Taguchi, SJ Glick - Plos one, 2023*
*[2] Theoretical comparison and optimization of cadmium telluride and gallium arsenide photon-counting detectors for contrast-enhanced spectral mammography. C Schaeffer, B Ghammraoui, K Taguchi, SJ Glick - Journal of Medical Imaging, 2023*

# Updated PCTK

# X-Thor detector - PCD-CT benchtop



| Sensor | CdTe |
| --- | --- |
| Pixel size | 100 um |
| Size | 5 x 30 cm**2 |
| Thickness | 750 um |
| Thresholds | Two |
| Operation Modes | Charge summing mode + standard mode |

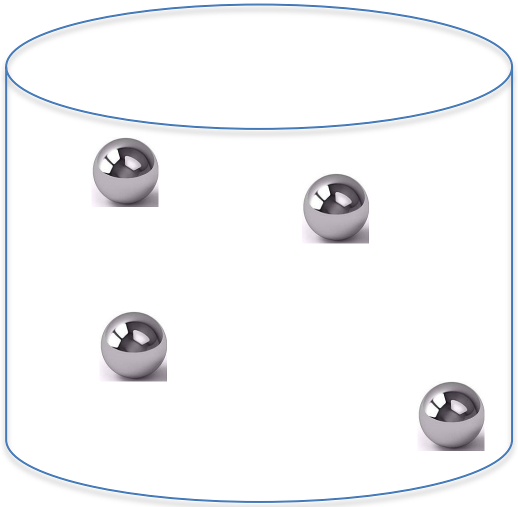
# PCD-CT benchtop

- Study 1: An empirical method for the geometric calibration of a photon counting detector-based cone beam CT system
  - Standard method are not applicable due to the relatively small detector size.
  - Three figure of merits was used to iteratively find or evaluate the accurate geometrical parameters of a cone beam PCD-CT:

The sphericity (ψ) of a reconstructed BB :

