独立行政法人 医薬品医療機器総合機構
Pharmaceuticals and Medical Devices Agency

Latest updates on CADe/CADx medical device review requirement in Japan

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7 October 2024

Topics

- Guidance for CAD in Japan
- The fundamental CAD review concept

  ～ Review Point for Computer-Aided Diagnosis Program to Support Interpretation of Medical Images ～

  https://www.std.pmda.go.jp/stdDB/Data_en/InfData/Infetc/samd05.pdf

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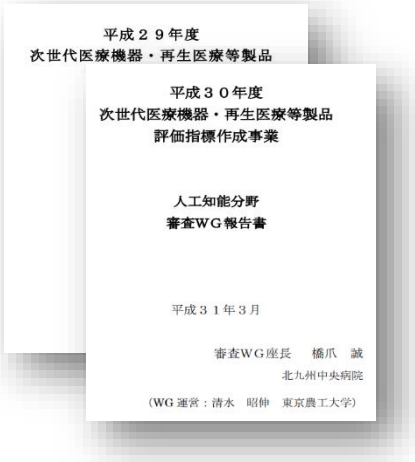
Guidance for Next Generation Evaluation

- ○ This project is designed to accelerate the review process by identifying key review pathways and confirmation points for the transition from non-clinical test to clinical test.
- ○ The guidance for CADe/CADx evaluation was first published in 2011.
- ○ After that, the guidance for CADe/CADx evaluation including machine learning was republished in 2019.

2017～2018

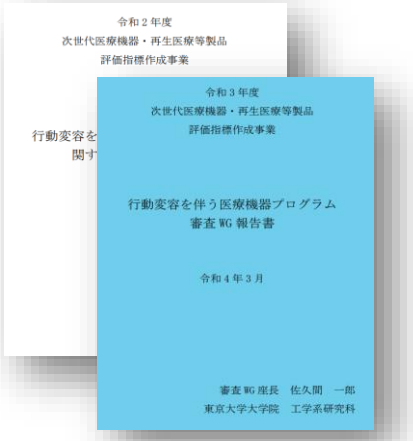
< AL/ML- enabled CAD>



https://dmd.nihs.go.jp/jisedai/tsuuchi/Guidance_for_evaluation_of_AI_assisted_systems.pdf

2020～2021

< SaMD for behavior change>



Review Points / Certification Criteria for SaMD

- ○ In this project, PMDA summarizes and discloses the key review points (e.g., test conditions and evaluation points for efficacy and safety) in order to improve predictability for manufacturers.
- ○ Five review points have been disclosed since 2022.
- ○ In 2023, the review points for the CADe for radiological images and endoscopic images were disclosed.

< Certification Criteria >

Class	Disclosure date	Medical Device Nomenclature
III	2023 /3/7	Software for radiation planning
II	2023/3/7	Supporting software for respiratory treatment
II	2023/10/18	Surporting software for external fixators treatment plan criteria

< Review Points >

Class	Disclosure date	Medical Device Nomenclature
III	2022/9/30	Software for peritoneal dialysis treatment
II	2022/11/2	Supporting software for dental implant treatment
III	2023/3/3	Software for ophthalmic surgery treatment planning
II	2023/3/10	Computer-Aided Detection for endoscopy
II	2023/3/10	Computer-Aided Detection for medical imaging

https://www.std.pmda.go.jp/stdDB/Data_en/InfData/Infetc/samd01.pdf
https://www.std.pmda.go.jp/stdDB/Data_en/InfData/Infetc/samd02.pdf
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https://www.std.pmda.go.jp/stdDB/Data_en/InfData/Infetc/samd04.pdf
https://www.std.pmda.go.jp/stdDB/Data_en/InfData/Infetc/samd05.pdf

The Science Board

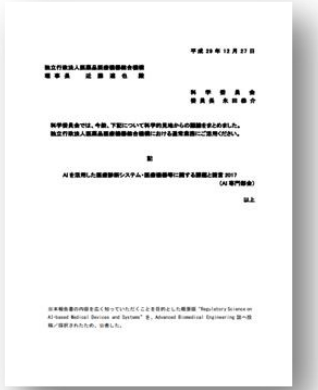
○ The purposes of the Science Board are, advancing regulatory science and evaluate products with advanced science and technology in appropriate manner by enhancing cooperation and communication with academia and medical institutions

○ The outcome document entitled “Regulatory Science on AI-based Medical Devices and System” was first published in 2017.

