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

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OUTLINE

- CAD devices types
- CAD assessment framework
- Some lessons learned
  - and how they might apply to autonomous AI/ML

COMPUTER-AIDE DIAGNOSIS (CAD)

CADe	• Computer aided detection: Aids in localizing/marking regions of that may reveal specific abnormalities
CADx	• Computer aided diagnosis: Aids in characterizing/assessing disease, disease type, severity, stage, progression
CADe/x	• Computer aided detection/diagnosis : Aid in localizing and characterizing conditions
CADt	• Computer aided triage: Aids in prioritizing/triaging time sensitive patient detection and diagnosis
CADa/o	• Computer-aided acquisition/optimization: Aid in the acquisition/optimization of images/diagnostic signals

These CAD device types are general not organ/disease specific

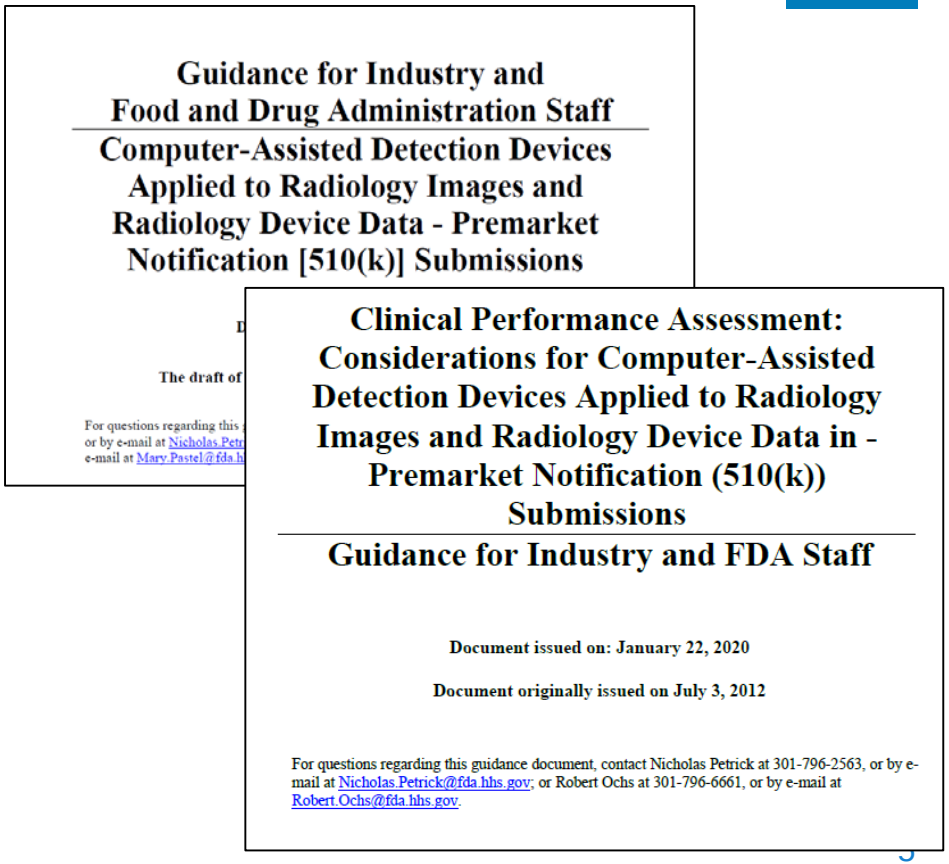
Initial Screener

- Initial Screener
  - Automated cervical cytology slide reader
    - BD FocalPoint GS (P950002-S002)
      - Selects up to 25% of Pap smear slides that need no further review

*https://www.bd.com/en-us/offerings/capabilities/cervical-cancer-screening/cytology-instruments/focalpoint-gs-imaging-system

CAD Device Assessment

- Two CADe guidance documents
  - Clinical assessment guidance
    - Updated 1/22/2020 to reflect CADe reclassifications



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

The draft of

For questions regarding this
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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

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Basic CADe Assessment Framework

- Detailed Descriptions
- Verification and Validations (V&V)
  - Standalone performance assessment
  - Clinical performance assessment
  - …
- Labeling
- …

