AI-POWERED BREAST RADIOLOGY

Medical Whitepaper

Lunit INSIGHT MMG

Lunit

Perfecting Intelligence, Transforming Medicine.

About Us

Lunit, abbreviated from “learning unit,” is a medical AI software company devoted to developing advanced medical image analytics and novel imaging biomarkers via cutting-edge deep learning technology.

Founded in 2013, Lunit has been internationally acknowledged for its advanced, state-of-the-art technology and its application in medical images.
Lunit is based in Seoul, South Korea.

Our Mission

Perfecting Intelligence, Transforming Medicine.
Through our unprecedented AI technology, we seek to provide AI solutions that open a new era of diagnostics and therapeutics. We are especially focused on conquering cancer, one of the leading cause of death worldwide.

Lunit INSIGHT MMG

Lunit INSIGHT MMG

Breast cancer is one of the most common disease that takes up 25% of the entire cancer and is the leading cause of death, at 15%, among women worldwide.[1] Screening mammography is the only single modality proven to improve breast cancer survival, with a mortality reduction rate of around 20%.[2]

However, accuracy of screening mammography is low, with false negative rates of 10-30%[3] and false positive rates around 95%.[4] Proportion of breast specialists reading screening mammograms is also low.

Lunit INSIGHT MMG provides solution to this problem by detecting breast cancer lesions with 97% accuracy within seconds. It has been trained by 200,000 mammography cases of which approximately 50,000 cases were from breast cancer patients. Our recent reader study results show that with Lunit INSIGHT MMG, radiologists saw an increase in breast cancer detection (24%) and a decrease in false positive recall (12%).

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Regulatory Status
(as of November 2019)

- **Korea MFDS**: Approved, July 2019
- **FDA**: Expected within 2020
- **CE**: Expected in late 2019

You can login to **https://insight.lunit.io** to freely upload images
and get real-time analysis results conducted by **Lunit INSIGHT** in no time.

1 Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin 2015;65:87-108.
2 Myers ER, Moorman P, Gierisch JM, et al. Benefits and harms of breast cancer screening: a systematic review. JAMA 2015;314:1615-34.
3 Majid AS, de Paredes ES, Doherty RD, Sharma NR, Salvador X. Missed breast carcinoma: pitfalls and pearls. Radiographics 2003; 23: 881-95.
4 http://breastscreening.cancer.gov.

Internal Validation
(Korea, United States, United Kingdom)

Lunit INSIGHT MMG was validated internally throughout various countries with different ethnicity. Validation dataset consists of approximately 3,200 patients of mammography exams from 3 countries, of which 1,858 patients from Korea (KR), 750 from United States (US), and 654 from United Kingdom (UK).

Performance Summary: ROC AUC, Sensitivity, Specificity

Avg. Performance 95% C.I (Low, High)	ROC AUC	Sensitivity	Specificity
KR	0.970 (0.963, 0.978)	0.903 (0.880, 0.926)	0.917 (0.901, 0.932)
US	0.953 (0.938, 0.968)	0.936 (0.906, 0.966)	0.802 (0.767, 0.837)
UK	0.938 (0.918, 0.958)	0.917 (0.881, 0.954)	0.768 (0.729, 0.808)

Density Sub-Group Analysis: ROC AUC

Entirely Fatty	Scattered Fibroglandular Tissue	Heterogeneously Dense	Extremely Dense
0.975	0.965	0.954	0.925

False Positive Analysis: FPPI*

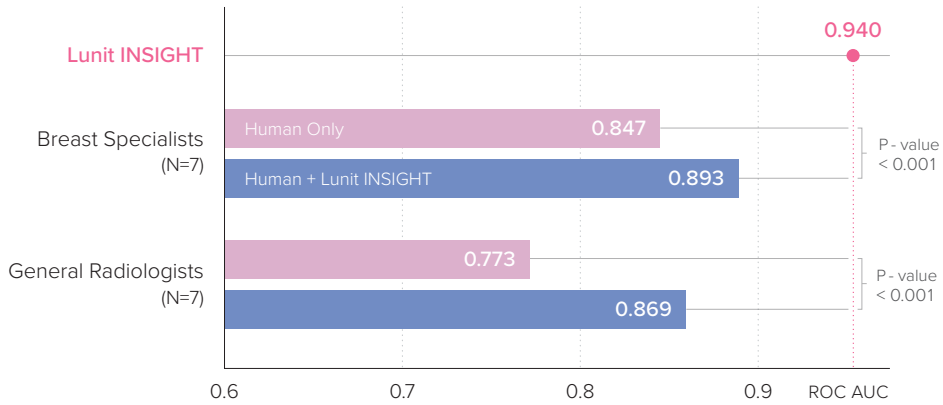
Cancer Breast	Benign Breast	Normal Breast
0.350	0.117	0.031

** False-Positive Per Image (FPPI) represents number of FP findings per image; extremely low especially in non-cancer breasts.*

