

# Imaging Management In Clinical Trials

Achala Vagal, MD,MS

Professor of Radiology

Associate Dean of Clinical and Translational Research

Executive Vice Chair and Vice Chair of Research

University of Cincinnati Medical Center

# Disclosures

- NIH/NINDS NS103824
- NIH NINDS/NIA NS117643
- NIH/NINDS NS100417
- NIH/NINDS NS 069763
- NIH/NINDS NS120493
- NIH/NINDS U01 NS120910
- NIH/NINDS U01NS100699
- NIH/NINDS U01NS110772
- NIH/NINDS U01NS117450
- PI, Imaging Core Lab, ENDOLOW Trial, Cerenovus
- Consultant, Viz.ai, Inc

## Learning objectives

1. To understand the imaging workflow in a clinical trial
2. To understand practical considerations when designing a clinical trial
3. To be familiar with common imaging challenges

*Practical tips and strategies*

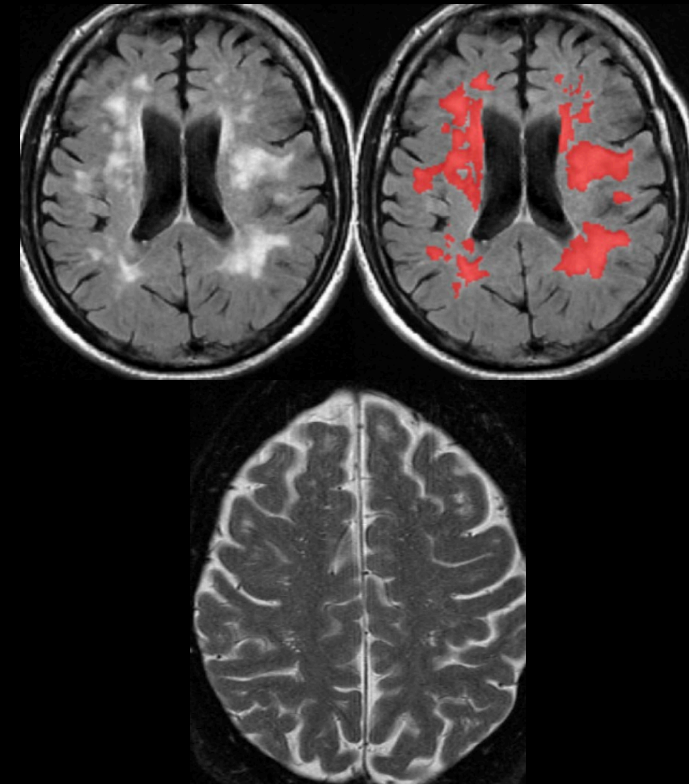
# Imaging Management Center University of Cincinnati



- **National Imaging Management Center for NIH StrokeNET**
- Long standing history (over 20 years) in being the imaging core lab for clinical trials in ischemic stroke, ICH, brain health
- Multiple NIH and industry clinical trials and population-based studies: IMS 3, CLEAR, CLEAR-ER, PRISMS, ERICH, GERFHS, ROSE-ICH, ROSE-LAWN, MOST, FASTEST, ROSE-LAWN, ERICH-Gene, APRISE, APRISE-Dementia, VERIFY, CAPTIVA, CAPTIVA MR, TESTED, SISTER, STEP, upcoming REASSESS MRI and TR2
- Dedicated imaging research personnel with deep expertise

# Need for comprehensive imaging solutions for clinical research

- **Massive amount of imaging data** in clinical trials and clinical research
- Centralized solutions to easily collect, search, sort, and create imaging data cohorts
- Reduce the number of imaging protocol deviations
- Avoid delays in imaging data transfer
- Maintain consistency and accuracy of imaging data interpretation and analysis