$$\psi = \frac{\pi^{1/3}\left(6V_p\right)^{2/3}}{A_p}$$

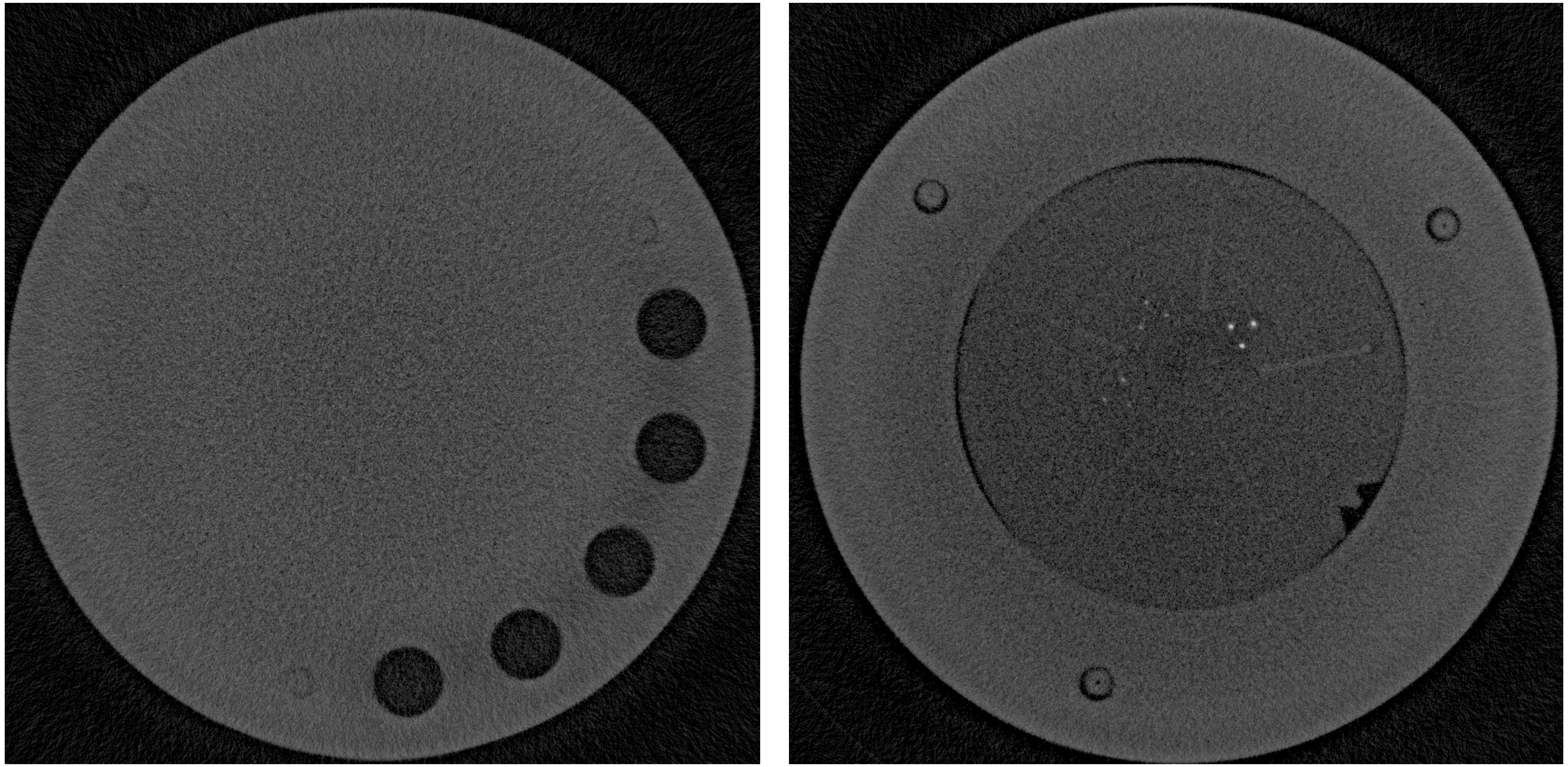
Symmetricity: Standard deviation among the estimated volumes of reconstructed BBs $\{V_{p1}, V_{p2}, \ldots V_{pi}, V_{pN}\}$



Physical phantom with ball-bearing spheres

*Development of an iterative method for the geometric calibration of a photon counting detector-based cone beam CT system. MU Ghani, A Makeev, JL Manus, SJ Glick… - Medical Imaging 2023: Physics of Medical Imaging, 2023*

