Lunit

Applying Advanced Technology in Clinical Practice:

Regulatory Approval Cases of AI Software “Lunit INSIGHT”

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VP of Regulation, Co-founder

IMDRF/DITTA
September 2019

Contents

Our company

Problem

30%

Annual growth of medical imaging[1]

4%

Annual growth of radiologists[2]

20-30%

False negatives in chest radiography & mammography[3,4]

95%

False positives in screening mammography

1,2 China Market INSIGHT 健康界 (China)
3 NLST trial, NEJM 2012
4 Breast Cancer Screening Consortium

Vision

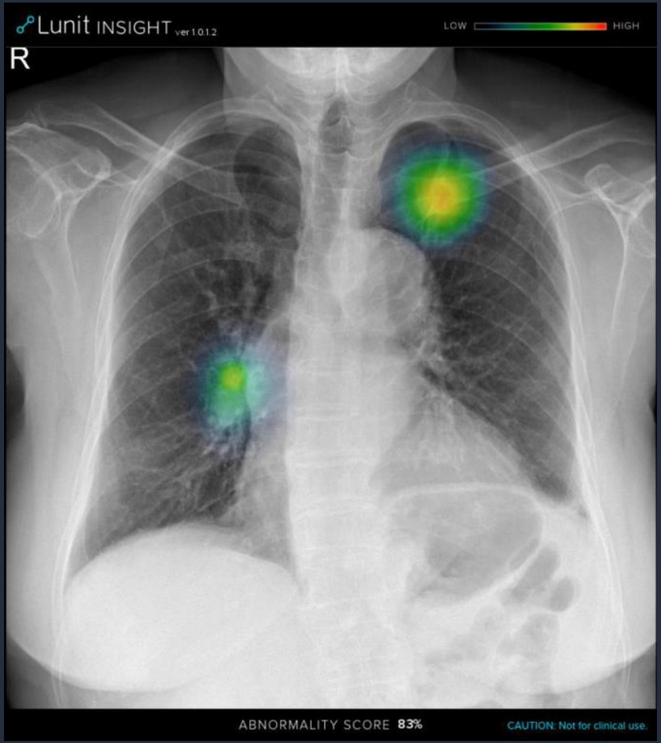
Lunit

Perfecting Intelligence, Transforming Medicine

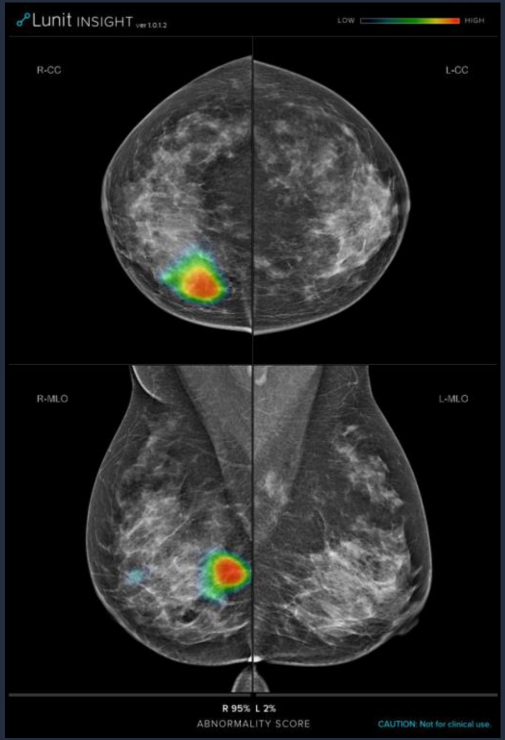
Our products

Product pipeline

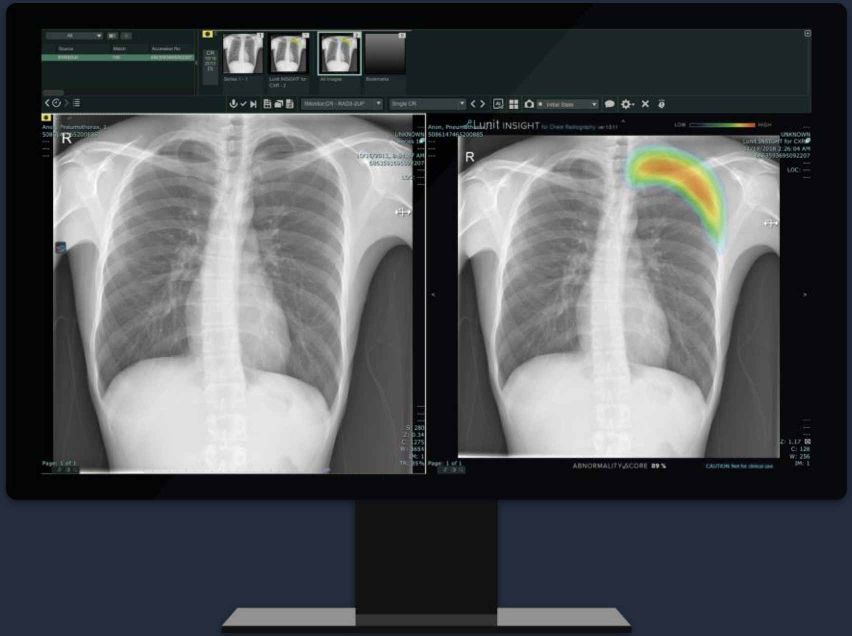
Lunit INSIGHT CXR
chest radiography