○ In 2023, the outcome document, summarize " test data reuse", "AI/ML bias" and "database", etc., has been published.

2017

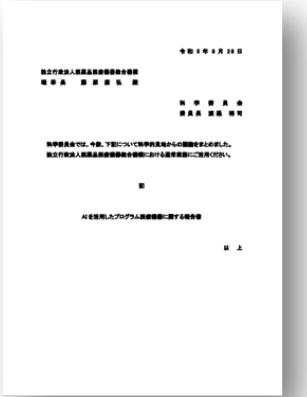
< Regulatory Science on AI-based Medical Devices and System>



https://www.jstage.jst.go.jp/article/abe/7/0/7_7_118/_pdf/-char/en

2023

< Regulatory Science on SaMD enabled machine learning >



https://www.pmda.go.jp/files/000266099.pdf

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- **The fundamental CAD review concept**

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Definition

CADe : Computer-Aided Detection

- Software as a Medical Devices or Software in a Medical Devices with a function of automatically detecting the portions of images with suspected lesions by computerized systems, and marking their positions.
- They support the **detection of lesions or abnormal values** by computerizing a medical image data alone or both a medical image data and an examination data.

CADx : Computer-Aided Diagnosis

- Software as a Medical Devices or Software in a Medical Devices with a function of outputting quantitative data such as differential diagnosis of benign and malignant lesions and disease progression related to lesion candidates as numerical values, graphs, etc. in addition to detecting the portions of suspected lesions or a device incorporating such software.
- This includes those that **provide diagnostic support** by providing candidate diagnostic results, information on risk assessment, etc.

Definition

CADe : Computer-Aided Detection

The scope of this review point

- Software as a Medical Devices or Software in a Medical Devices with a function of automatically detecting the portions of images with suspected lesions by computerized systems, and marking their positions.
- They support the **detection of lesions or abnormal values** by computerizing a medical image data alone or both a medical image data and an examination data.

- Second Reader and Concurrent Reader (include)
- To detect objects with multiple disease pathologies (include)
- To demonstrate for the classification of detecting disease pathologies (not include)

Overall structure

§2 Explanation for application product
- The role in clinical practice
- Design concept

§3 Evaluation Package
- Evaluation for clinical effectiveness
- Evaluation for clinical performance
- Evaluation for other functions

§4 Test Design Considerations
- Test sample
- Handle the data derived from human
- Variation of test dataset
- Reference standard
- Scoring
- Endpoint
- Reviewing clinician（reader study）etc.

§5 Additional Points to Consider for Products Using Machine Learning
- The relation between training data and test data
- Consideration for variation

2. Explanation for application product

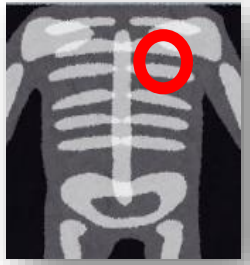
2.1. Summarize the role in clinical practice

2.2. Design concept

One-day consultation ～the role in clinical practice and Evaluation～

Applicant

- We develop a software to detect lung nodule on X-ray images using AI technology
- As shown here, the software notifies the user the location of lung nodule by placing ○
- The sensitivity and specificity show high results, 85% and 90%, respectively.