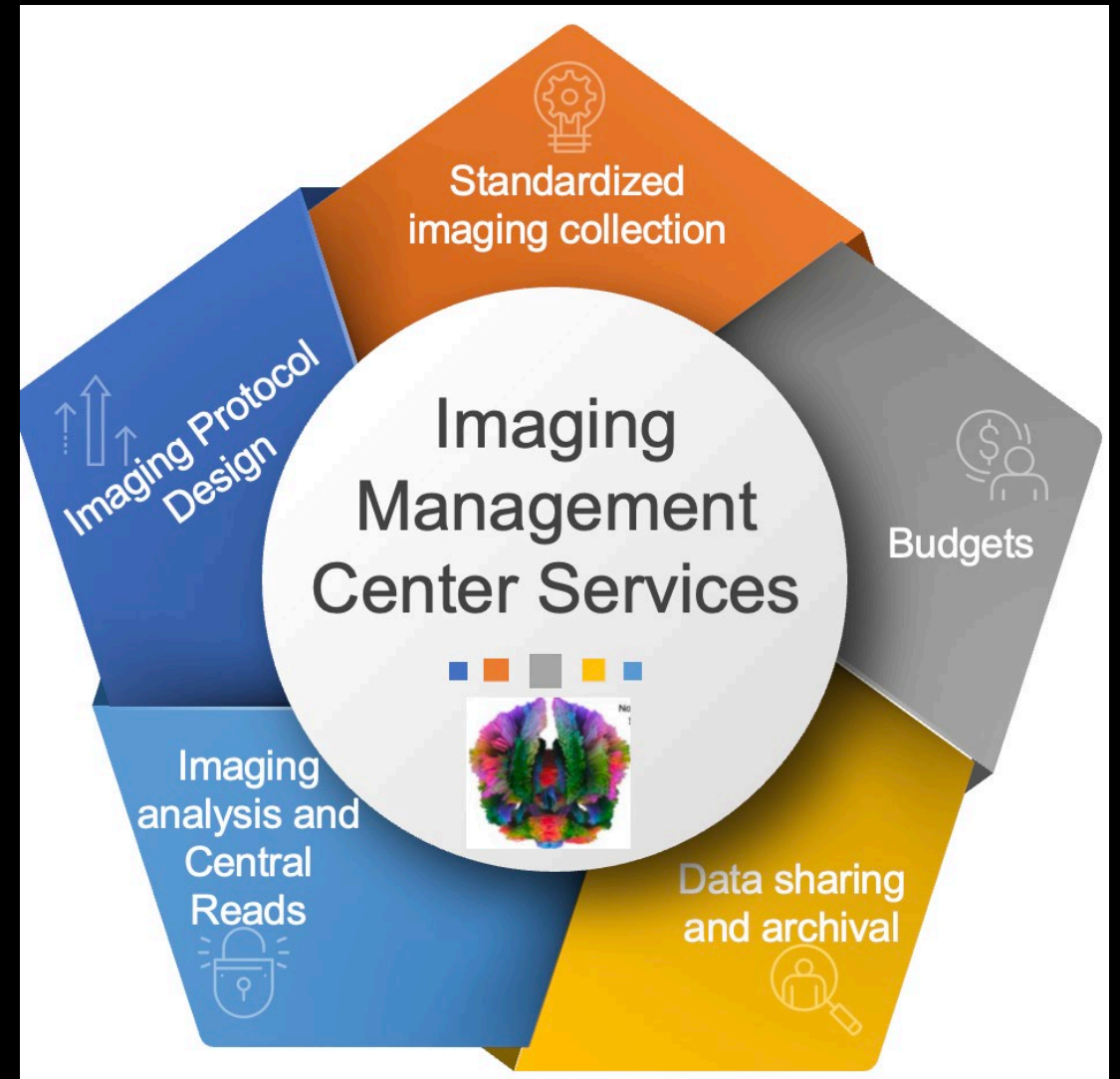
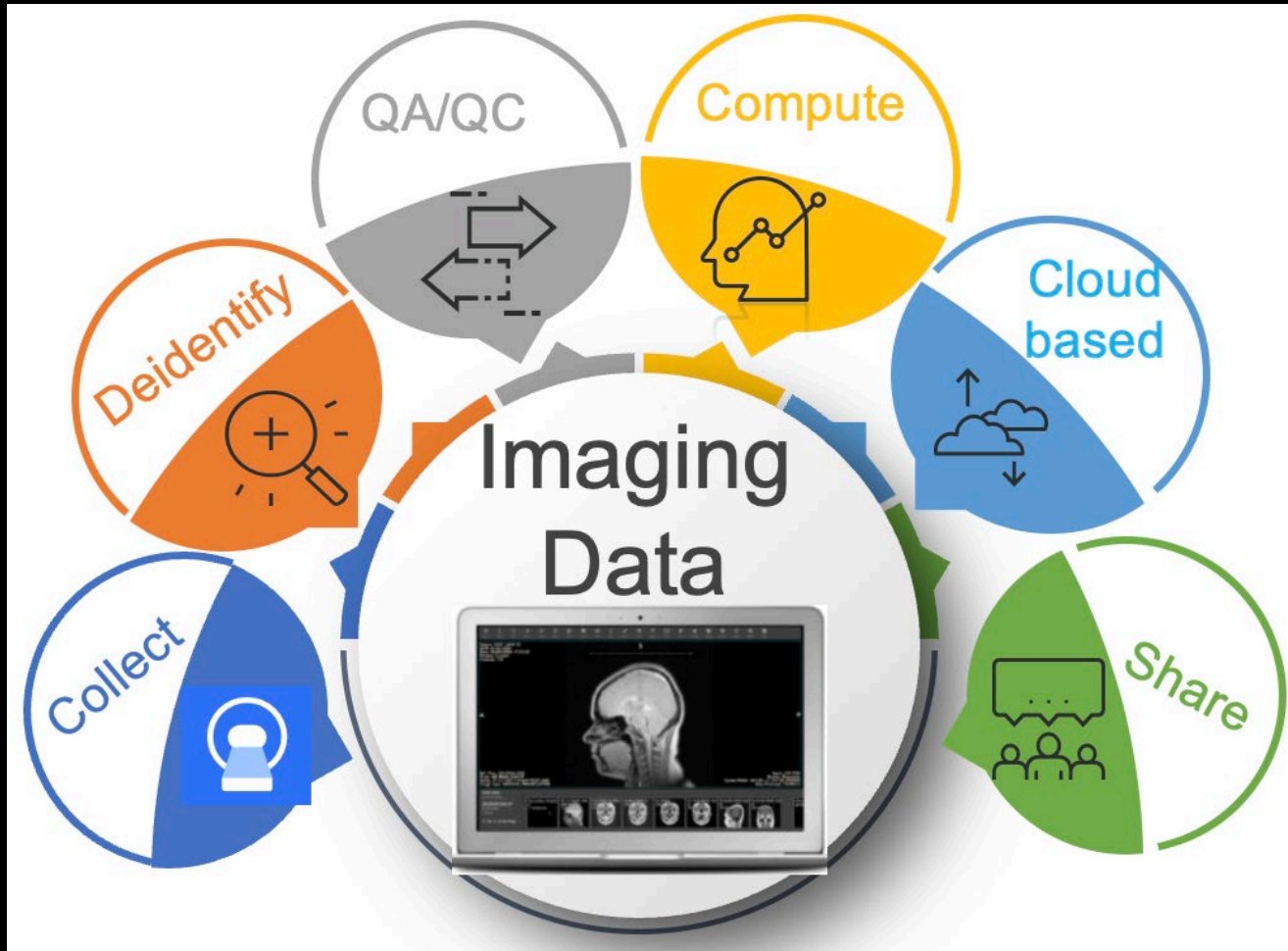
# Most important Takeaway