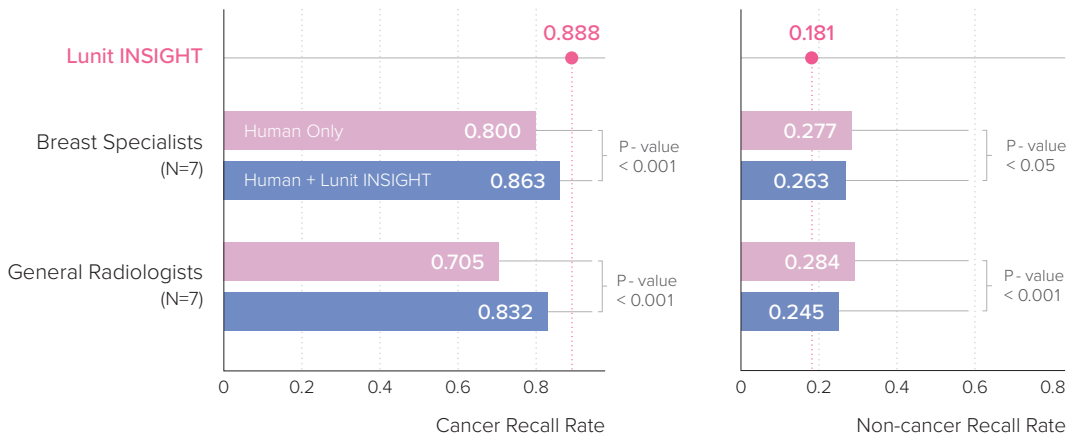
Reader Study Results
(Korea Ministry of Food and Drug Safety)

Yonsei University Severance Hospital & Soon Chun Hyang University Hospital, Feb. 2019

Diagnostic Performance: ROC AUC (N=320)



Recall Rate: Cancer (N=160), Non-Cancer (N=160)



Subgroup Analysis: Breast Density

Avg. Performance		Radiologist Only (N=14)	Radiologist + Lunit INSIGHT (N=14)	Lunit INSIGHT Only
ROC AUC (N=320)	Fatty (A,B)	0.861	0.905	0.948
	Dense (C,D)	0.782	0.866	0.932
Cancer Recall Rate (N=160)	Fatty (A,B)	0.792	0.841	0.864
	Dense (C,D)	0.738	0.850	0.897
Non-cancer Recall Rate (N=160)	Fatty (A,B)	0.205	0.168	0.067
	Dense (C,D)	0.326	0.305	0.250

A: Entirely Fatty / B: Scattered Fibroglandular Tissue / C: Heterogeneously Dense / D: Extremely Dense

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Reader Study Results
(Diagnostic Performance and Reading Time)

Soon Chun Hyang University Hospital, Oct. 2019

Performance Summary: ROC AUC, Recall Rate, Reading Time

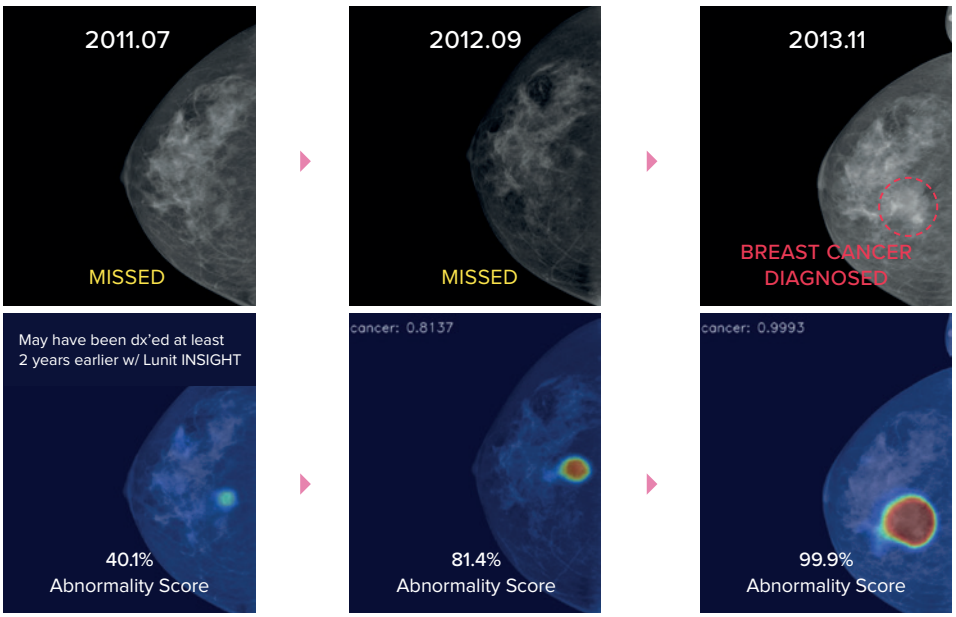
Avg. Performance		Radiologist Only (N=5)	Radiologist + Lunit INSIGHT (N=5)	Lunit INSIGHT Only
ROC AUC (N=200)		0.751	0.850	0.915
Recall Rate	Cancer (N=100)	0.660	0.816	0.870
	Non-cancer (N=100)	0.348	0.306	0.210
Reading Time	Cancer (N=100)	71.97 sec	60.89 sec	-
	Non-cancer (N=100)	71.00 sec	60.88 sec	-

Early-Stage Cancer Detection

Below examples show the performance evaluation of Lunit INSIGHT MMG in terms of early-stage cancer detection. Both examples consist of biopsy-proven cancer case and its previous studies. In each example, original images were shown on the first row with the ground-truth location of cancer lesions, and the same images analyzed by Lunit INSIGHT MMG were shown on the second row with its detection of cancer lesions presented in heatmaps.

