# **About the Authors**



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# Revolutionizing Breast Imaging: Artificial Intelligence's Role in Precisely Differentiating Benign from Malignant Lesions

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#### Introduction

Recent advancements in artificial intelligence (AI) have leveraged computer science with large datasets to improve predictive and classification capabilities, which are crucial for problem-solving in radiology.<sup>1</sup> Machine Learning (ML), the driving force behind AI's effectiveness, harnesses computational models and algorithms to analyze raw data for classification and prediction tasks.<sup>2</sup> AI utilizes a multi-layered network of interconnected nodes emulating the intricate neuronal structure of the human brain. These include an input layer that initially receives data, a hidden layer that discerns data patterns, and an output layer that presents the results of the processed data.<sup>2</sup>

The evolution of AI has propelled us from a reliance on manually intensive ML techniques to the more autonomous realms of deep learning (DL). This shift has reduced our dependence on extensive engineering knowledge and domain-specific expertise, particularly in extracting features from raw data.<sup>3</sup> This progression has proved pivotal in managing large-scale datasets, enhancing results, and augmenting performance with increased data exposure. Within the spectrum of DL methodologies, convolutional neural networks have emerged to transform image analysis and have particularly revolutionized the use of AI applications in radiology. The advancements of Al in the domain of clinical radiology are notably evident, with breast imaging emerging as a key beneficiary of this technological progress.<sup>4,5</sup>

The application of AI in breast imaging presents a range of clinical uses, from improving breast cancer screening and risk stratification,<sup>6-8</sup>

to aiding in making treatment decisions by predicting axillary involvement,<sup>9</sup> neoadjuvant therapy responses,<sup>10</sup> and recurrence risks.<sup>11</sup> A significant breakthrough in the application of AI in breast imaging lies in its potential to boost the specificity of breast imaging tests, enabling accurate discrimination between benign and malignant breast lesions.

A recent systematic review and meta-analysis looked at radiomic analyses of preoperative diagnostic imaging of the breast. Data from 31 studies was analyzed,<sup>12</sup> with 17 studies contributing to the meta-analysis. The study included 8,773 patients, with a cohort comprised of 56.2% malignant breast cancers and 43.8% benign breast lesions. The findings showed that nine of the included studies reported the value of radiomic properties from MRI to differentiate malignant and benign breast cancer, with a sensitivity of 0.91 (95% CI: 0.89-0.92) and a specificity of 0.84 (95% CI: 0.82–0.86). In the four studies that included mammography, the sensitivity was 0.79 (95% CI: 0.76-0.82) with a specificity of 0.81 (95% CI: 0.79-0.84), and in the three studies that included ultrasound, the sensitivity was 0.92 (95% CI: 0.90-0.94) with a specificity of 0.85 (95% CI: 0.83–0.88) in differentiating between malignant and benign lesions.

Additionally, in a validation study, Lee et al.<sup>13</sup> compared the effectiveness of commercial Al software, assessing its performance and reading time against the proficiency of both breast and general radiologists. The Al model surpassed the diagnostic accuracy of radiologists across all levels of expertise, with an area under the curve (AUC) of Al alone, breast radiologist, and general radiologist groups of 0.915 (95% CI:

0.876-0.954), 0.813 (95% CI: 0.756–0.870), and 0.684 (95% CI: 0.616–0.752), respectively. Further, the use of AI assistance notably reduced the reading time for breast radiologists from 82.73 seconds to 73.04 seconds, p < 0.001, while it increased the reading time for general radiologists from 35.44 seconds to 42.52 seconds, p < 0.001.

Moreover, a multicentric study which included 144,231 screening mammograms from 85,580 U.S. women and 166,578 screening mammograms from 68,008 Swedish women, revealed that AI algorithms combined with a radiologist's review showed an AUC of 0.942 with a significantly improved specificity of 92.0% and an unchanged sensitivity.<sup>14</sup> This study demonstrates the potential of AI as an adjunctive tool in interpreting mammographic screenings. Furthermore, AI's efficacy in breast cancer detection extends to modalities beyond digital mammography, including digital breast tomosynthesis, ultrasound, and MRI.<sup>14</sup>

In fact, within AI-based computer-aided systems, two distinct classifications have emerged: computer-aided detection (CADe), which identifies lesions, and computer-aided diagnosis (CADx), which classifies the identified lesions as benign or malignant.<sup>15</sup> Radiologists can utilize these tools to assess if abnormalities detected by CADe or CADx require further investigation. Therefore, CADx can increase specificity by distinguishing lesion types, and CADe can improve sensitivity in mammography screenings, acting as a triage tool to highlight suspicious cases and confirm cancer-free diagnoses, thereby streamlining workflows.<sup>15</sup>

This shift from traditional mammography to CAD systems, which have often led to increases in unnecessary follow-ups without better cancer detection,<sup>15–17</sup> to more effective AI-CAD systems that equal or even exceed the diagnostic performance of radiologists is a significant development.<sup>17,18</sup> These CAD systems can both address the global shortage of radiologists skilled in breast imaging, minimize the dependence on specialized radiologists to interpret breast images, while potentially reducing unnecessary biopsies and treatments, which represents a movement toward precision medicine. For patients, the use of AI in radiology could alleviate the psychological impact and anxiety associated with false-positive results.<sup>19,20</sup> Operationally, these AI models, designed to process extensive imaging data efficiently, can ease the workload of radiologists and promote cost-effective healthcare resource

allocation. This efficiency could lead to significant cost savings, potentially re-allocating funds to improve other aspects of patient care and medical research.