 **Involve Radiology/Imaging group  
EARLY in your study**



# Imaging Management Center/Imaging Core Lab



# Imaging workflow in a clinical trial

- Trial design and planning (imaging biomarkers/imaging endpoints)
- Regulatory and administrative tasks
- Imaging infrastructure setup, customization – **Imaging Charter**
- Site selection and training (imaging specific questions)
- Imaging acquisition and data ingestion
- Deidentification of the imaging data
- **QA and QC of imaging data (protocol adherence and query missing images)**



# Imaging workflow in a clinical trial (continued)

- Imaging case report forms
- Central reads (trained readers) versus site reads (training)
- Safety monitoring workflow
- Imaging data processing and quantitative measurements
- Imaging data lock, data integration and analysis
- Imaging data storage and long term archival
- Data sharing



**U.S. FOOD & DRUG**  
ADMINISTRATION




















← [Home](#) / [Regulatory Information](#) / [Search for FDA Guidance Documents](#) / [Clinical Trial Imaging Endpoint Process Standards Guidance for Industry](#)

GUIDANCE DOCUMENT

# Clinical Trial Imaging Endpoint Process Standards Guidance for Industry

APRIL 2018

# Cloud based Imaging Solutions

Actions				
		<div>0</div>	Completed ▾	
Images	Download	Reports ▾		
		<div>0</div>	Ready to be Read ▾	
Images	Download	Reports ▾		
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Images	Download	Reports ▾		



# Backend activities - Imaging data backup

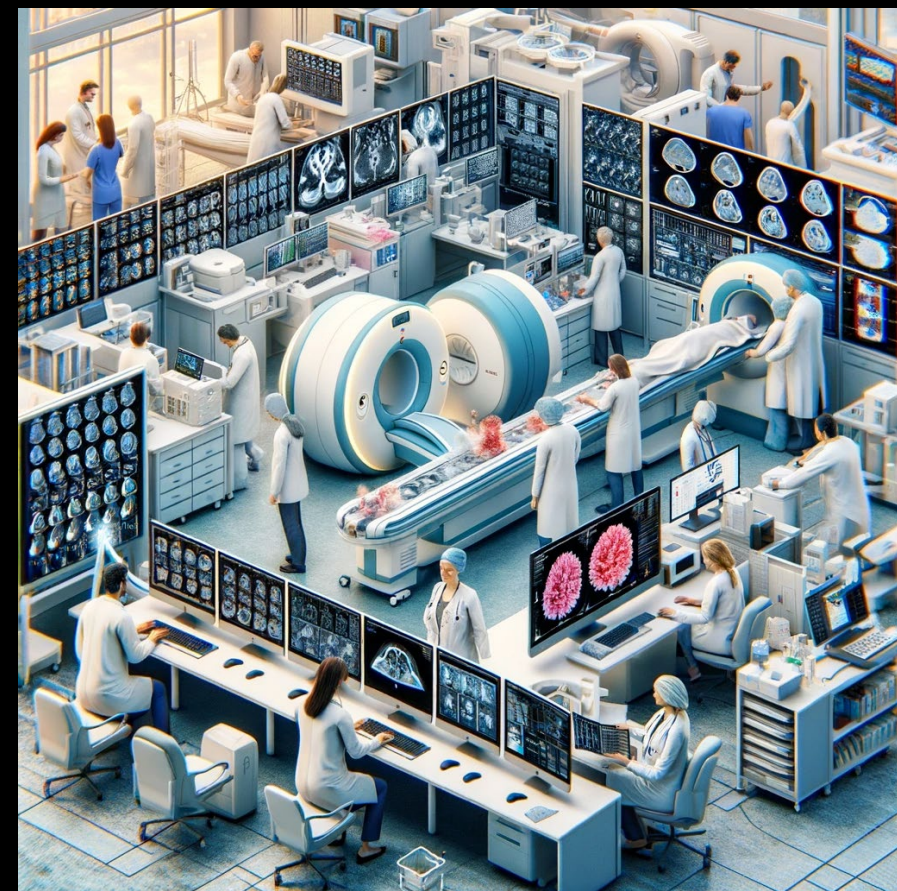
Automated system backups imaging data and CRF data from all studies.

DICOM Images converted to Nifti and pushed to trial directories, where applicable, for segmentation and analysis.

All attachments, masks and annotations in cloud-based system saved locally.

CRF data from HTML extracted and saved in database.