# PCD-CT benchtop

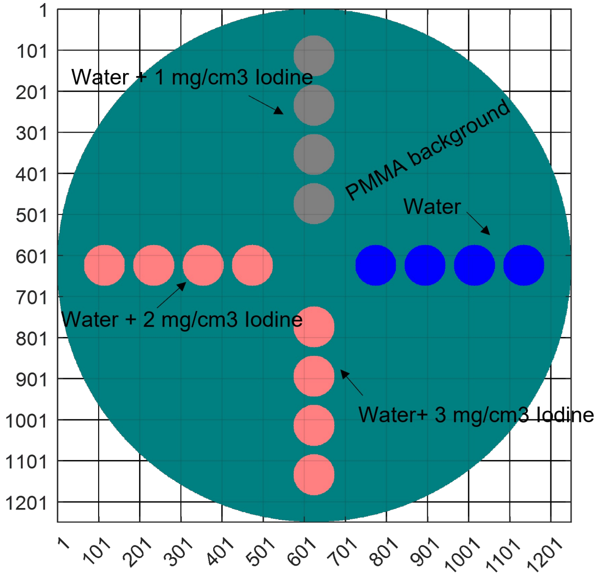


Reconstructed images of the ACR phantom

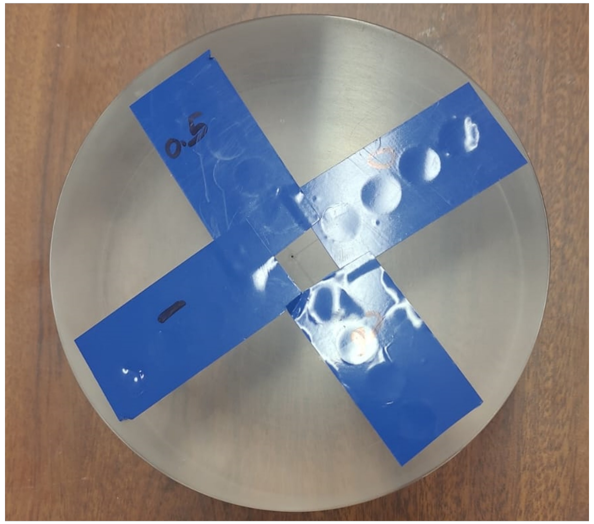
# PCD-CT benchtop

- Study 2: Assessing Spectral Efficiency in Quantitative Contrast-Enhanced Breast CT Using a CdTe Photon-Counting Detector: An Experimental Approach

(a)



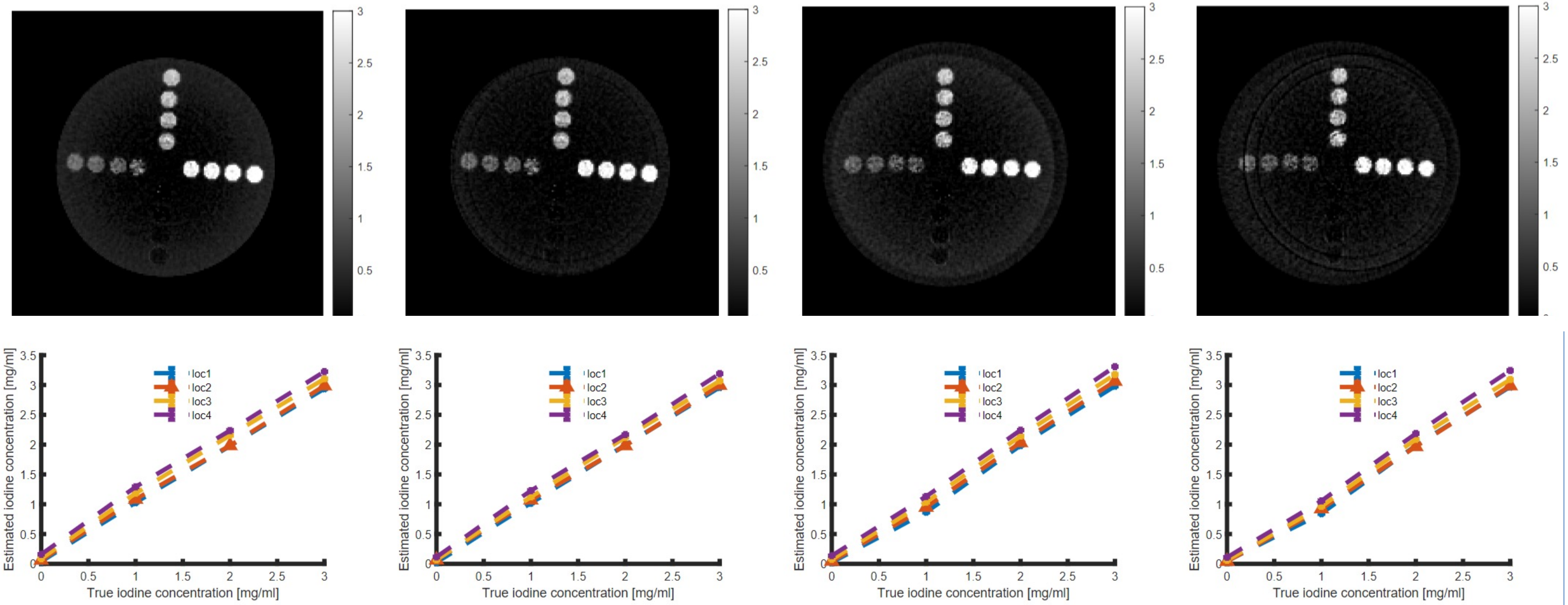

(b)



Physical phantom

*Assessing Spectral Efficiency in Quantitative Contrast-Enhanced Breast CT Using a CdTe Photon-Counting Detector: An Experimental Approach. Bahaa Ghammraoui, MU Ghani, JL Manus, SJ Glick… - In preparation*