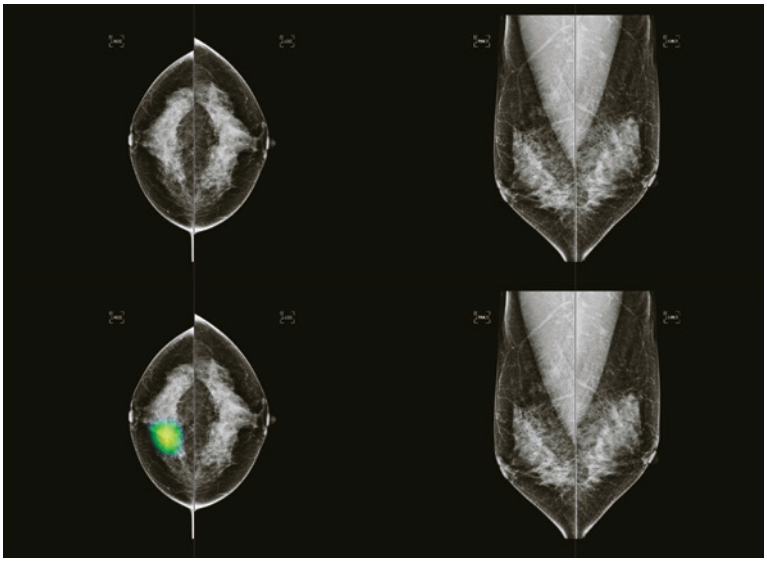
Example 1

Example 2

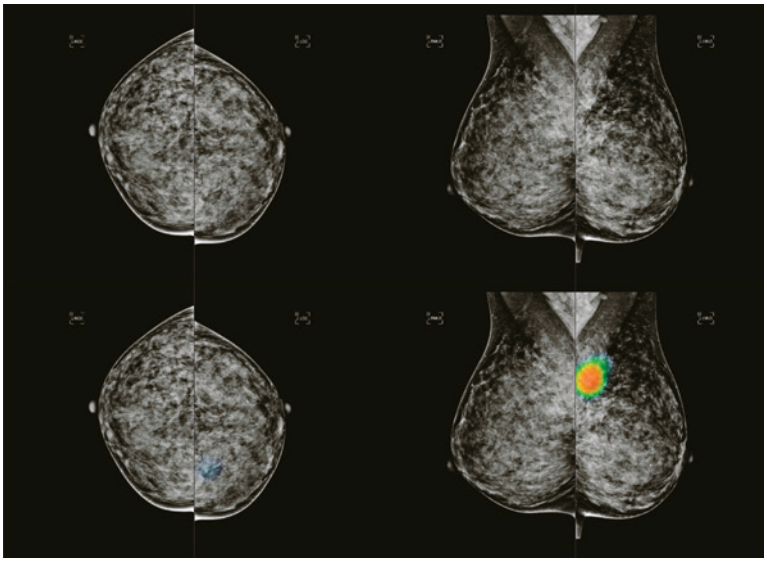


Sample Cases

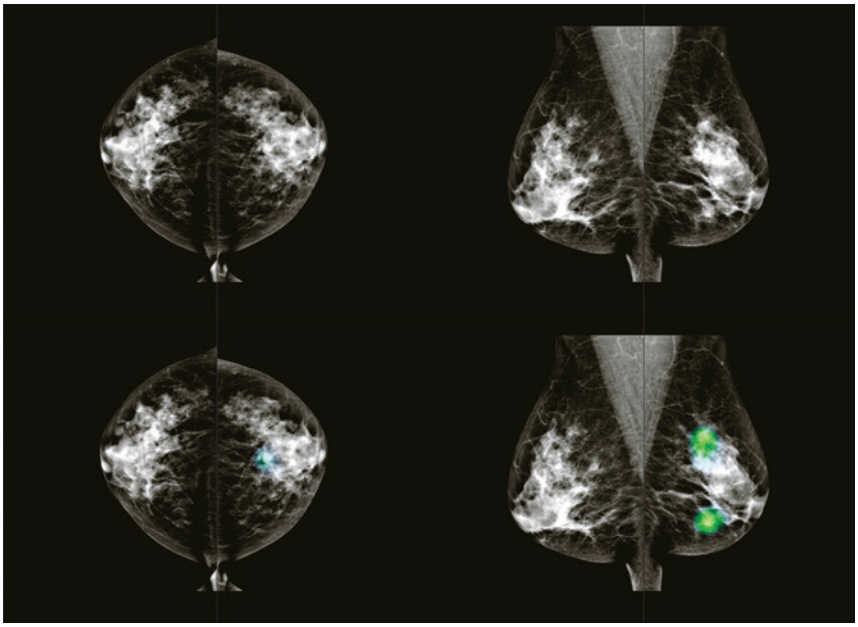
Below sample cases show how radiologists were able to detect more breast cancer after using Lunit INSIGHT MMG. In the parenthesis, on the left are the number of radiologists that detected breast cancer without any AI assistance, whereas on the right is the number of radiologists who correctly detected breast cancer with Lunit INSIGHT MMG. (Total number of radiologists=14)