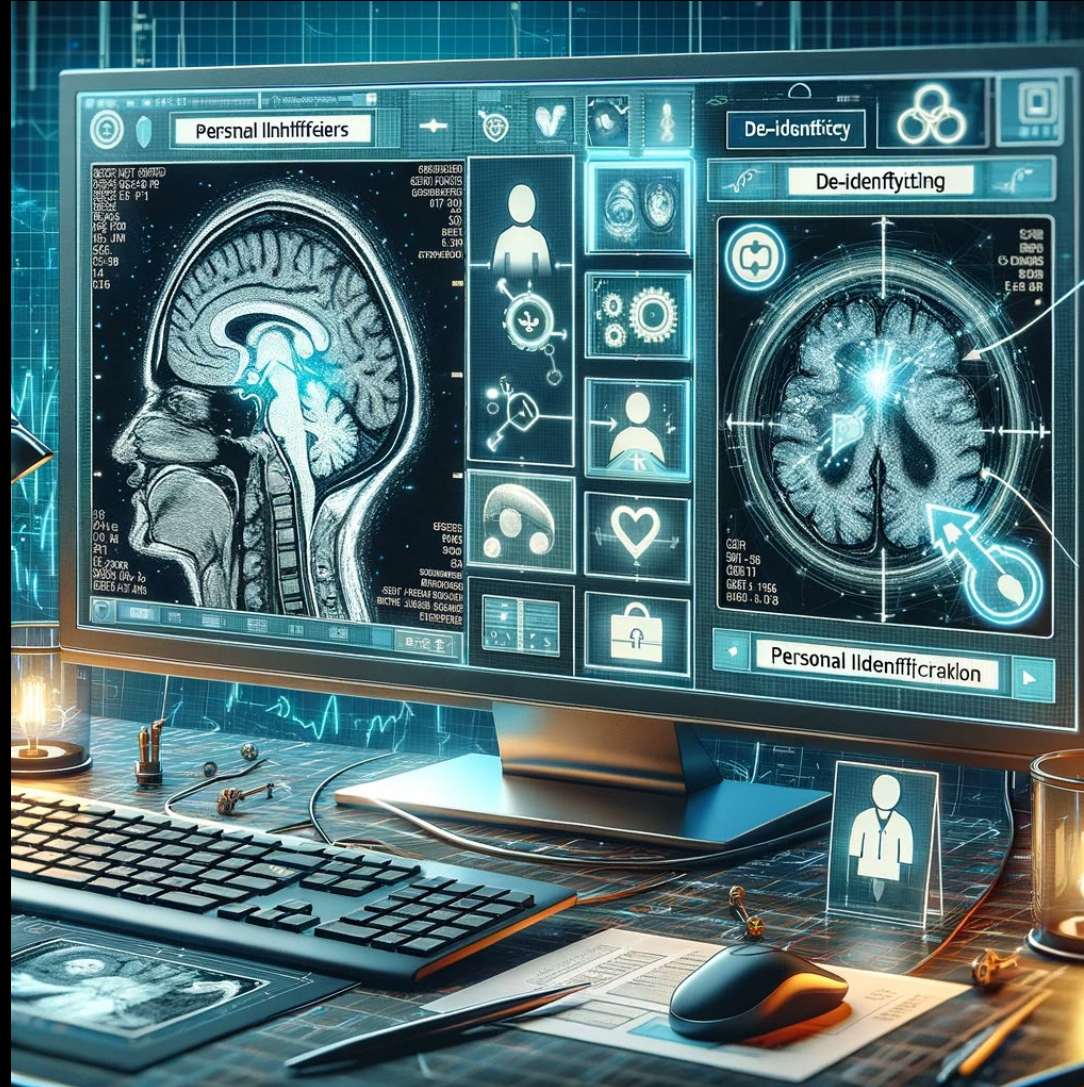
# Key Takeaway



**Do NOT underestimate the complexity  
of imaging workflow in a clinical trial**



# Deidentification





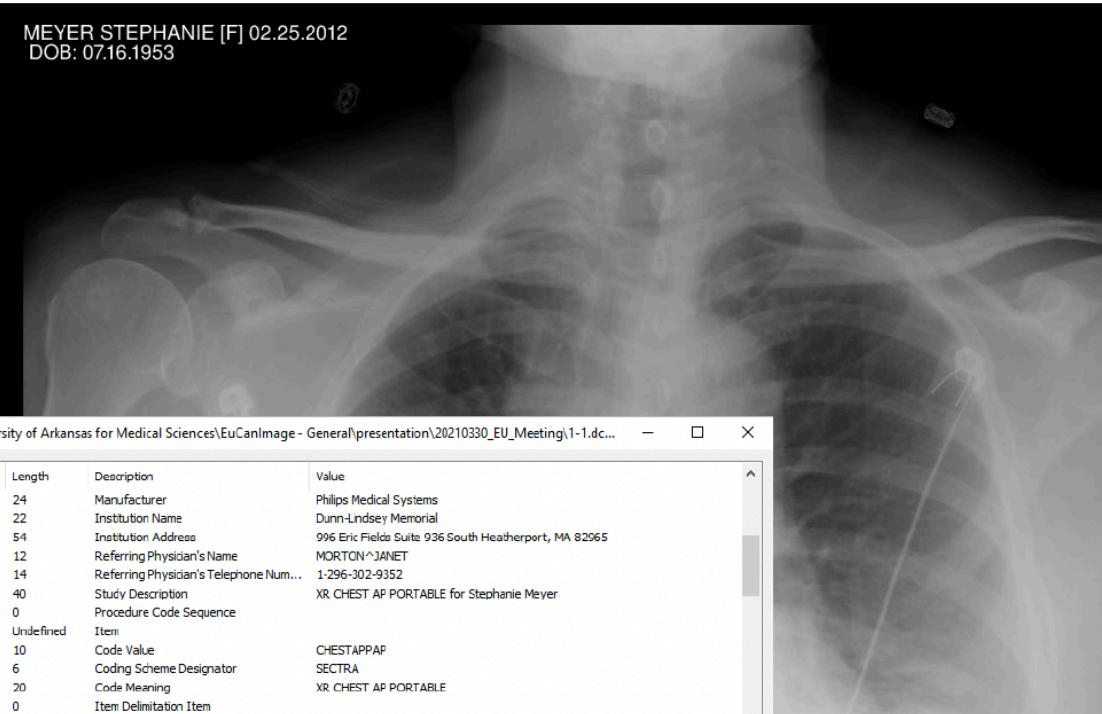
# Medical Imaging

- **DICOM**

(Digital Imaging and Communications in Medicine)

- Metadata (Header)
- Pixel Data
  - Content
    - Implants
  - Recognizable Features
    - Faces
  - Embedded
    - Burned-in Text
    - Watermark

MEYER STEPHANIE [F] 02.25.2012  
DOB: 07.16.1953



DICOM Tags (D:\Cloud\University of Arkansas for Medical Sciences\EuCanImage - General\presentation\20210330\_EU\_Meeting\1-1.dc...