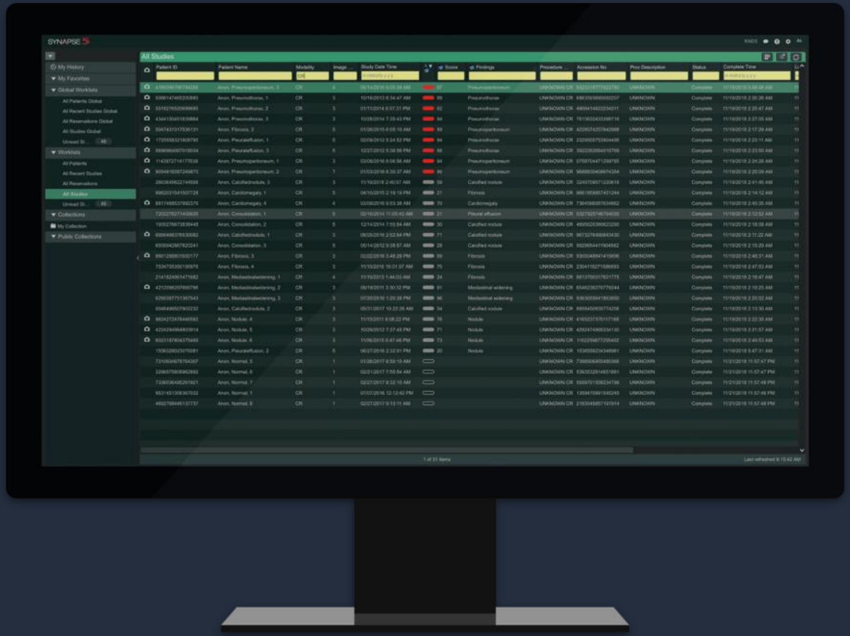
Lunit INSIGHT MMG
mammography



Lunit INSIGHT



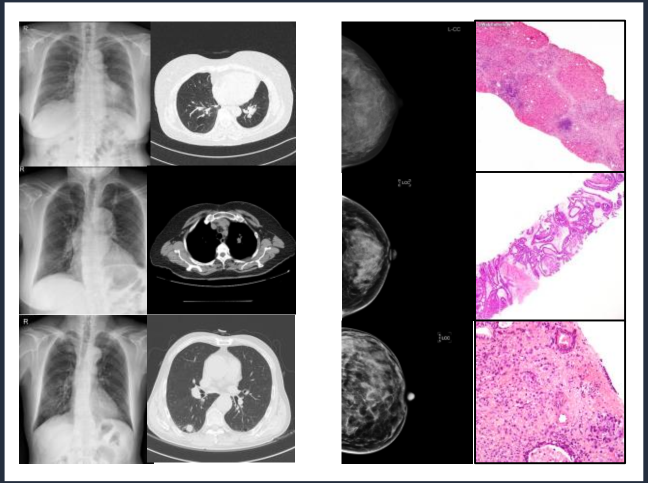
Diagnostic Support



Worklist Prioritization

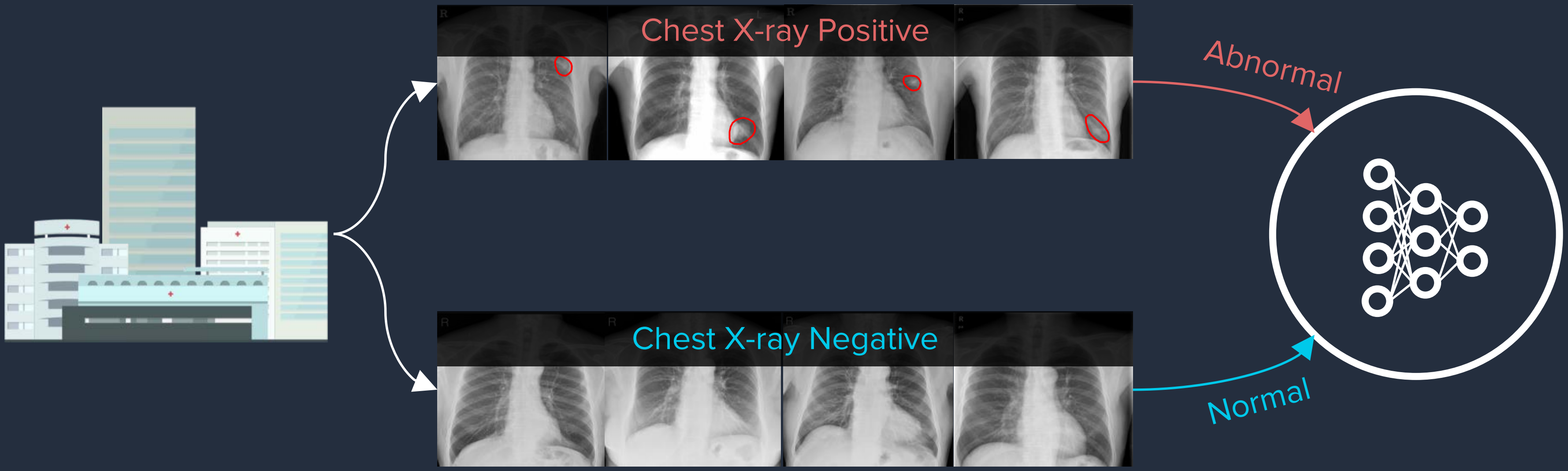
Training data

4+ million images

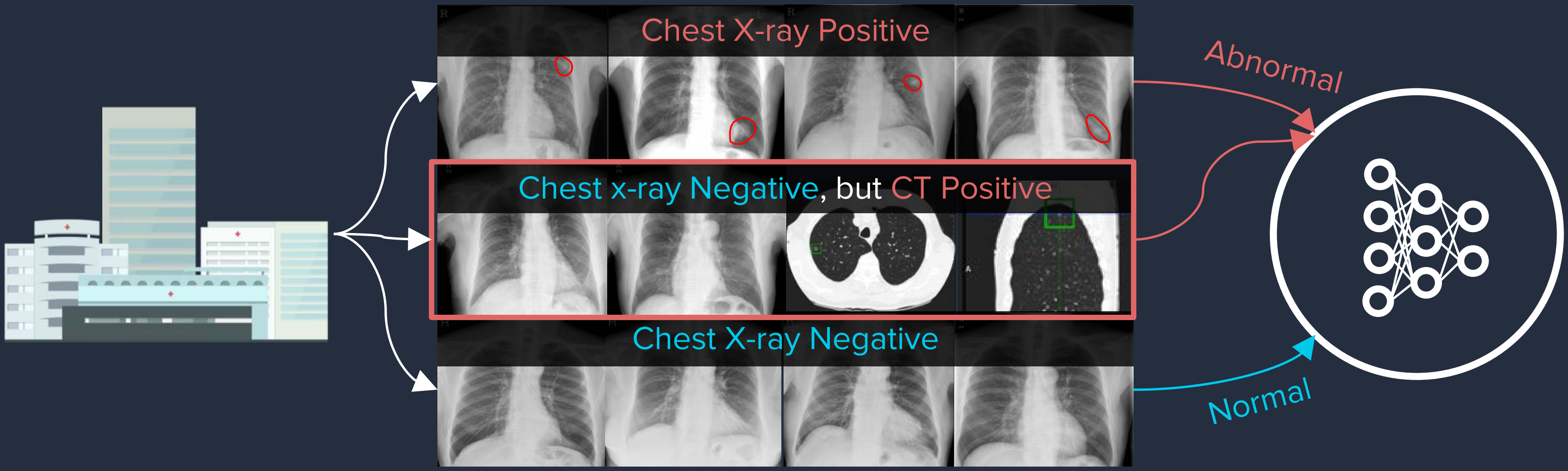


Paired with CT / biopsy

Training data

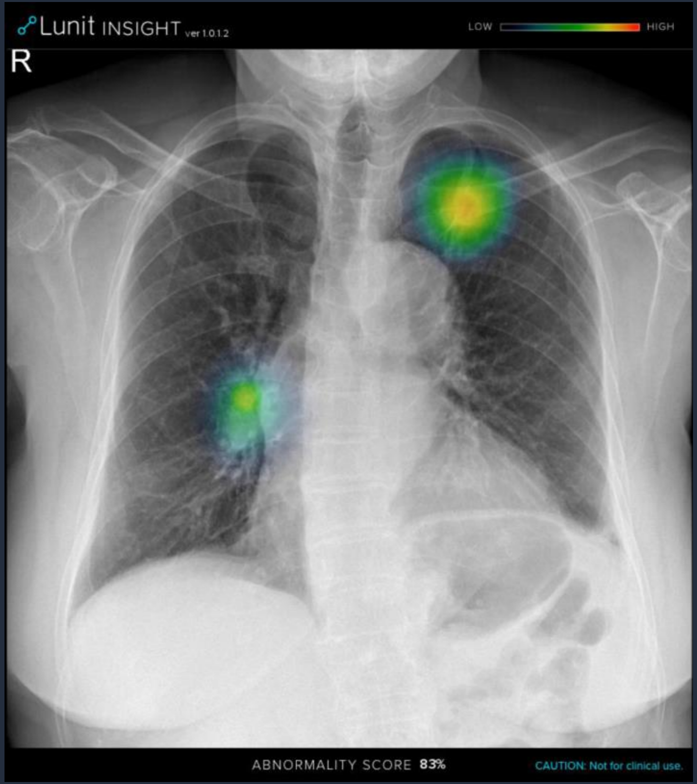


Training data



Lunit INSIGHT CXR

Lunit INSIGHT CXR

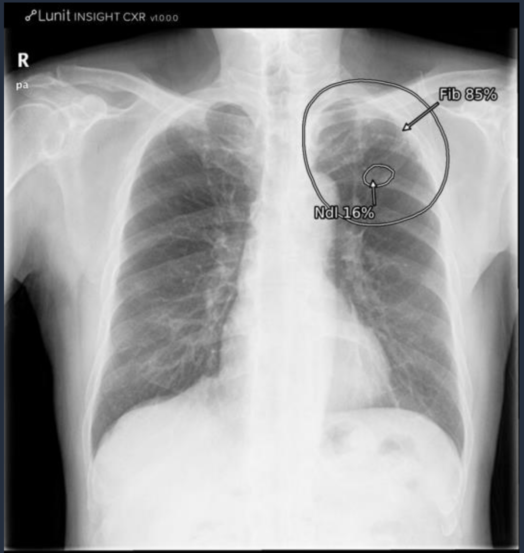


MFDS-approved
- Nodule

MFDS-submitted
- Consolidation
- Pneumothorax

- Calcification
- Fibrosis
- Pneumoperitoneum
- Cardiomegaly
- Pleural Effusion
- Mediastinal Widening
- Atelectasis
- Tuberculosis Screening

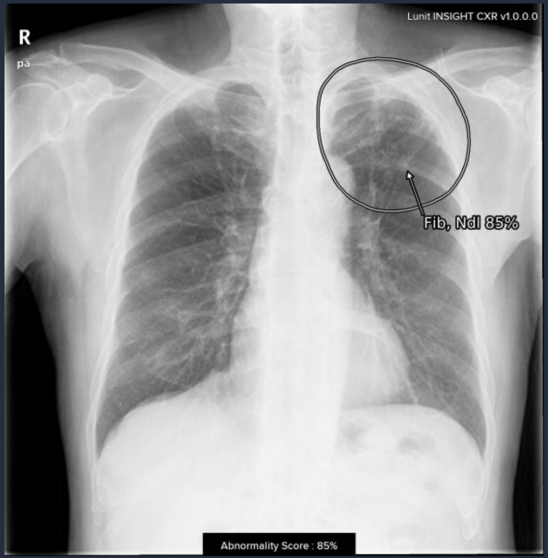
Lunit INSIGHT CXR



CASE REPORT

Abnormality Score 85%

Atl	Atelectasis	Low	-