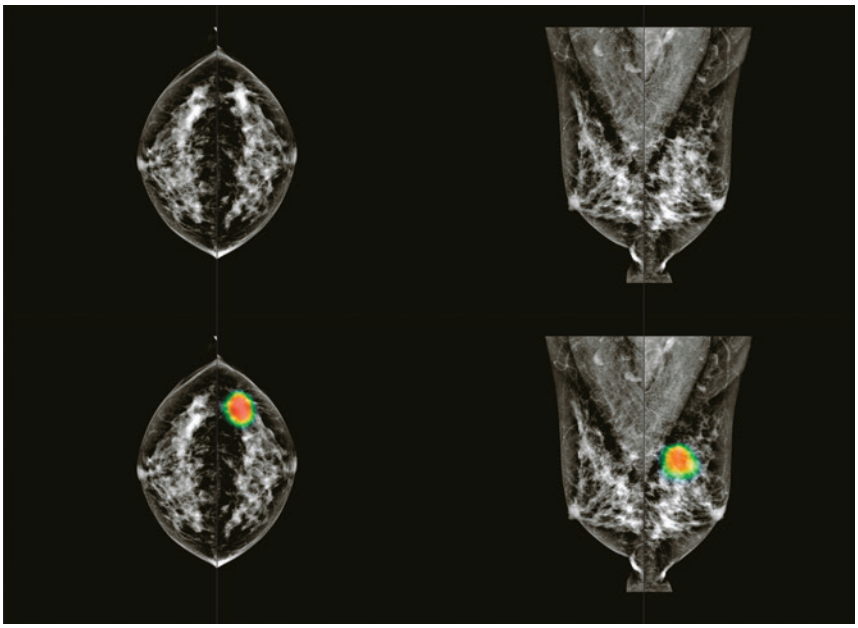
CASE 1 A small obscured mass (w/o Lunit 4 → w/ Lunit 13)



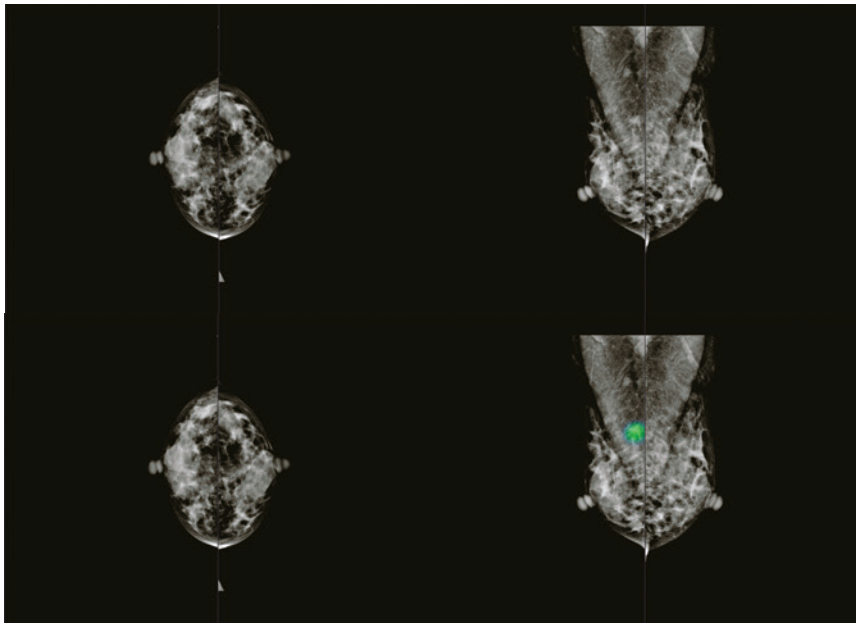
CASE 2 A small obscured mass (w/o Lunit 7 → w/ Lunit 14)