Tag ID	VR	VM	Length	Description	Value
(0008,0070)	LO	1	24	Manufacturer	Philips Medical Systems
(0008,0080)	LO	1	22	Institution Name	Dunn-Lindsey Memorial
(0008,0081)	ST	1	54	Institution Address	996 Eric Fields Suite 936 South Heatherport, MA 82965
(0008,0090)	PN	1	12	Referring Physician's Name	MORTON^JANET
(0008,0094)	SH	1	14	Referring Physician's Telephone Num...	1-296-302-9352
(0008,1030)	LO	1	40	Study Description	XR CHEST AP PORTABLE for Stephanie Meyer
(0008,1032)	SQ	0	0	Procedure Code Sequence	
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(0008,0102)	SH	1	6	Coding Scheme Designator	SECTRA
(0008,0104)	LO	1	20	Code Meaning	XR CHEST AP PORTABLE
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(FFFF,E000)		0	0	Sequence Delimitation Item	
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(0010,0020)	LO	1	10	Patient ID	8548156246

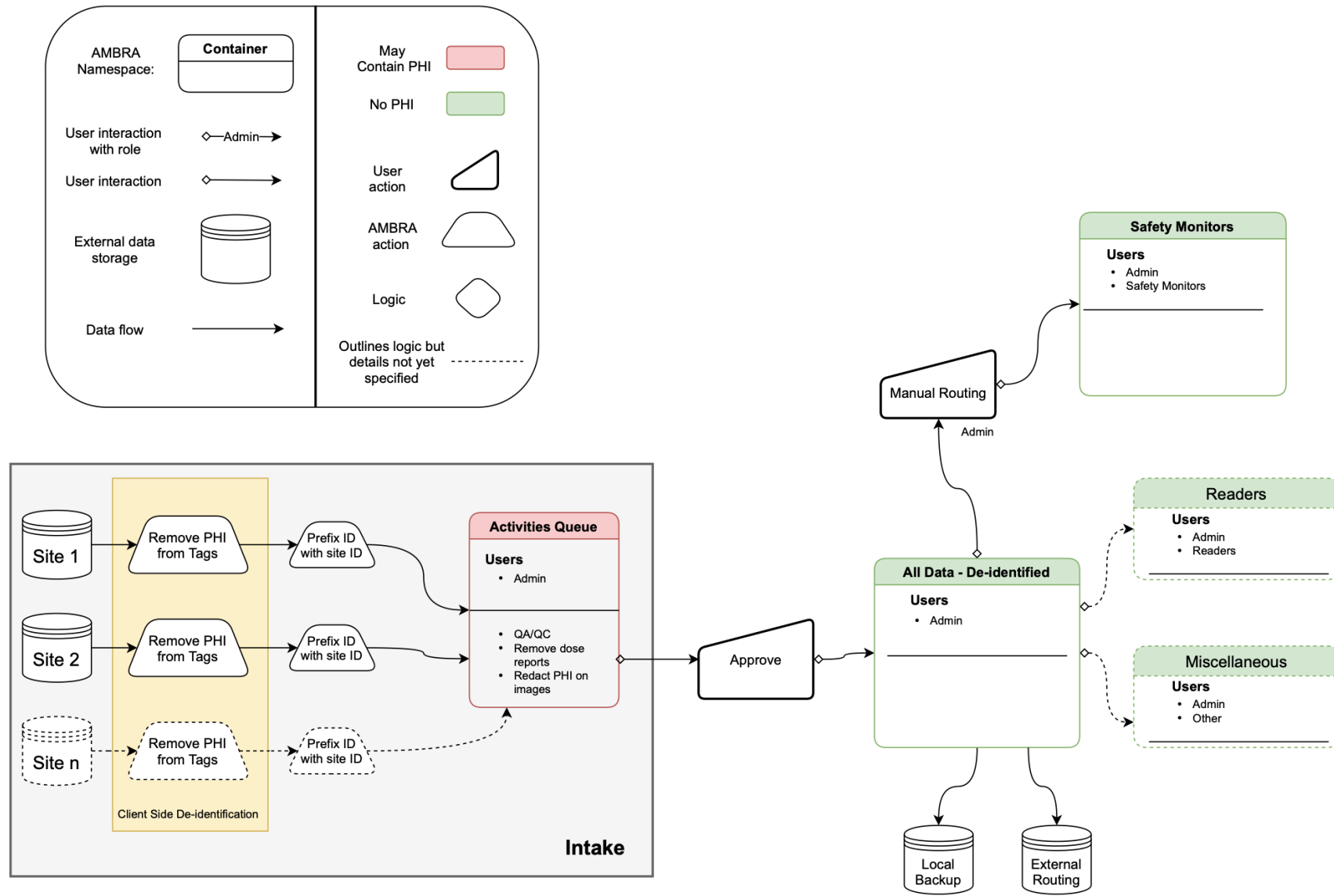
Find text... Close

Rutherford M, Mun SK, Levine B, Bennett W, Smith K, Farmer P, Jarosz Q, Wagner U, Freyman J, Blake G, Tarbox L, Farahani K, Prior F. *A DICOM dataset for evaluation of medical image de-identification*. Sci Data. 2021 Jul 16;8(1):183.

# Image De-identification for Open Access Data Sharing

- Open access or shared research data must comply with regulations that govern patient privacy.
  - Health Insurance Portability and Accountability Act (HIPAA) in the US
  - General Data Protection Regulation (GDPR) in the EU
- These regulations require the removal of protected health information (PHI) and other personally identifiable information (PII) from datasets before they can be made publicly available.
- Covered entities (US) or Data Controllers (EU) are legally responsible for compliance, even if the data publisher is exempt.