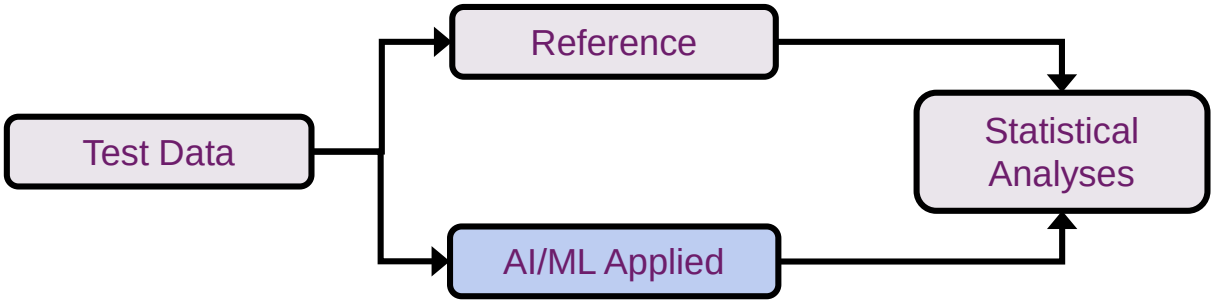
*Based on information in the CADe Guidances

Detailed Descriptions

- CAD algorithm and component
  - Device usage and patient population
  - Algorithm design and function
  - Training process
    - Training/tuning datasets
  - …
- Performance testing protocols and dataset(s)
  - Statistical analysis plan
  - Validation dataset(s)
    - Independent of training/tuning datasets & only accessed after algorithm finalized
  - Reference standard
  - Scoring method
  - …

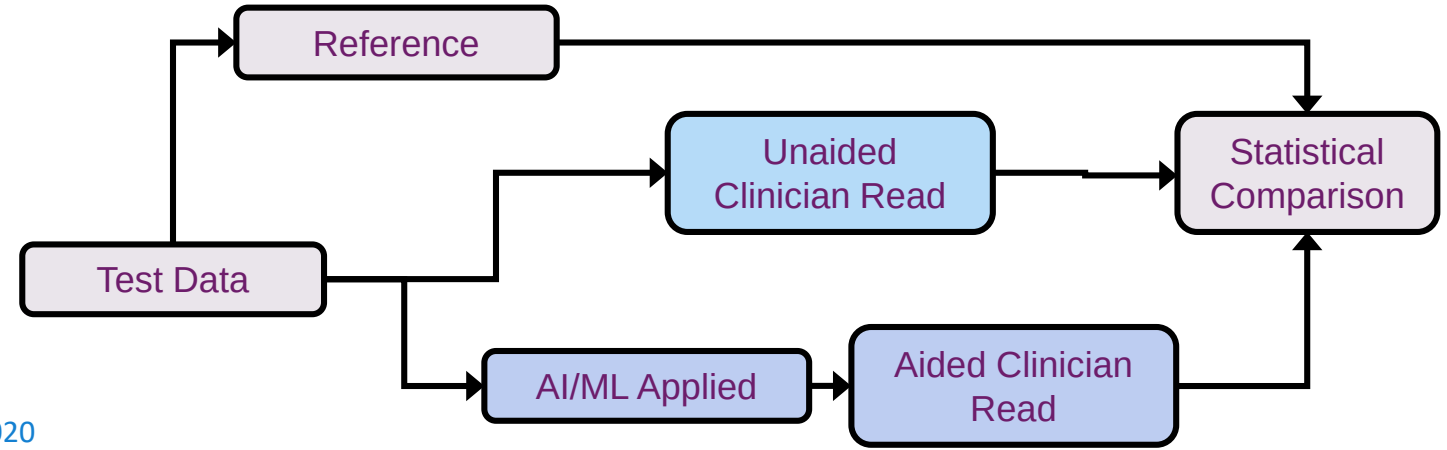
Standalone Performance Assessment

- Benchmark performance (includes CIs)
- Facilitate generalizability analysis



Clinical Performance Assessment

- Clinicians' performance utilizing the device
  - Multi-reader multi-case designs
  - Prospective/retrospective