Although we have been slowly incorporating Al into clinical practice, and some Al algorithms have received FDA approval,<sup>21</sup> numerous challenges remain when applying these developments effectively in clinical practice. These challenges include the generalizability and transferability of AI research, which may be hampered by a limited number of multicentric studies and a lack of diverse population demographics.<sup>22</sup> Transparency issues, notably the "black box" nature of AI neural networks, hinder the acceptance of AI systems, which necessitate the development of methodologies for rigorous peer review and validation.<sup>23</sup> Moreover, the focus of AI studies on diagnostic metrics needs a shift toward tangible clinical outcomes, such as mortality rates or surrogates, to provide concrete evidence of Al's benefits.<sup>24</sup> Also, from a liability standpoint, different legal responsibilities have been raised during the integration of AI into clinical practice. Regarding liability in cases where AI can replace the radiologist, especially considering that the algorithm development process usually involves many steps with different experts, it is critical to define who should be held responsible for the results in situations where Al misinterpretation could potentially cause patient harm.<sup>2</sup> Governance also emerges as a critical barrier, with regulatory bodies such as Health Canada<sup>25</sup> and the FDA<sup>26</sup> demanding clear guidelines and stringent testing for AI medical devices, to ensure their safety and efficacy before clinical adoption. These challenges underscore the complexity of integrating AI into healthcare and the need for careful consideration to maintain patient trust and the integrity of medical services.

#### Conclusion

In conclusion, the integration of AI in breast imaging is set to refine the workflow and efficiency of breast radiologists and help to manage the growing caseload without overwhelming the professionals. While AI assists in diagnostic tasks, it is important to keep in mind that it will not supplant radiologists due to their role in decision-making and other complex tasks; rather, the synergy between human expertise and AI promises to enhance patient care and diagnostic accuracy. This integration represents a significant



**Figure 1.** Impact of AI in the Breast Imaging Lifecycle; *image courtesy of Vivanne Freitas, MD, MSc.* and Renata Pinto, MD, MSc.

advancement in imaging, potentially impacting the entire breast imaging lifecycle. (**Figure 1**.) Addressing the challenges of integrating AI into clinical practice is essential to leverage its full potential for enhancing patient care.

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#### **Financial Disclosures**

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#### References

- Hu Q, Giger ML. Clinical artificial intelligence applications: breast imaging. Radiol Clin North Am. 2021;59(6):1027-I043. doi: 10.3322/caac.21552.
- Pesapane F, Codari M and Sardanelli F. Artificial intelligence in medical imaging: threat or opportunity? Radiologists again at the forefront of innovation in medicine. Eur Radiol Exp. 2018;2:35. doi: 10.1186/ s41747-018-0061-6.
- 3. LeCun Y, Bengio Y, Hinton G. Deep learning. Nature. 2015;521(7553):436-444. doi: 10.1038/nature14539
- Sahiner B, Pezeshk A, Hadjiiski LM, Wang X, Drukker K, Cha KH, et al. Deep learning in medical imaging and radiation therapy. Med Phys. 2019;46(1):el-e36. doi: 10.1002/mp.
- Mazurowski MA, Buda M, Saha A, Bashir MR. Deep learning in radiology: an overview of the concepts and a survey of the state of the art with focus on MRJ. J Magn Reson Imaging. 2019;49(4):939-954. doi: 10.1002/jmri.26534.
- Yala A, Lehman C, Schuster T, Portnoi T, Barzilay R. A deep learning mammography-based model for improved breast cancer risk prediction. Radiology. 2019;292(1):60-66. doi: 10.1148/radiol.2019182716.
- Dembrower K, Liu Y, Azizpour H, Eklund M, Smith K, Lindholm P, et al. Comparison of a deep learning risk score and standard mammographic density score for breast cancer risk prediction. Radiology. 2020;294(2):265-272. doi:10.1148/radiol.2019190872.
- Yala A, Mikhael PG, Strand F, Lin G, Smith K, Wan YL, et al. Toward robust mammography-based models for breast cancer risk. Sci Transl Med. 2021;13(578):eaba4373. doi: 10.1126/scitranslmed. aba4373