Calc	Calcification	Low	-
Cm	Cardiomegaly	Low	-
Csn	Consolidation	Low	-
Fib	Fibrosis	85%	Left Upper Zone
MW	Mediastinal Widening	Low	-
Ndl	Nodule	16%	Left Upper Zone
Ppm	Pneumoperitoneum	Low	-
Ptx	Pneumothorax	Low	-
PEf	Pleural effusion	Low	-



1.0M+
training cases

0.8M+
positive cases

97-99%
performance level (AUC)

Clinical study - CXR nodule

September 2018

Radiology

ORIGINAL RESEARCH • THORACIC IMAGING

Development and Validation of Deep Learning–based Automatic Detection Algorithm for Malignant Pulmonary Nodules on Chest Radiographs

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From the Department of Radiology and Institute of Radiation Medicine, Seoul National University Hospital and College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Republic of Korea (J.G.N., E.J.H., J.M.G., C.M.P.); Lunit Incorporated, Seoul, Republic of Korea (S.P.); Department of Radiology, Armed Forces Seoul Hospital, Seoul, Republic of Korea (J.H.L.); Department of Radiology, Seoul National University Boramae Medical Center, Seoul, Republic of Korea (K.N.J.); Department of Radiology, National Cancer Center, Goyang, Republic of Korea (K.Y.L.); Department of Radiology and Biomedical Imaging, University of California, San Francisco, San Francisco, Calif (T.H.V., J.H.S.); and Department of Industrial & Information Systems Engineering, Seoul National University of Science and Technology, Seoul, Republic of Korea (S.H.). Received January 30, 2018; revision requested March 20; revision received July 29; accepted August 6. **Address correspondence to** C.M.P. (e-mail: *cmpark.morphius@gmail.com*).