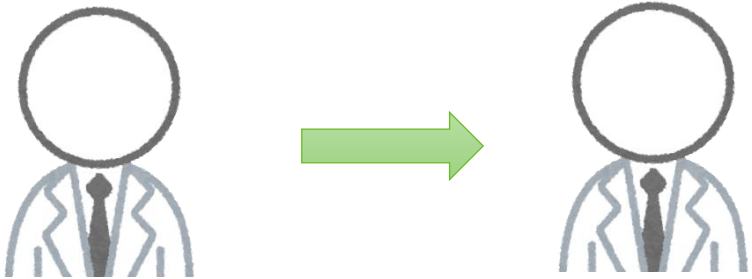
Please explain the role in clinical practice of this software

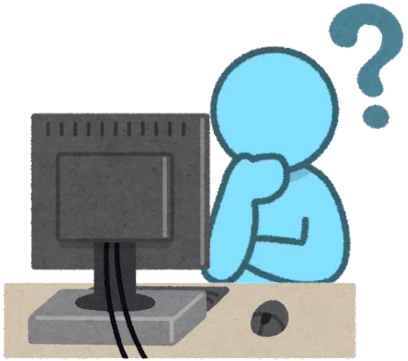
Reviewer

I just told you?

Applicant

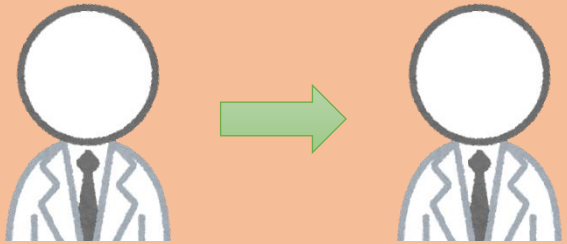
The role in clinical practice and evaluation



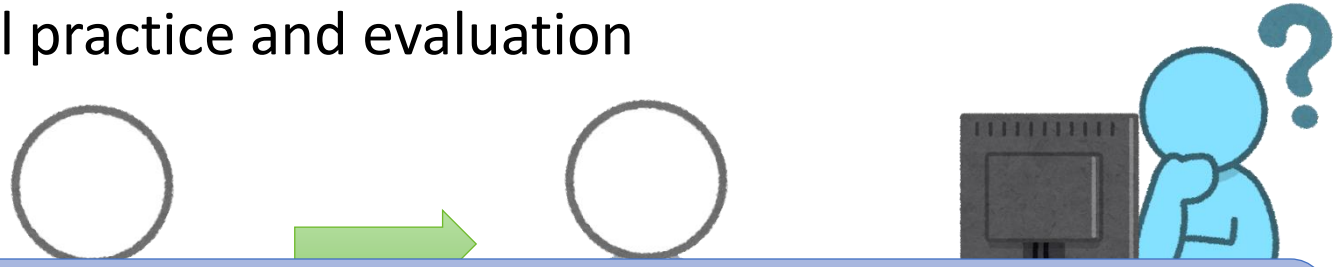


【Image Ⅰ】

Maintain the double reading system, and
improve the diagnostic skills of each physician



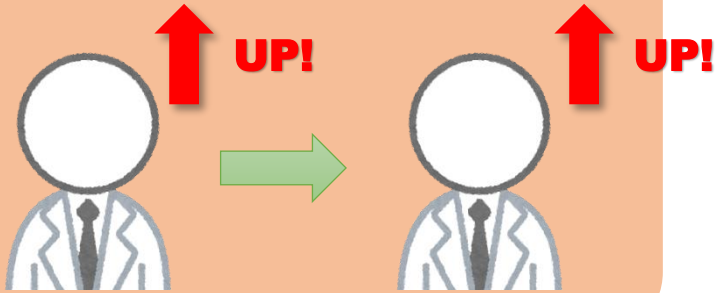
The role in clinical practice and evaluation



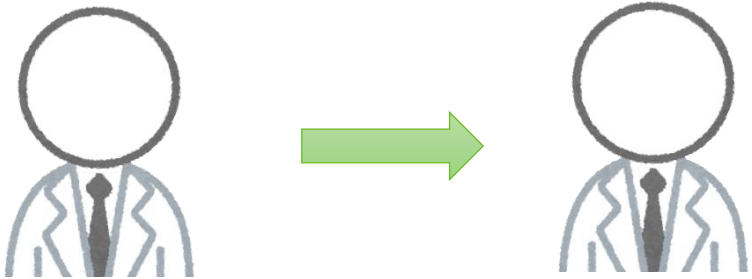
Improve the results of the nodule detection by each physician with CAD ?