- Brunetti N, Calabrese M, Martinoli C, Tagliafico AS. Artificial intelligence in breast ultrasound: from diagnosis to prognosis-a rapid review. Diagnostics (Basel). 2022;13(1):58. doi: 10.3390/ diagnostics13010058.
- Liang X, Yu X, Gao T. Machine learning with magnetic resonance imaging for prediction of response to neoadjuvant chemotherapy in breast cancer: a systematic review and meta-analysis. Eur J Radiol. 2022;150:110247. doi: 10.1016/j.ejrad.2022.110247.
- Davey MG, Davey MS, Ryan ÉJ, Boland MR, McAnena PF, Lowery AJ, et al. Is radiomic MRI a feasible alternative to OncotypeDX<sup>®</sup> recurrence score testing? A systematic review and meta-analysis. BJS Open. 2021;5(5):zrab081. doi: 10.1093/bjsopen/zrab081.
- Oh KE, Vasandani N, Anwar A. Radiomics to differentiate malignant and benign breast lesions: a systematic review and diagnostic test accuracy metaanalysis Cureus. 2023;15(11):e49015. doi: 10.7759/ cureus.49015
- Lee JH, Kim KH, Lee EH, An JS, Ryu JK, Park YM, et al. Improving the performance of radiologists using artificial intelligence-based detection support software for mammography: a multi-reader study. Korean J Radiol. 2022;23(5):505-516. doi: 10.3348/ kjr.2021.0476.
- 14. Schaffter T, Buist DSM, Lee CI, Nikulin Y, Ribli D, Guan Y, et al. Evaluation of combined artificial intelligence and radiologist assessment to interpret screening mammograms. JAMA Netw Open. 2020;3(3):e200265. doi: 10.1001/ jamanetworkopen.2020.0265.
- Yoon JH, Kim EK. Deep learning-based artificial intelligence for mammography. Korean J Radiol. 2021;22(8):1225-1239. doi: 10.3348/kjr.2020.1210
- Lee HJ, Nguyen AT, Ki SY, Lee JE, Do LN, Park MH et al. Classification of MR-detected additional lesions in patients with breast cancer using a combination of radiomics analysis and machine learning. Front Oncol. 2021;11:744460. doi: 10.3389/fonc.2021.744460.
- Le EPV, Wang Y, Huang Y, Hickman S, Gilbert FJ. Artificial intelligence in breast imaging. Clin Radiol. 2019;74(5):357-366. doi: 10.1016/j.crad.2019.02.006.
- Bahl M. Artificial intelligence: a primer for breast imaging radiologists. J Breast Imaging. 2020;2(4):304-314. doi: 10.1093/jbi/wbaa033.
- Dabbous FM, Dolecek TA, Berbaum ML, Friedewald SM, Summerfelt WT, Hoskins K, et al. Impact of a false-positive screening mammogram on subsequent screening behavior and stage at breast cancer diagnosis. Cancer Epidemiol Biomarkers Prev. 2017;26(3):397-403. doi: 10.1158/1055-9965.EPI-16-0524

- Nelson HD, Pappas M, Cantor A, Griffin J, Daeges M, Humphrey L. Harms of breast cancer screening: a systematic review to update the 2009 U.S. Preventive Services Task Force recommendation. Ann Intern Med. 2016;164(4):256-267. doi: 10.1158/1055-9965. EPI-16-0524.
- U.S. Food & Drug Administration. Machine Learning (AI/ML)-Based Software as a Medical Device (SaMD) Action Plan. [Internet] US Food and Drug Administration [Published September 22, 2021, Accessed January 09, 2024] Available from: https:// www.fda.gov/medical-devices/software-medicaldevice-samd/artificial-intelligence-and-machinelearning-software-medical-device..
- Chan HP, Samala RK, Hadjiiski LM, Zhou C. Deep learning in medical imaging analysis. Adv Exp Med Biol. 2020;1213:3-21. doi: 10.1007/978-3-030-33128-3\_1.
- Haibe-Kains B, Adam GA, Hosny A, Khodakarami F, Massive Analysis Quality Control (MAQC) Society Board of Directors, Waldran L, et al. Transparency and reproducibility in artificial intelligence. Nature. 2020;586(7829):E14-E16. doi: 10.1038/s41586-020-2766-y.
- Facciorusso A, Ferrusquía J, Muscatiello N. Lead time bias in estimating survival outcomes. Gut. 2016;65(3):538-539. doi:10.1136/gutjnl-2015-310199
- Health Canada. Medical Devices Active License Listing (MDALL) - Your reference tool for licensed medical devices in Lead time bias in estimating survival outcomes Canada. [Internet]. Health Canada. [Accessed 2023 September 24, cited 2021 January 06]. Available from: https://health-products.canada. ca/mdall-limh/
- U.S. Food & Drug Administration. Artificial Intelligence and Machine Learning (AI/ML)-Enabled Medical Devices. [Internet]. [Accessed 2022 September 24, cited 2021 September 22]. Available from: Artificial Intelligence (AI) and Machine Learning (ML) in Medical Devices (fda.gov)