# Data workflow- Deidentification





# Terminology

- Deidentification
- Anonymization
- Pseudoanonymization






# Canadian Association of Radiologists White Paper on De-Identification of Medical Imaging: Part 1, General Principles


**William Parker, MD, BMSc<sup>1,2</sup>** , **Jacob L. Jaremko, MD, PhD, FRCPC<sup>3</sup>**,  
**Mark Cicero, MD, BSc, FRCPC<sup>4,5</sup>**, **Marleine Azar, MSc<sup>6</sup>**,  
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**Benoit Desjardins, MD, PhD, FACR<sup>11</sup>**, **Andrea Lum, MD, FRCPC, CCPE<sup>12</sup>**,  
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and **Rebecca Bromwich, PhD, LLM, LLB<sup>18</sup>**

Artificial Intelligence / Intelligence artificielle

# Canadian Association of Radiologists White Paper on De-identification of Medical Imaging: Part 2, Practical Considerations

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Canadian Association of  
Radiologists' Journal  
2021, Vol. 72(1) 13-24  
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# De-Identification, Anonymization, Pseudonymization

- **De-identification** of medical record data refers to the removal or replacement of personal identifiers so that it would be **difficult** to re-establish a link between the individual and his or her data. (Kushida, et al. <https://doi.org/10.1097/mlr.0b013e3182585355> (2012).)
  - the removal of **specified individual identifiers** as well as **absence of actual knowledge** by the covered entity that the remaining information could be used alone or in combination with other information to identify the individual. (HIPAA, 45 CFR [Part 160](#) and [Part 164](#).)
- **Anonymization** refers to the irreversible removal of the link between the individual and their medical record data to the degree that it would be virtually impossible to reestablish the link
  - To achieve anonymization under GDPR, **re-identification of a data subject must be impossible**.
  - **Anonymized data is excluded from GDPR regulation** altogether because anonymized data is no longer “personal data.”
- **Pseudonymization** replaces personal identifiers with nonidentifying references or keys so that anyone working with the data is unable to identify the data subject without the key.
  - This type of data may enjoy fewer processing restrictions under GDPR.

<https://www.jdsupra.com/legalnews/the-edata-guide-to-gdpr-anonymization-95239/>

Slide Courtesy: Fred Prior Presentation. NCI 2023 Medical Image De-Identification Workshop  
<https://wiki.nci.nih.gov/display/MIDI/2023+Medical+Image+De-Identification+Workshop>



A blurred photograph of a city street at night, showing the motion of cars and pedestrians. The background is dark with streaks of light from city lights and vehicle headlights. The title text is overlaid in a large, bold, white font.