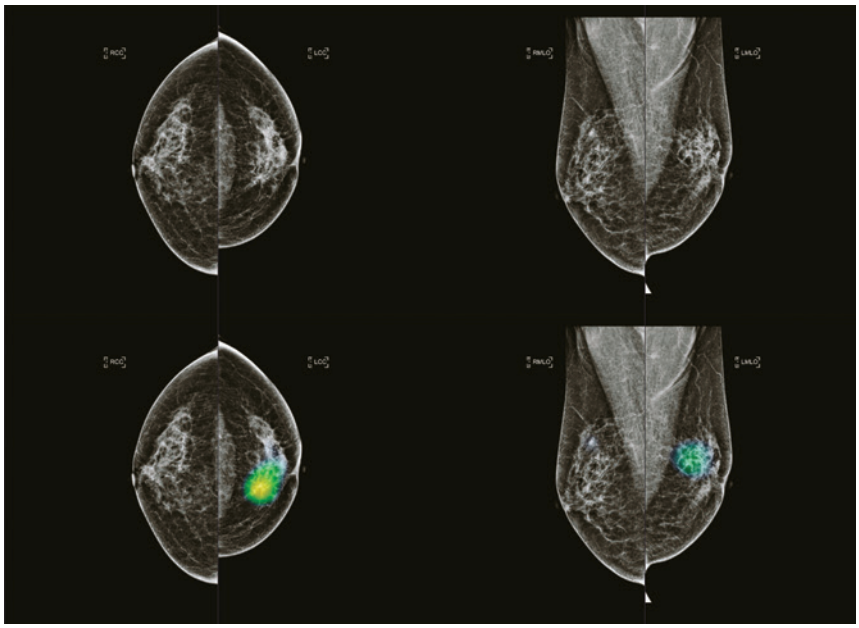
CASE 3 A small obscured mass with clustered microcalcifications
(w/o Lunit 2 → **w/ Lunit 11**)



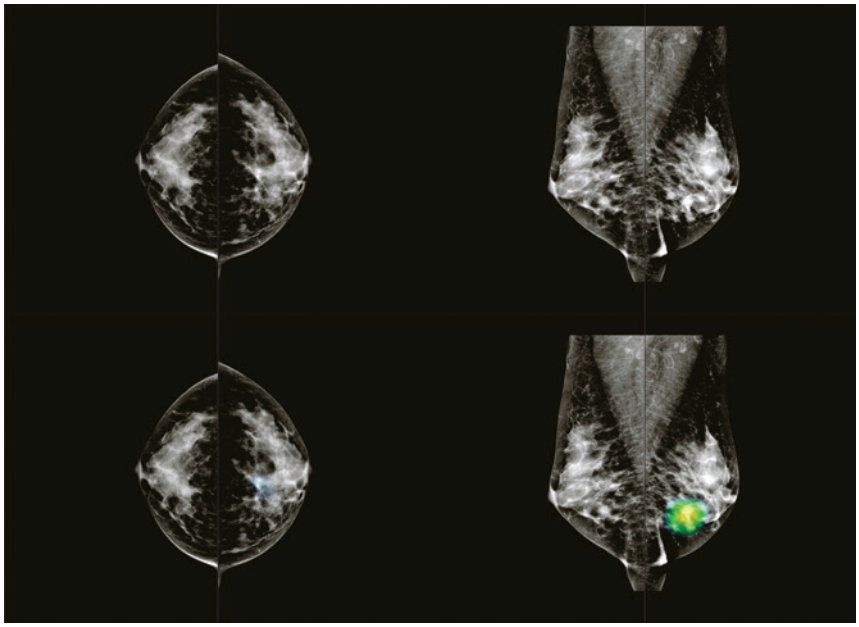
CASE 4 A small obscured mass with clustered microcalcifications
(w/o Lunit 5 → **w/ Lunit 12**)



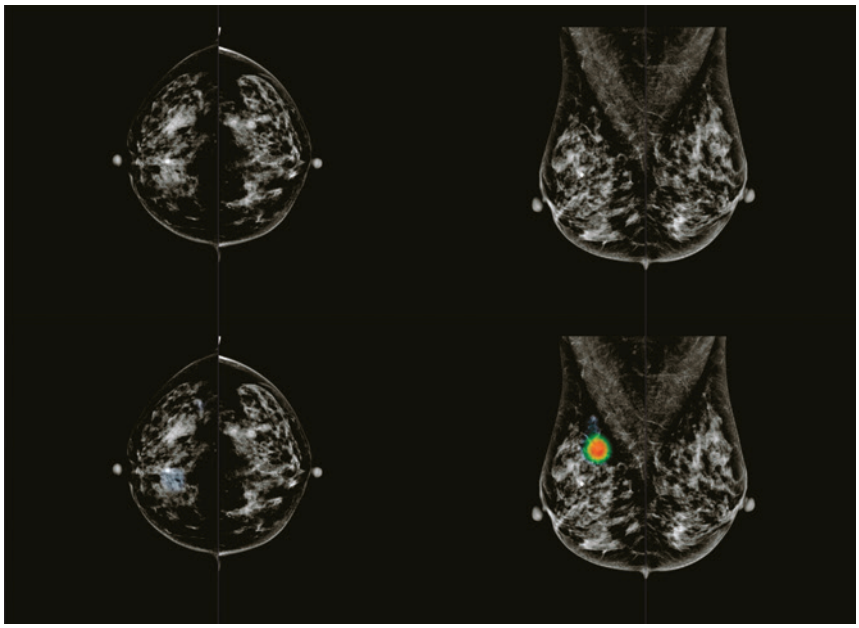
CASE 5 A small spiculated mass (w/o Lunit 7 → w/ Lunit 14)