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*J.G.N. and S.P. contributed equally to this work.

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

Radiology 2018; 00:1–11 • https://doi.org/10.1148/radiol.2018180237 • Content codes: IN CH

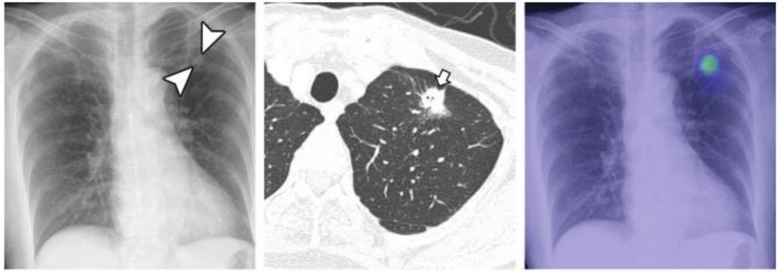
Purpose: To develop and validate a deep learning–based automatic detection algorithm (DLAD) for malignant pulmonary nodules on chest radiographs and to compare its performance with physicians including thoracic radiologists.

Materials and Methods: For this retrospective study, DLAD was developed by using 43 292 chest radiographs (normal radiograph–to–nodule radiograph ratio, 34 067:9225) in 34 676 patients (healthy-to-nodule ratio, 30 784:3892; 19 230 men [mean age, 52.8 years; age range, 18–99 years]; 15 446 women [mean age, 52.3 years; age range, 18–98 years]) obtained between 2010 and 2015, which were labeled and partially annotated by 13 board-certified radiologists, in a convolutional neural network. Radiograph classification and nodule detection performances of DLAD were validated by using one internal and four external data sets from three South Korean hospitals and one U.S. hospital. For internal and external validation, radiograph classification and nodule detection performances of DLAD were evaluated by using the area under the receiver operating characteristic curve (AUROC) and jackknife alternative free-response receiver-operating characteristic (JAFROC) figure of merit (FOM), respectively. An observer performance test involving 18 physicians, including nine board-certified radiologists, was conducted by using one of the four external validation data sets. Performances of DLAD, physicians, and physicians assisted with DLAD were evaluated and compared.

Results: According to one internal and four external validation data sets, radiograph classification and nodule detection performances of DLAD were a range of 0.92–0.99 (AUROC) and 0.831–0.924 (JAFROC FOM), respectively. DLAD showed a higher AUROC and JAFROC FOM at the observer performance test than 17 of 18 and 15 of 18 physicians, respectively ($P < .05$), and all physicians showed improved nodule detection performances with DLAD (mean JAFROC FOM improvement, 0.043; range, 0.006–0.190; $P < .05$).

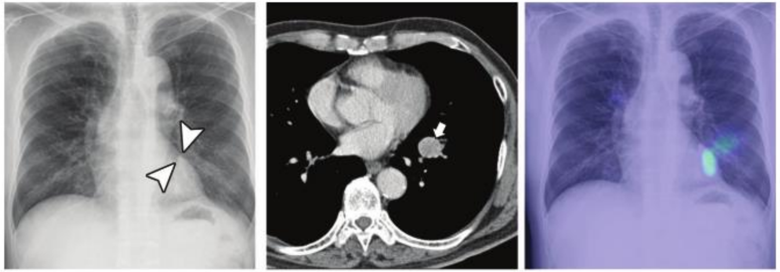
Conclusion: This deep learning–based automatic detection algorithm outperformed physicians in radiograph classification and nodule detection performance for malignant pulmonary nodules on chest radiographs, and it enhanced physicians' performances when used as a second reader.

Online supplemental material is available for this article.



a. b. c.

Figure 1: Images in a 78-year-old female patient with a 1.9-cm part-solid nodule at the left upper lobe. **(a)** The nodule was faintly visible on the chest radiograph (arrowheads) and was detected by 11 of 18 observers. **(b)** At contrast-enhanced CT examination, biopsy confirmed lung adenocarcinoma (arrow). **(c)** DLAD reported the nodule with a confidence level of 2, resulting in its detection by an additional five radiologists and an elevation in its confidence by eight radiologists.



a. b. c.

Figure 2: Images in a 64-year-old male patient with a 2.2-cm lung adenocarcinoma at the left upper lobe. **(a)** The nodule was faintly visible on the chest radiograph (arrowheads) and was detected by seven of 18 observers. **(b)** Biopsy confirmed lung adenocarcinoma in the left upper lobe on contrast-enhanced CT image (arrow). **(c)** DLAD reported the nodule with a confidence level of 2, resulting in its detection by an additional two radiologists and an elevated confidence level of the nodule by two radiologists.