Other CAD Assessment Frameworks

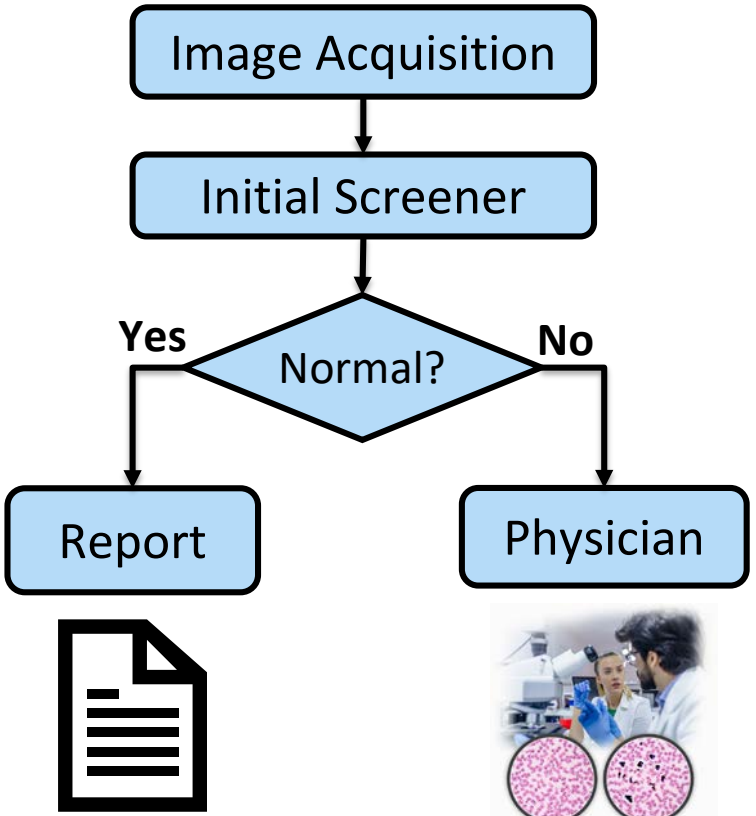
- Special Controls
  - CADx: DEN170022 Quantitative Insights QuantX
  - CADe+CADx: DEN180005 Imagen OsteoDetect
    - Generally consistent with CADe Guidance approaches
  - CADt: DEN170073 Viz.AI ContraCT
    - Detailed Descriptions
      - …
    - V&V
      - Standalone performance testing
      - Performance testing that demonstrate device will provide effective triage
      - …
    - Labeling
  - CADa/o: DEN190040 Bay Labs Caption Guidance

LESSON 1

- CAD assessment framework largely applicable to autonomous AI/ML
  - Important differences
    - CADe/CADx
      - Includes standalone and clinical reader performance
      - Generally utilizes enriched dataset
    - Autonomous AI/ML
      - Include standalone/benchmark performance
      - Include clinical comparison with standard of care (?)
      - Representative dataset likely required

Initial Screener

- Initial Screener (AI/ML+Reader)
  - Normal: AI/ML or reader determine “Neg”
  - Positive: Both AI/ML & reader determine “Pos”
- Properties
  - Se AI/ML+Reader ≤ Se SOC
    - AI/ML may miss cancers
  - Sp AI/ML+Reader ≥ Sp SOC
    - SOC reader may misdiagnose normal cases determined correctly by AI/ML
- Assuming reader performance same before/after introducing initial screener



LESSON 2

- Makeup of validation dataset impacts safety and effectiveness assessment

Common Test Dataset Types

- Enriched datasets
  - Challenging cases to probe differences in modalities
  - Enriched subgroups to assess generalizability
    - Technological subgroups
    - Patient subgroups
- Representative datasets
  - Representative of clinical population
  - Representative of imaging acquisition landscape

CAD Test Datasets

- Evaluating CADs in FDA submissions
  - Generally not measuring aid under clinical conditions
  - Generally not comparing devices across different datasets

  - Standalone
    - Representative (somewhat) to benchmark performance
      - Limited number of sites, likely some selection bias
    - Enriched subgroups/imaging technologies
      - Informs labeling and facilitates generalizability analyses

  - Clinical reader study
    - Typically enriched with challenging cases
    - Clinical readers generally not truly representative of reader population

AUTONOMOUS AI/ML TEST DATASETS

- Evaluating autonomous AI/ML in FDA submissions
  - Likely want ability to direct compare algorithms across different datasets
  - Standalone
    - Representative of patient population and clinical image acquisitions
      - More sites, minimize potential selection bias
    - Enriched patient or imaging technologies subgroups
      - Inform labeling, determine limitations, generalizability analysis
  - Standard-of-Care comparison study
    - Representative of clinical population, clinical image acquisitions, clinical readers
      - Automated Pap smear reader device used a two-arm prospective intended use study at five cytology laboratories