CASE 6 Focal asymmetry (w/o Lunit 5 → w/ Lunit 13)



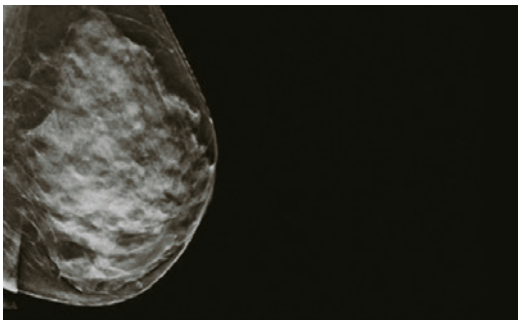
CASE 7 Focal asymmetry (w/o Lunit 5 → w/ Lunit 13)



CASE 8 Focal asymmetry (w/o Lunit 7 → w/ Lunit 14)

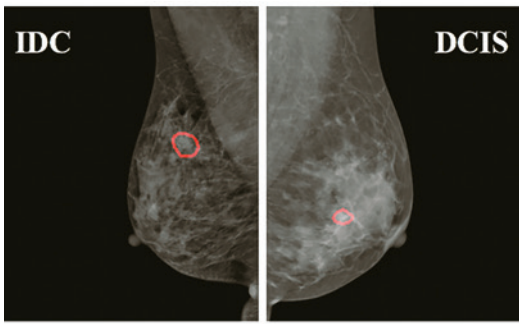
Other Research in Breast Radiology

Digital Breast Tomosynthesis



Digital Breast Tomosynthesis (DBT) has been demonstrated by various large-scale studies to be superior to mammography in terms of breast cancer detection performance. We are using our experience in mammography research to develop a highly accurate diagnostic algorithm for breast cancer detection in DBT.

IDC and DCIS on Mammography



Up to 56% of Ductal carcinoma in situ (DCIS) cases proven by biopsy have been upstaged to micro-invasive or Invasive ductal carcinoma (IDC) upon final surgical pathology, leading to likely additional invasive procedures.
We are investigating whether preoperative assessment is possible by distinguishing DCIS and IDC on mammography.

Increase of cancer detection rate and reduction of false-positive recall in screening mammography using artificial intelligence – a multi-center reader study

PURPOSE

To assess feasibility of artificial intelligence (AI) based diagnostic-support software whether it can be used to improve radiologists' diagnostic performance in terms of cancer detection and false-positive recall in breast cancer screening.

METHOD AND MATERIALS

A total of 400 exams of screening mammograms were retrospectively collected from two institutions. For each institution, 100 cancer, 40 benign, and 60 normal exams were collected. All cancer exams were proven by biopsy. Half of the benign exams were proven by biopsy (i.e. recalled benign) while the remainder were proven by at least 2 years of follow-up imaging. 80% of the exams were randomly selected respectively from each category and each institution (e.g., 16 recalled benign for each institution). All exams were 4-view paired. A blinded multi-reader multi-case study was performed with a group of 14 radiologists for the selected 320 exams. Each radiologist reads each case without and then with aid of Lunit INSIGHT for Mammography (Lunit Inc., South Korea), a deep learning-based software which shows per-breast malignancy scores as well as region-ofinterests (ROIs) for suspicious malignant lesions (Fig.1). The difference of readers' decision without and with AI in terms of likelihood-of-malignancy (LOM; DMIST 7-pt score) and recall-ness (recall or not) was analyzed.

AI-based diagnosis-support software which shows per-breast malignancy scores (on the right-side panel) and ROIs for suspicious malignant lesions (heatmaps).

RESULTS

Significant improvement of diagnostic performance was shown for all 14 radiologists; average LOM-based ROC AUC was 0.810 and 0.881 without and with AI, respectively (p-value=0.0000047, C.I.=95%). Based on readers' binary decision whether each exam should be recalled or not, average cancer detection rate was increased from 75.3% to 84.8% while false-positive recalls (i.e. non-cancer recalls) were decreased from 28.0% to 25.4% where 20% of non-cancer exams were recalled benign cases.

CONCLUSION

This reader study showed a statistically significant improvement of diagnostic performance (0.071 increase in ROC AUC). Cancer detection rate was increased by 12.6% and false-positive recall rate was decreased by 9.6% with assistance of AI-based diagnostic-support software.

CLINICAL RELEVANCE / APPLICATION

With increase of cancer detection rate and decrease of false-positive recall rate, AI-based diagnostic-support software can be practically used in routine breast cancer screening.

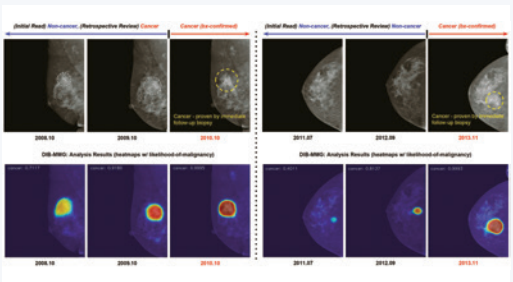
Data-driven Imaging Biomarker for Breast Cancer Screening in Mammography – Early Detection of Breast Cancer

PURPOSE

To assess feasibility of data-driven imaging biomarker in mammography (DIB-MMG; an imaging biomarker derived from large-scale mammography data based on deep learning technology) whether it can be used for early detection of breast cancer.

