

Artificial Intelligence Risk Model (Mirai) Delivers Robust Generalization and Outperforms Tyrer-Cuzick Guidelines in Breast Cancer Screening

TO THE EDITOR:

Recently, Yala et al¹ reported on the validation of an artificial intelligence (AI)-aided breast cancer risk model called Mirai on the basis of traditional mammograms across multiple international cohorts. To the best of our knowledge, this is the first study suggesting that the AI-based breast cancer screening model developed on a large-scale data set across seven hospitals with at least five races can deliver impressively robust transferability. Such extensive cross-regional validation is challenging because of interethnic heterogeneity of breast cancer, device bias from different institutions, and completeness of patient clinical data.² To overcome these challenges, this study developed a risk factor predictor that could produce risk factors referred in the Tyrer-Cuzick (TC) guidelines and then combined these factors with mammographic images. This study also leveraged a conditional-adversarial training scheme to eliminate the bias caused by different mammography machines. As a result, Mirai maintained high performance (range, 0.75-0.84) and could accurately identify high-risk subsets across all test cohorts. Moreover, this AI model shows better performance than the widely used traditional TC model in improving early detection and reducing overtreatment of breast cancer. Thus, this study concluded that Mirai has the potential to replace current breast cancer risk assessment models recommended by clinical guidelines for magnetic resonance imaging screening.

Although this study demonstrated encouraging and promising findings, some issues should be noted. First, women with extremely dense breast tissue have double the risk of developing breast cancer as compared with the general screening population.³ Meanwhile, the dense breast tissue limits the sensitivity of mammography,⁴ causing a high number of interval cancers. Thus, we need to pay more attention to women with extremely dense breast tissue during breast cancer screening. However, the ability of the Mirai model in predicting breast cancer via mammography images presenting extremely dense breast tissue remains unclear. It would be clinically relevant to report the rate of extremely dense breast tissue in all data sets and conduct analysis to evaluate the performance of Mirai in predicting the risk of breast cancer in such patients. If Mirai has unsatisfactory

performance, it should be leveraged with caution and the eligibility for supplemental magnetic resonance imaging or ultrasound should be determined to improve early detection and reduce interval cancers.^{4,5} Second, risk prediction models are often evaluated by both calibration and discrimination, whereas this study used the area under the curve (AUC) and the concordance index (C-index) as discrimination metrics for evaluating the predictive performance of the Mirai model, which is not enough since calibration is not fully captured by AUC and C-index. The calibration reflects the consistency between the true probability and the model-predicted probability of cancer.⁶ Calibration is a crucial property of a prediction model because it can assess the extent to which a model correctly estimates the absolute risk.⁷ Models with poor calibration may overestimate the risk of cancer. Thus, both discrimination and calibration statistics are suggested to be used to evaluate the performance of the Mirai model. Third, this study used discriminative metrics AUC and C-index to compare the performance of the Mirai model and the TC model, whereas additional indicators such as integrated discrimination improvement and net reclassification index are helpful to evaluate the risk prediction improvement of the Mirai model compared with the TC model.⁸ Finally, given the different results of Mirai between the populations screened annually and biennially, this model should provide appropriate risk thresholds to comply with local policies and procedures. In regions where screening is performed annually, Mirai should provide higher specificity to avoid supplemental screening, whereas in regions where screening is performed once every two or more years, Mirai should provide higher sensitivity to improve early detection.

Despite the abovementioned issues, we still appreciate Yala et al¹ for their outstanding work on the development and broadest validation of the Mirai model across race and ethnicity categories, which provided a more robust mammography-based breast cancer risk model. We look forward to further works to improve the validity and clinical utility of the Mirai model in real-world settings. The application of Mirai in breast cancer screening is still a long way from having the accuracy and generalizability required for its implementation into clinical practice.⁹

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

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