DATASET SIZE

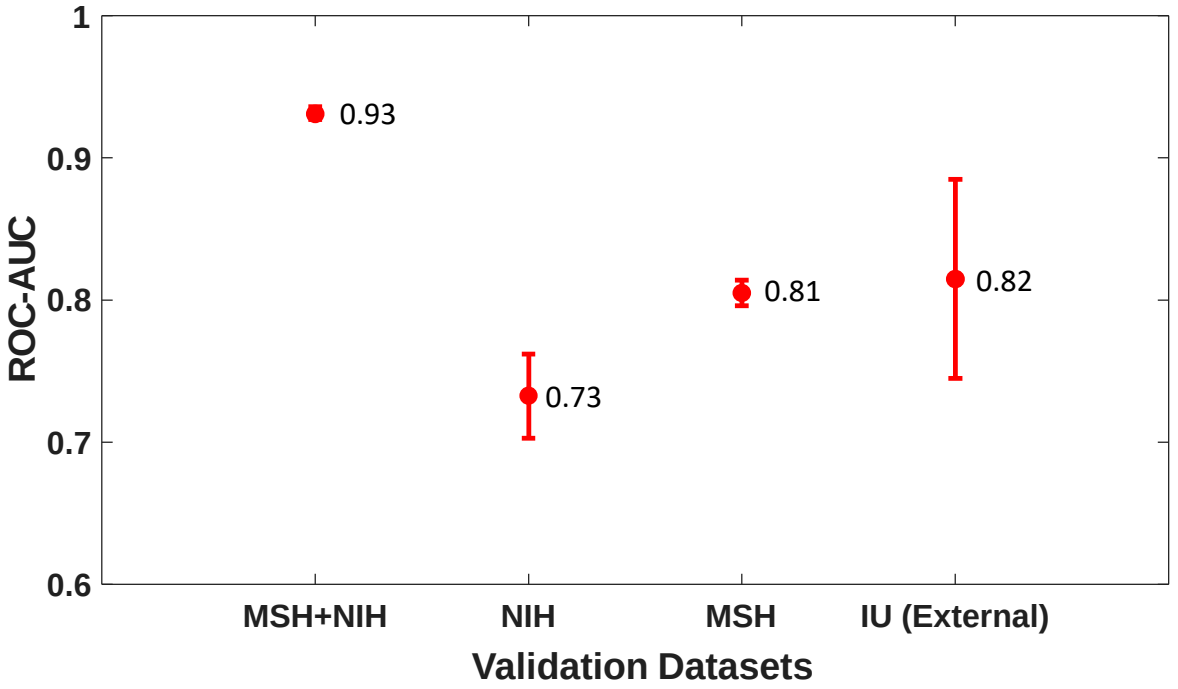
- How much data is enough?

CAD has generally uses modest sized enriched validation datasets

Automatous AI/ML likely to require larger representative validation datasets

LIMITS OF AUTONOMOUS AI/ML TESTING

- Zech et al*, CNN pneumonia screener for chest X-rays
  - Training MSH & NIH
    - Train:109,922 cases
    - Tune: 15,144
  - Validation
    - NIH: 22,062
    - MSH: 8,388
    - IU: 3,807
  - Pneumonia prevalence
    - NIH: 1.2%
    - MSH: 34.2%
    - IU: 1.0%

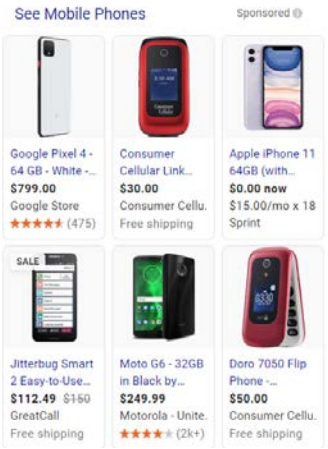


*Zech et al, PLOS-Medicine, 2018

LIMITS OF AUTONOMOUS AI/ML TESTING

- Limits of benchmarking AI/ML performance

Extend to new imaging devices without new studies?



Extend to other patient groups without new studies?

Adults

Children

LESSON 3

- Quality control (QC) is critical for automated AI/ML
  - QC as safety control

AUTOMATED PAP SMEAR INITIAL SCREENER

- Automated QC checks on inputs & AI/ML processing
  - To ensure real-time adequacy of algorithm processing
- Clinical QC
  - To confirm ongoing AI/ML functionality
    - System identifies up to 15% of successfully processed slides for full manual rescreening

Summary of CAD Lessons

- For autonomous AI/ML
  - CAD assessment framework largely applicable
  - Large representative validation dataset likely needed
  - Ongoing quality control may be a useful safety control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