# Deidentification 201: A lawyer's guide to pseudonymization and anonymization



May 28, 2020



Save This

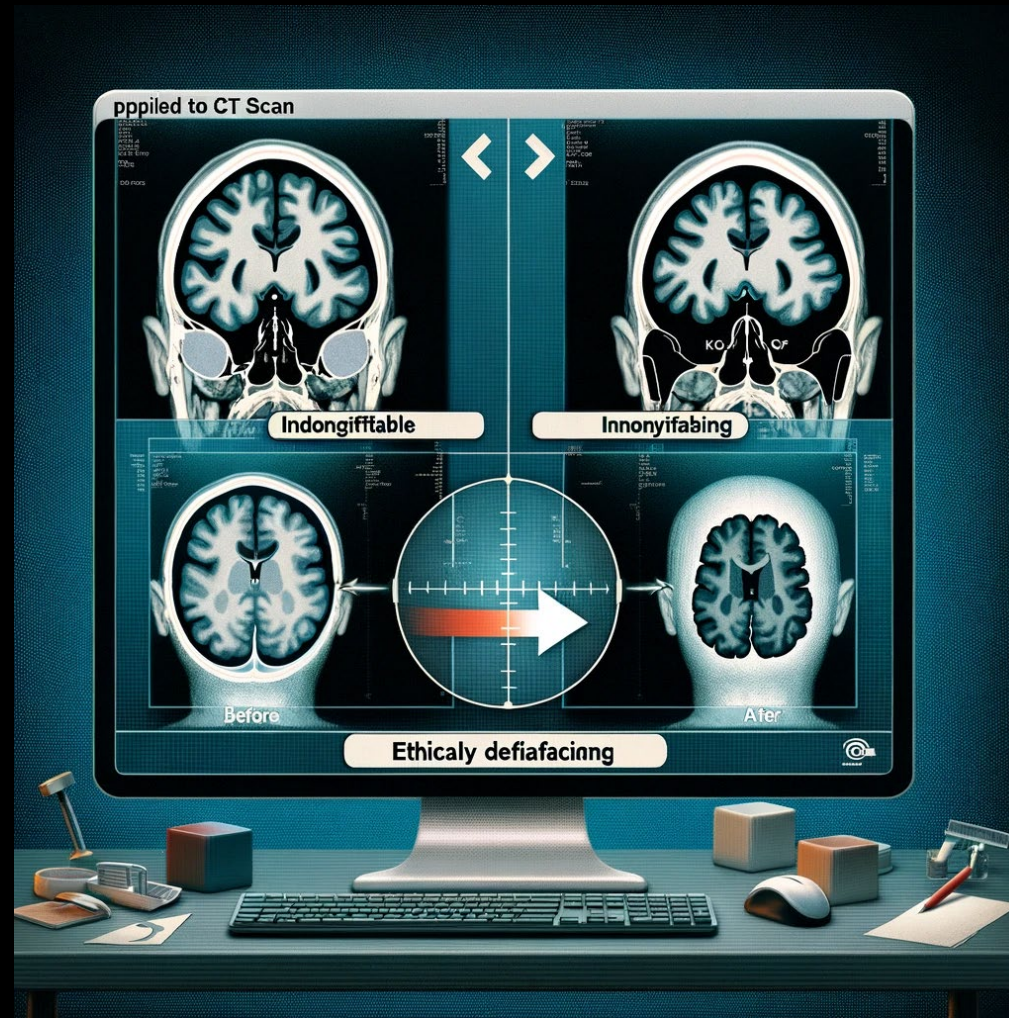


## **Key Takeaway** ***Terminology***

***De-identification ≠ Anonymization***

# De-Facing

Particularly important for neuroimaging



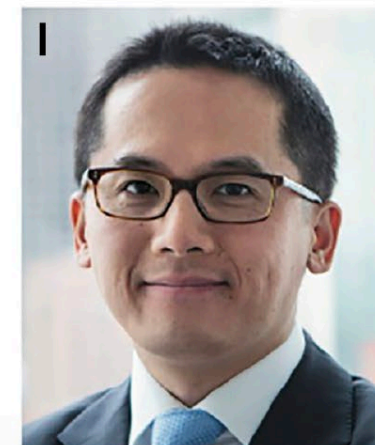
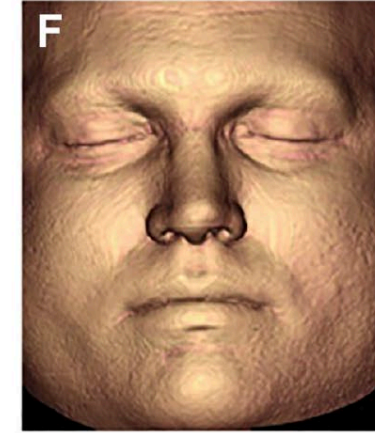
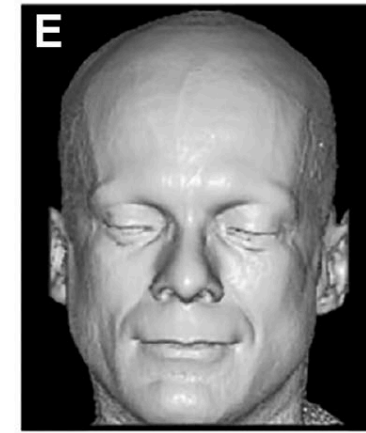
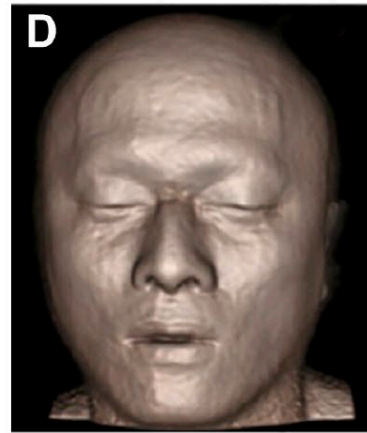
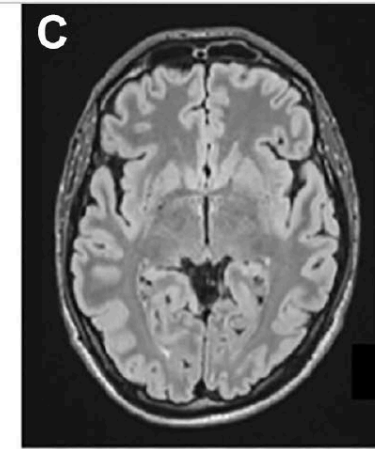
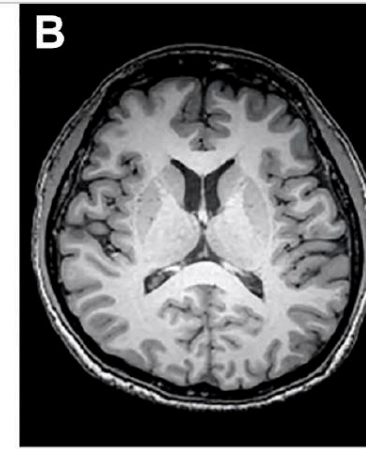
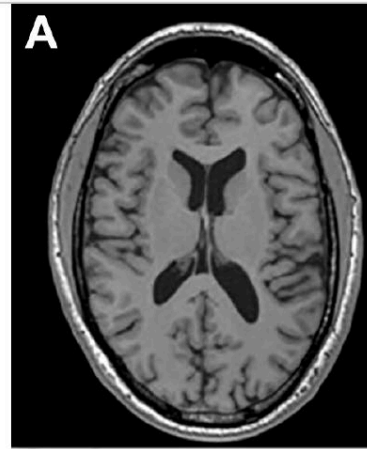
# Is De-facing (Face-Deidentification) required?

- Public sharing of imaging data is increasing and at times required
- Typical deidentification only removes text metadata
- Imagery of faces are kept intact
- Even more critical in MRI head, CT/CTA with 3D reconstructions
- MRI, CT, PET all have identifiable images!
- RISK of re-identification
- Area of active research



## Canadian Association of Radiologists White Paper on De-identification of Medical Imaging: Part 2, Practical Considerations

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Answers: 1) a-f-g. 2) b-d-i. 3) c-e-h.