METHOD AND MATERIALS

A total of 105,592 exams of 4-view digital mammograms were retrospectively collected from multiple institutions for developing DIB-MMG, where 22,456 were cancer (confirmed by biopsy), 36,821 were benign (confirmed by biopsy or at least 1 year of follow-up imaging), and 46,315 were normal exams. Based on external validation in a separate institution with 3,696 exams of mammograms (1,073 were cancer; one for each patient), DIB-MMG showed 0.963, 94.1%, 80.2% of AUC, sensitivity, specificity, respectively. Among the 1,073 cancer patients, 85 patients had 116 exams of prior mammograms which were diagnosed as non-cancer at that time. A breast radiologist retrospectively reviewed the 116 exams and re-classified into three categories – 1) Missed (46 exams; 47 cancer / 45 non-cancer breasts): retrospectively seen in previous mammogram (mmg-p) and also seen in mammogram at diagnosis (mmg-d), 2) Interval (55; 61/49): retrospectively not seen in mmg-p but seen in mmg-d, and 3) Occult (15; 17/13): not seen both in mmg-p and mmg-d. DIB-MMG was analyzed for the Missed, Interval, and Occult cancers, respectively.



Each patient (left and right) was diagnosed as cancer (right most column), where the cancer lesion was seen at diagnosis. Their prior mammograms (first and second columns) were reviewed retrospectively by a breast radiologist who already knows location of the biopsy-confirmed cancer lesions.
1) Missed cancer (left): previously negative but retrospectively positive, **2) Interval cancer (right):** previously negative and retrospectively negative.

RESULTS

Per-breast AUC, sensitivity, specificity were used since all the data is positive in exam-level. Per-breast AUC was 0.841, 0.676, 0.620 for the Missed, Interval, Occult, respectively. Sensitivity (w/ specificity) at different operating points 0.05, 0.10 were 68.1% (88.9%), 55.3% (91.1%) for Missed, 49.2% (83.7%), 37.7% (91.8%) for Interval, and 41.2% (69.2%), 17.7% (84.6%) for Occult, respectively. Original operating point of DIB-MMG for routine screening was 0.10. Fig.1 shows examples of the Missed and Interval cancers.

CONCLUSION

This retrospective study showed feasibility of DIB-MMG for early detection of breast cancer on mammography, where 32 out of 47 missed cancers, 30 out of 61 interval cancers, 7 out of 17 occult cancers were detected by DIB-MMG. Overall AUC was 0.738. Further clinical validation with observer performance study is needed.

CLINICAL RELEVANCE / APPLICATION

With further clinical validation, DIB-MMG can be used as an effective diagnostic-support tool for early detection of breast cancer in screening mammography.

Data-driven Imaging Biomarker for Breast Cancer Screening in Mammography – Prediction of Tumor Invasiveness in Mammography

PURPOSE

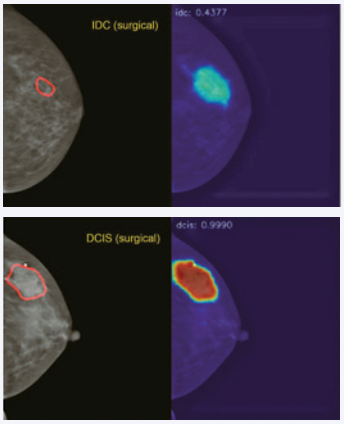
To assess feasibility of data-driven imaging biomarker in mammography (DIB-MMG; an imaging biomarker derived from large-scale mammography data based on deep learning technology) whether prediction of tumor invasiveness is applicable on mammography – discrimination of ductal carcinoma in situ (DCIS), DCIS with microinvasion (DCIS-MI), and invasive ductal carcinoma (IDC).

METHOD AND MATERIALS

A total of 151,764 exams of 4-view mammograms were collected from multiple institutions for developing DIBMMG, where 31,776 were cancer (confirmed by biopsy), 49,644 were benign (confirmed by biopsy or at least 1 year of follow-up imaging), and 70,344 were normal exams (confirmed by at least 1 year of follow-up imaging). Surgical assessment of tumor invasiveness (459 DCIS, 373 DCIS-MI, and 6,365 IDC) was collected for 7,197 out of 31,776 cancer exams. A separate set of 777 cancer exams (46 DCIS, 49 DCIS-MI, 682 IDC) were used for evaluation. Previously, we assessed the feasibility of DIB-MMG as a diagnostic-support tool for breast cancer screening in mammography. In this study, we further investigated whether DIB-MMG is applicable to predict tumor invasiveness in mammography. DIB-MMG-TI (i.e. Tumor Invasiveness) was developed via two stages of training – 1) training with diagnosis labels (normal, benign, cancer), followed by 2) fine-tuning with invasiveness labels (DCIS, DCIS-MI, IDC) on the subset of cancer exams. We exploited the location of cancer lesions (6,229 among 7,197 exams) for the purpose of attention (i.e. attention mechanism in AI) in order to predict the invasiveness in more effective way.