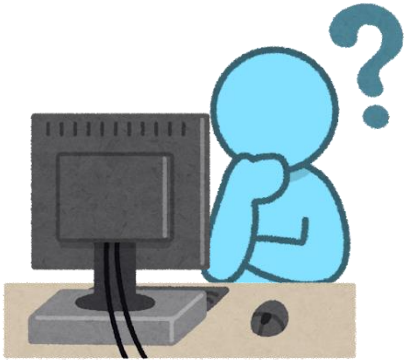
【Image I】

Maintain the double reading system, and improve the diagnostic skills of each physician



The role in clinical practice and evaluation





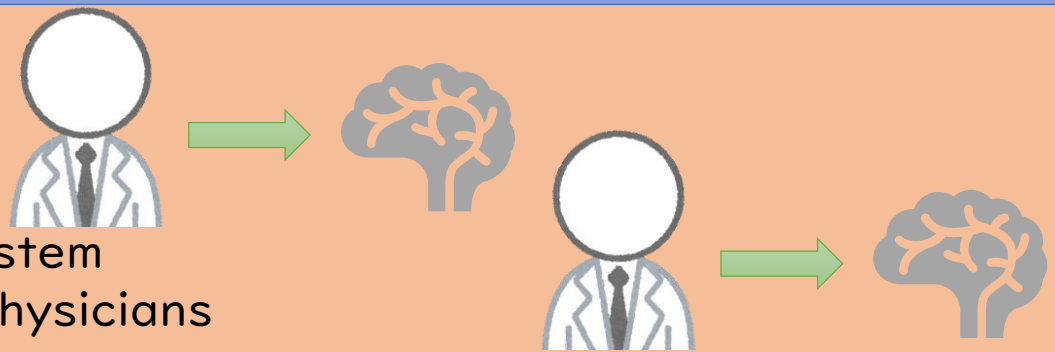
【Image2】

Resolve the double reading system
because of the shortage of physicians

The role in clinical practice and evaluation

“Double reading” vs “physician + CAD” shows the equivalent result ?
Conservative thinking, dose it mean “Resident + CAD” ?
It may affect existing guidelines ?
What do we coordination with medical societies ?

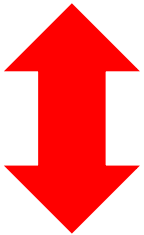
【Image2】



Resolve the double reading system
because of the shortage of physicians

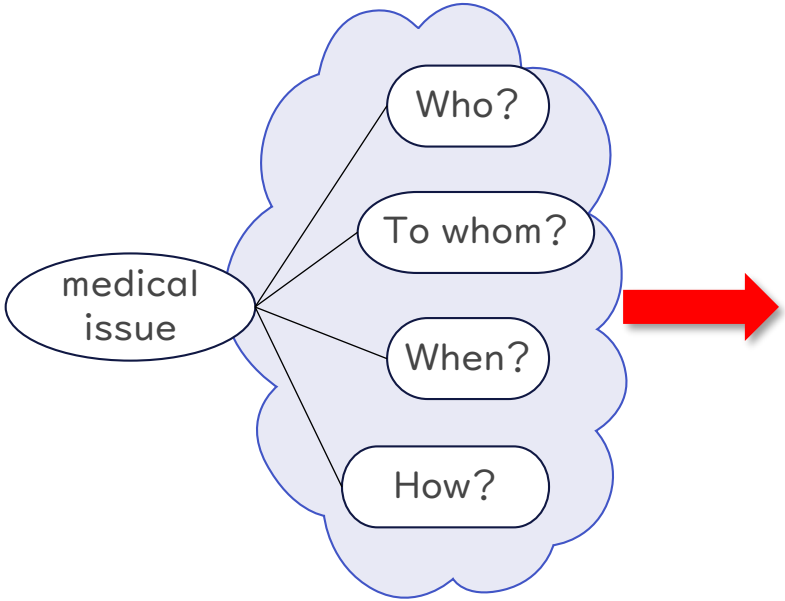
Evaluation depends on the role in clinical practice

For what purpose and To whom, the application product is used in clinical environment



What the application product should show

Design concept



Cluse 2.1 the role in clinical practice

2.2 design concept (specification of the product)

Function
- input
- detection target
- analysis methodology
- output etc.