# Face recognition performance after de-facing



Input MRI

153/157  
97%



*mri\_deface*

52/157  
33%



*pydeface*

59/157  
38%



*fsl\_deface*

44/157  
28%



*mri\_reface*

11/157  
7%

Slide Courtesy: Christopher Schwarz presentation, NCI 2023 Medical Image De-Identification Workshop  
<https://wiki.nci.nih.gov/display/MIDI/2023+Medical+Image+De-Identification+Workshop>



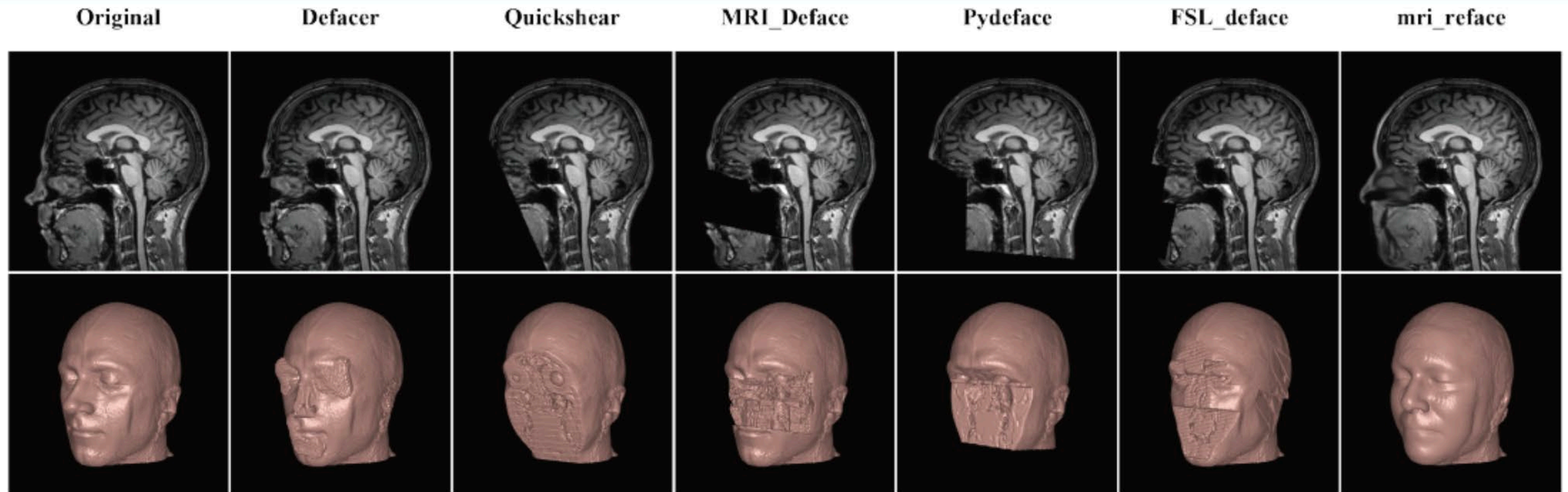
# Effects of Defacing Whole Head MRI on Neuroanalysis

Chenyu Gao<sup>a,\*</sup>, Linghao Jin<sup>b,\*</sup>, Jerry L. Prince<sup>a,b,c</sup>, and Aaron Carass<sup>c</sup>

<sup>a</sup>Department of Biomedical Engineering, The Johns Hopkins University, Baltimore, MD 21218

<sup>b</sup>Department of Computer Science, The Johns Hopkins University, Baltimore, MD 21218

<sup>c</sup>Department of Electrical and Computer Engineering,  
The Johns Hopkins University, Baltimore, MD 21218





## **Key Takeaway** ***De-identification***

***De-identification is not a simple problem!***

No perfect turnkey off the shelf solution.  
Requires due diligence in de-identifying images.  
Tools and infrastructure must comply with local regulations.

# Practical imaging considerations in trial design



- Is imaging a primary/secondary endpoint or assessing safety in your study – sample size calculations?
- Imaging for diagnosis, monitoring, assess therapeutic response?
- Are imaging findings an important part of inclusion/exclusion?
- What all imaging needs to be collected?
- Standard of care or research imaging, timing and frequency?
- Feasibility? Site capabilities

# Practical imaging considerations in trial design



- Patient considerations - Imaging in informed consent?  
Radiation risk? Logistics?
- Do you need protocol harmonization/phantoms/site training?
- Do you need central reads/blinded/imaging analysis?
- What data points do you want to capture in imaging CRFs
- How will you handle missing data (motion/incomplete imaging)?
- Who will do the comprehensive imaging management?
- Imaging budget and resources?

# **Key Takeaway** *Budgets*



**Imaging is expensive!**  
*Discuss budgets with imaging group  
sooner than later*

# Research Challenges/Pain Points of Radiology Departments

- Large numbers of requests for imaging research
- Availability and accessibility - Clinical versus research scanners
- Busy scanners
- Minimal to no dedicated research time for clinical technologists
- Need investment in personnel and resources for multiple activities:
  - ✓ Site feasibility
  - ✓ Review of imaging requirements
  - ✓ Phantom testing
  - ✓ Imaging protocol build
  - ✓ Scheduling
  - ✓ Incidental finding reads
  - ✓ Deidentification and uploads
  - ✓ Resolving imaging queries



## Key Takeaway



***Make sure to have at least one best friend in Radiology (more the better)!***

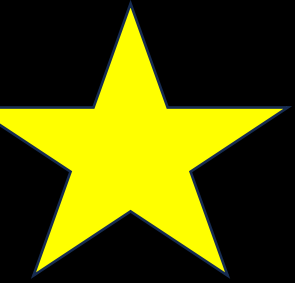
# Future directions

- **Big data** – AI/ML tools, clinically relevant algorithms
- Development of **advanced post processing tools**
- **Open science** - Share curated imaging data with investigators, collaborating consortia and big data projects worldwide (*FAIR – Findability, Accessibility, Interoperability, Reuse of data*)
- Vast opportunities for **training in medical imaging**

## Conclusion

- Imaging is a critical piece of clinical research.
- Comprehensive imaging management is key.
- Imaging workflows are complex but when well done and efficiently can save time for the PI/sites/sponsors.
- Include imaging in your trial budget.

# Final Takeaway



**Always involve Radiology/Imaging  
experts EARLY in your study**