Clinical study - CXR nodule/consolidation/pneumothorax

March 2019

JAMA Network Open

JAMA Network Open

Original Investigation | Imaging

Development and Validation of a Deep Learning–Based Automated Detection Algorithm for Major Thoracic Diseases on Chest Radiographs

Eui Jin Hwang, MD; Sunggyun Park, MS; Kwang-Nam Jin, MD; Jung Im Kim, MD; So Young Choi, MD; Jong Hyuk Lee, MD; Jin Mo Goo, MD, PhD; Jaehong Aum, PhD; Jae-Joon Yim, MD; Julien G. Cohen, MD; Gilbert R. Ferretti, MD; Chang Min Park, MD, PhD; for the DLAD Development and Evaluation Group

Abstract

IMPORTANCE Interpretation of chest radiographs is a challenging task prone to errors, requiring expert readers. An automated system that can accurately classify chest radiographs may help streamline the clinical workflow.

OBJECTIVES To develop a deep learning–based algorithm that can classify normal and abnormal results from chest radiographs with major thoracic diseases including pulmonary malignant neoplasm, active tuberculosis, pneumonia, and pneumothorax and to validate the algorithm's performance using independent data sets.

DESIGN, SETTING, AND PARTICIPANTS This diagnostic study developed a deep learning–based algorithm using single-center data collected between November 1, 2016, and January 31, 2017. The algorithm was externally validated with multicenter data collected between May 1 and July 31, 2018. A total of 54 221 chest radiographs with normal findings from 47 917 individuals (21 556 men and 26 361 women; mean [SD] age, 51 [16] years) and 35 613 chest radiographs with abnormal findings from 14 102 individuals (8373 men and 5729 women; mean [SD] age, 62 [15] years) were used to develop the algorithm. A total of 486 chest radiographs with normal results and 529 with abnormal results (1 from each participant; 628 men and 387 women; mean [SD] age, 53 [18] years) from 5 institutions were used for external validation. Fifteen physicians, including nonradiology physicians, board-certified radiologists, and thoracic radiologists, participated in observer performance testing. Data were analyzed in August 2018.

EXPOSURES Deep learning–based algorithm.

MAIN OUTCOMES AND MEASURES Image-wise classification performances measured by area

Key Points

Question Can a deep learning–based algorithm accurately discriminate abnormal chest radiograph results showing major thoracic diseases from normal chest radiograph results?

Findings In this diagnostic study of 54 221 chest radiographs with normal findings and 35 613 with abnormal findings, the deep learning–based algorithm for discrimination of chest radiographs with pulmonary malignant neoplasms, active tuberculosis, pneumonia, or pneumothorax demonstrated excellent and consistent performance throughout 5 independent data sets. The algorithm outperformed physicians, including radiologists, and enhanced physician performance when used as a second reader.

Meaning A deep learning–based algorithm may help improve diagnostic accuracy in reading chest radiographs and assist in prioritizing chest radiographs, thereby increasing

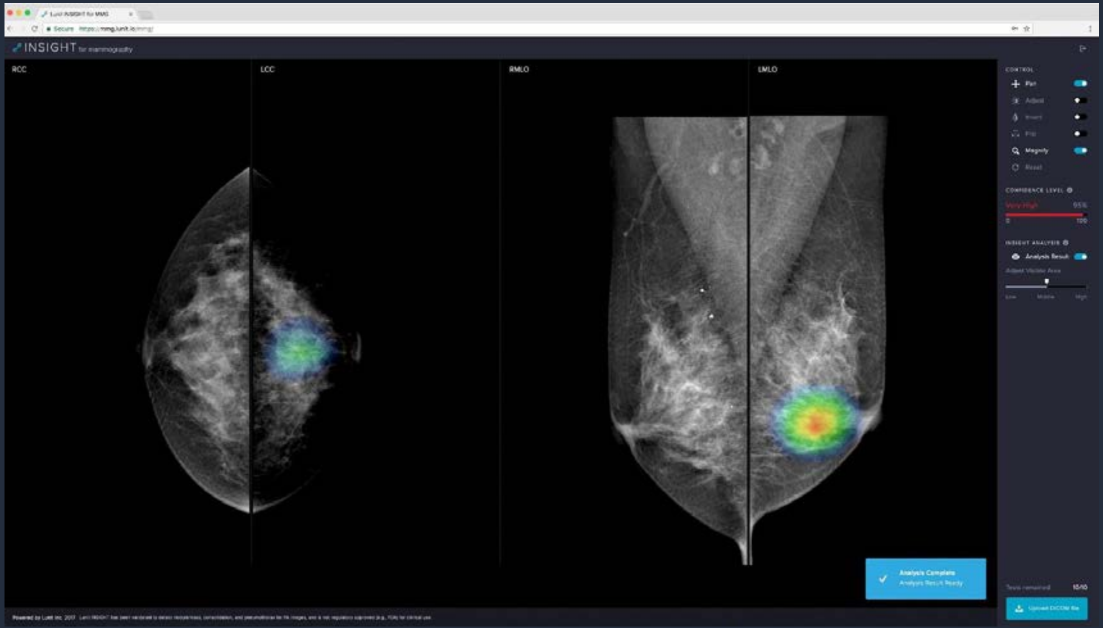
Representative Case From the Observer Performance Test (Malignant Neoplasm)
A, The chest radiograph (CR) shows nodular opacity at the right lower lung field (arrowhead), which was initially detected by 2 of 15 observers. B, The corresponding computed tomographic (CT) image reveals a nodule at the right middle lobe. C, The deep learning-based automatic detection algorithm (DLAD)