# PCD-CT benchtop




(i) 12 cm, STC (j) 12 cm, STC+ LEF (k) 16 cm, STC (l) 16 cm, STC+ LEF

# PCD-CT benchtop

- Study 1: Assessing Spectral Efficiency in Quantitative Contrast-Enhanced Breast CT Using a CdTe Photon-Counting Detector: An Experimental Approach

## Figure of Merits

The performance of the quantitative methods under study was evaluated using four metrics:

- Root-mean-square (RMS) error between the estimated iodine concentration $C_i$ and the known values $C_i^{true}$:

$$RMSE = \sqrt{\frac{\sum_{i=1}^{9}(C_i - C_i^{true})^2}{9}} \qquad (7)$$

- The correlation $C_r$ between the measured and known values.
- Precision of the iodine estimation, as measured by the population standard deviation ($\sigma_{ci}$) across different realizations and the standard deviation between locations ($\Sigma_{ci}$):

$$\sigma = \sqrt{\frac{\sum_{i=1}^{Nr}(C_i - C_i^{mr})^2}{Nr}}$$
$$\Sigma = \sqrt{\frac{\sum_{i=1}^{9}(C_i - C_i^{ml})^2}{9}} \qquad (8)$$

Where $C_i^{mr}$ and $C_i^{ml}$ represent the mean values of the estimated iodine concentration across different realizations and across the three different locations of the disks with the same known concentration, respectively.

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  - Miguel A. Lago

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# Regulatory Science Tools

## CDRH’s Office of Science and Engineering Labs (OSEL)

Contact at:
OSEL_CDRH@fda.hhs.gov

Website:
https://www.fda.gov/medical-devices/science-and-research-medical-devices/medical-device-regulatory-science-research-programs-conducted-osel

Tools Catalog:
https://www.fda.gov/medical-devices/science-and-research-medical-devices/catalog-regulatory-science-tools-help-assess-new-medical-devices

FDA U.S. FOOD & DRUG ADMINISTRATION

**Catalog of Regulatory Science Tools to Help Assess New Medical Devices**

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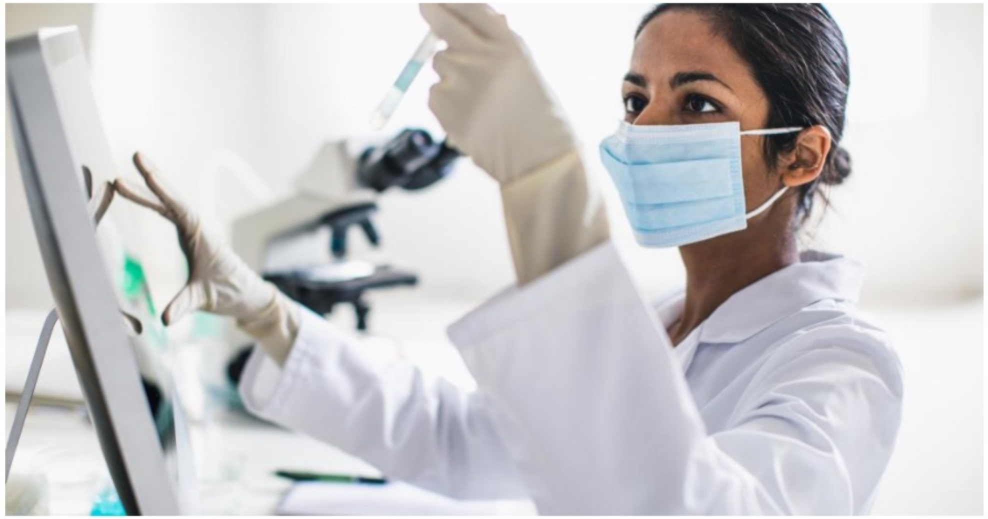

# Thank you!

# Questions?

- For more information on medical device regulations:

  https://www.fda.gov/training-and-continuing-education/cdrh-learn
  https://www.fda.gov/medical-devices/digital-health-center-excellence