Using method
- user
- using method

Performance
- performance

Summarize the role in clinical practice

- Intended disease and patient
- The problem of current medical treatment
- How will the product solve the problem
- How will the existing medical treatment be changed

3. Evaluation Package

3.1. Test to evaluate clinical effectiveness

3.2. Test to evaluate clinical function

3.3. Other functions

Conceptual requirements

1. The use of the results of analysis by the application product for the intended input data shall improve the diagnostic performance of the intended user.

2. The application product shall have clinically significant detection performance against the intended input data.

3. Processing shall be able to be completed within a clinically acceptable time frame.

4. Other functions shall operate as intended.

5. To manage software lifecycle properly

6. Appropriate cybersecurity measures are implemented.

Clinical effectiveness

Demonstrate the value by actually use?

Clinical performance

Achieved the required performance?

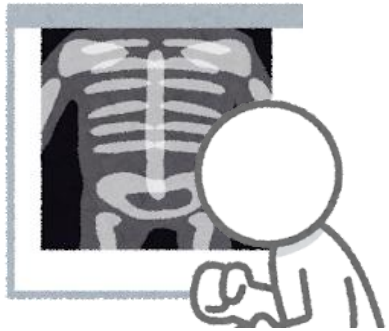
Essential performance

Realize the other functions ?

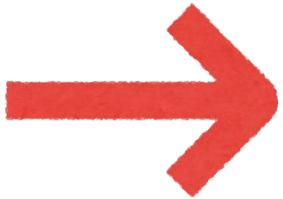
Evaluate the clinical effectiveness

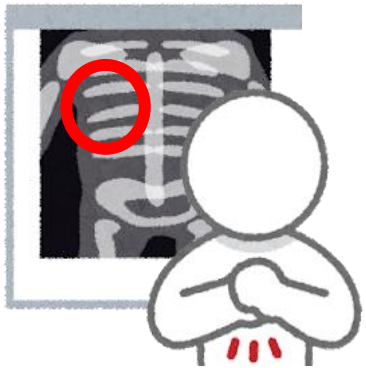
Evaluate the value of introducing the application product into clinical environment.

Example of Second Reader



Reading without CAD (Normal reading)





Reading with CAD (Prevention of oversight)

Evaluation for clinical performance

Evaluate the performance of the applied product itself

Conduct a test for all requirements?

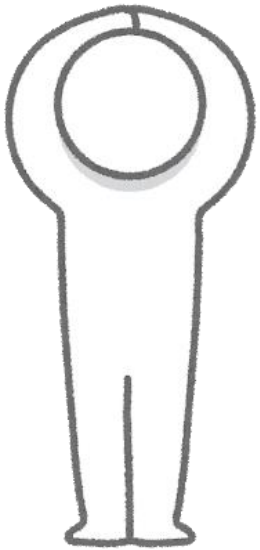
Example of evaluation strategy

「Conduct a evaluation」≠「Conduct a test」

Tests for clinical effectiveness

Tests for clinical performance

Test for essential performance



Consideration for clinical effectiveness

Tests for clinical performance

Test for essential performance

Evaluation for clinical performance

Evaluate the performance of the applied product itself

The purpose of the evaluation depends on the evaluation strategy.

① Verify the performance of the applied product.

② Verify the performance of the applied product meets the criteria of clinical significance.

4. 4. Test Design Considerations

Clarifying the matters

Tests for clinical effectiveness

Tests for clinical performance

Test for essential performance

Demonstrate a value when implementing in clinical environment?

Is there any results and features providing information to ensure that users correctly understand the performance, limitations.

5. Additional Considerations for the product using machine learning

Training Data and Test Data

Explain the rational for test data considering training data！

For example：

The applicant product
(MLMD)

Thank you for your attention