Representative Case From the Observer Performance Test (Pneumonia)
A, The chest radiograph (CR) shows subtle patchy increased opacity at the left middle lung field, which was initially missed by all 15 observers. B, The corresponding computed tomographic (CT) image shows patchy ground glass opacity at the left upper lobe. C, The deep learning-based automatic detection algorithm (DLAD) correctly localized the lesion (probability score, 0.371). Seven observers correctly detected the

Lunit INSIGHT MMG

Lunit INSIGHT MMG

MFDS-approved



200K+
training cases

50K+
biopsy-proven cancer cases

97%
performance level (AUC)

Internal simulation – MMG breast cancer

	Breast Specialists		General Radiologists	
unit: %	Sensitivity	Specificity	Sensitivity	Specificity
Single reading: 1 reader	80.0	72.3	70.5	71.6
Double reading: 3 readers	81.9	75.4	72.5	74.7
Single reading (1 reader) + AI	86.3	73.8	83.2	75.5

Internal simulation based on clinical study for MFDS, 2019 (unpublished)

Regulation approval cases

CADe(x) SaMD in MFDS (Korean FDA)

	Product Class	Lunit INSIGHT	
CADe	Class 2	Lunit INSIGHT CXR - Nodule (2018.08)	Detect radiologic finding(s)
CADx	Class 3	Lunit INSIGHT MMG (2019.07)	Detect and characterize suspicious lesions for breast cancer