RESULTS

AUC was summarized on two tasks: 1) discrimination of IDC from DCIS and DCIS-MI, and 2) discrimination of DCIS from DCIS-MI and IDC. For each task, per-exam AUC of DIB-MMG-TI on 777 exams of validation dataset was 0.781 and 0.690 respectively, while per-breast AUC for each task was 0.775 and 0.690. Fig.1 shows examples.



Examples of IDC (above) and DCIS (below) respectively, where red contour is the location of cancer lesions. For each case, attention map for respective subtype is shown as a heat-map.

CONCLUSION

This study showed that discrimination of DCIS-MI from DCIS is more difficult than that from IDC in mammography. Experimental results showed that DIB-MMG-TI is feasible to discriminate IDC from the rest. Further clinical validation with observer performance study is needed.

CLINICAL RELEVANCE / APPLICATION

With further clinical validation, DIB-MMG-TI can be used as a preoperative diagnostic-support tool for prediction of tumor invasiveness in mammography.

Data-driven Imaging Biomarker for Breast Cancer Screening in Digital Breast Tomosynthesis – Multidomain Learning with Mammography

PURPOSE

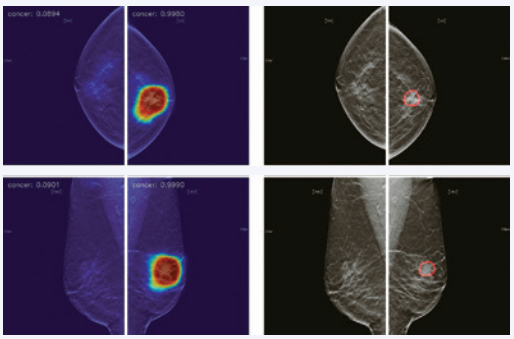
To assess feasibility whether mammography data is helpful for developing data-driven imaging biomarker in digital breast tomosynthesis (DIB-DBT; an imaging biomarker for detection of breast cancer, which is derived from DBT data based on deep learning technology).

METHOD AND MATERIALS

A total of 1,517 exams of 4-view digital breast tomosynthesis (DBT) and 49,577 exams of 4-view digital mammograms (MMG) were retrospectively collected from an institution. We divided 1,517 exams of DBT into 1,187 (970 cancer, 52 benign, 165 normal) and 330 (244 cancer, 34 benign, 52 normal) exams for training and validation, and 49,577 exams of MMG into 47,719 (5,599 cancer, 17,971 benign, 24,149 normal) and 1,858 (619 cancer, 620 benign, 619 normal) exams for training and validation, respectively. For external validation, we also collected 448 exams (148 cancer, 150 benign, and 150 normal) of 4-view DBT from another institution. Previously, we demonstrated that using DBT and MMG concurrently is effective for developing DIB-DBT, where it was first trained with (large-scale) MMG then fine-tuned with (small-scale) DBT. We further aimed to enhance the utilization of MMG by multi-domain learning to boost the performance of DIB-DBT. Two-stage training was adopted – 1) pre-training with MMG, followed by 2) multi-domain fine-tuning with both of DBT and MMG. A total of four different approaches was compared in order to find the best way to exploit MMG for developing DIB-DBT – (a) training only with DBT, (b-d) training with MMG and then fine-tuning with (b) DBT (previous work), (c) DBT and MMG, (d) DBT and MMG by multi-domain learning.

RESULTS

Per-exam AUC of DIB-DBT on the internal validation dataset was 0.890, 0.899, 0.901, 0.910 for each method of (a-d) respectively, while per-exam AUC on the external validation dataset was 0.871, 0.880, 0.899, 0.901 for (ad) respectively. Fig.1 shows an example of DIB-DBT (i.e. (d)).



For visual interpretability of the results, we showed heat-maps on a set of synthetic 2D images (just for visualization). (Left) Heat-maps from DIB-DBT, (Right) Ground-truth – cancer lesion confirmed by biopsy.

CONCLUSION

This study demonstrated that multi-domain learning with large -scale MMG is an effective way for developing DIB-DBT especially with small-scale DBT. Further clinical validation is needed to utilize DIB-DBT as a reliable diagnostic-support tool for breast cancer detection.

CLINICAL RELEVANCE / APPLICATION

With further clinical validation, DIB-DBT could be practically used as an effective diagnostic-support tool for breast cancer screening in digital breast tomosynthesis.

Deepen your INSIGHT
with AI-Powered Breast Radiology

With the help of our AI,
you can make the best decision in less duration of time.
Together, we can save more time, save cost, and save lives.

Partner with Us

We welcome research partnerships and other collaboration with medical institutions, healthcare providers and companies interested in implementing our software product. Currently, we have over 20 worldwide research partners throughout USA, UK, China and Korea.

We look forward to hearing from you!

Corporate Partners

FUJIFILM

Microsoft Azure

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NUANCE

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