Clinical evaluation

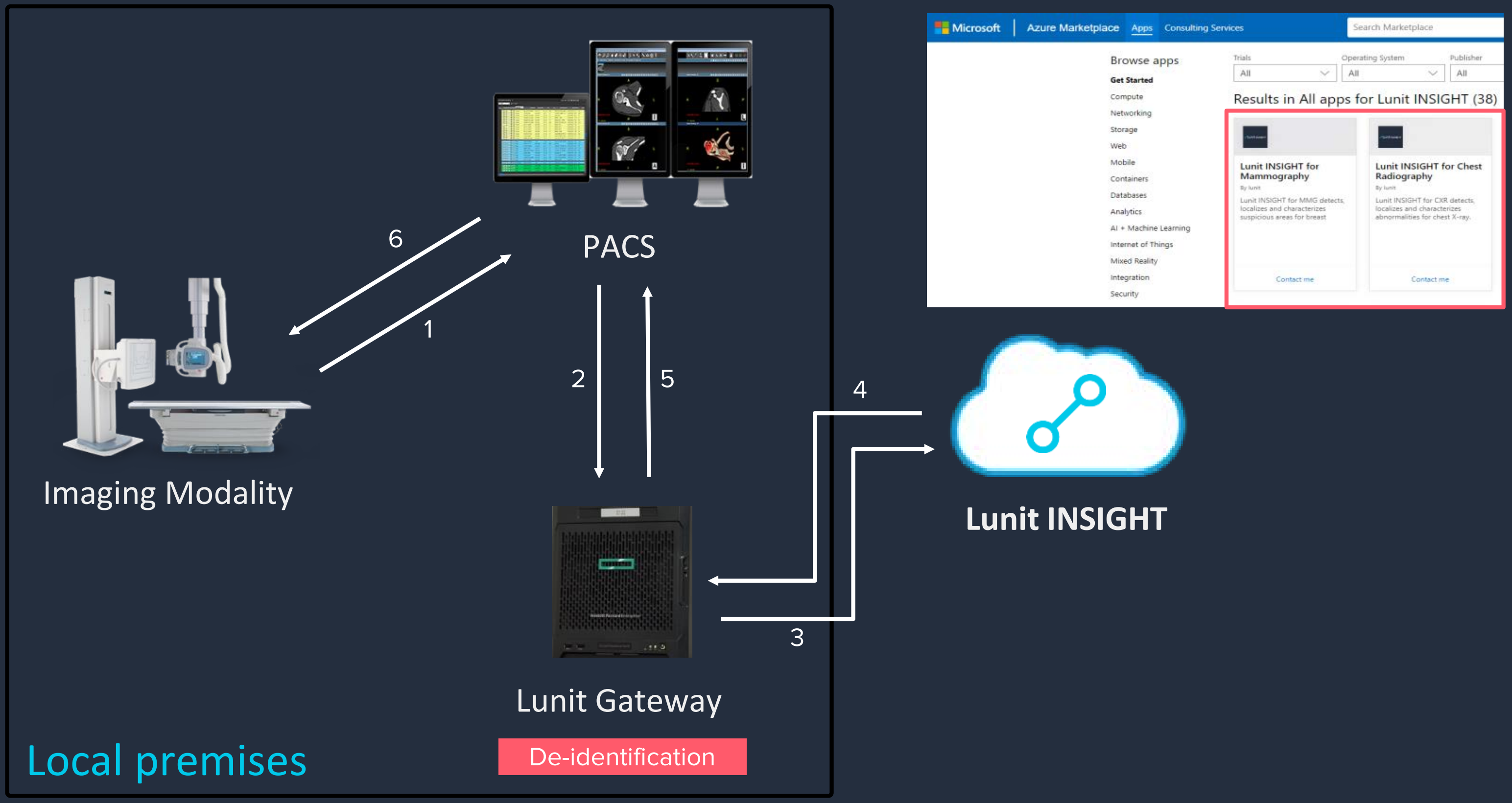
Internal performance validation

- Multi-national/center cases
- Standalone performance
  - Classification : AUROC / sensitivity / specificity
  - Localization : JAFROC / LROC

Clinical study

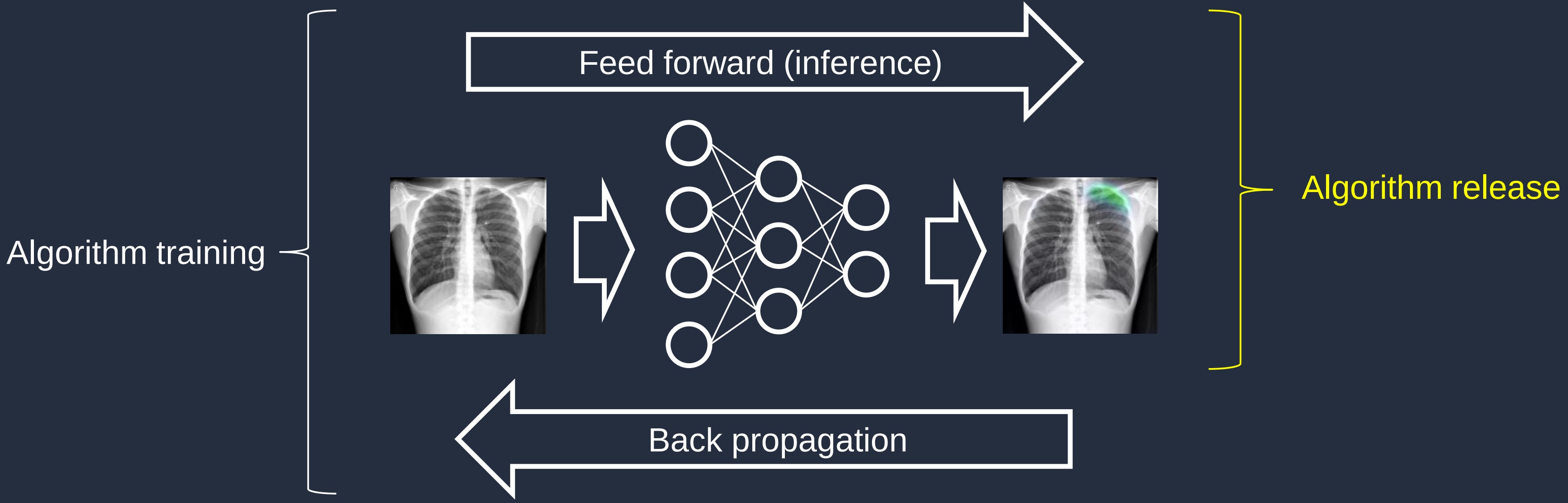
- Every product
- Retrospective clinical study
- Reader study (w/ CAD vs. w/o CAD)
  - AUROC + Localization

Integration & Data security



Change control

- Analysis algorithm is locked for each SW version



For MFDS (Korean FDA), if only training data is added to the same architecture, vendors can manage their own minor changes.

Further direction

- Global regulatory approvals (e.g. CE, FDA)

- Extend capabilities of indications
    - Lunit INSIGHT CXR
        - Nodule + Consolidation / Pneumothorax + 7 more radiologic findings

- Diversification of intended use
    - CADe/x , CADt (Triage), Worklist prioritization, etc.

- Other modalities
    - CT, DBT (Digital Breast Tomosynthesis)

Q&A

Lunit

Thank you

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