# Machine learning intratumoral and axillary lymph node magnetic resonance imaging radiomics for predicting axillary lymph node metastasis in patients with early-stage breast cancer (RBC-01 Study)


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## Abstract Background


In current clinical practice, the routine approaches of axillary lymph node (ALN) status evaluation through sentinel lymph node biopsy (SLNB) is unsatisfied with high false-negative rate and brings significant complications. We aimed to develop a preoperative magnetic resonance imaging (MRI) radiomic-based signature for predicting ALN metastasis in a non-invasive way.

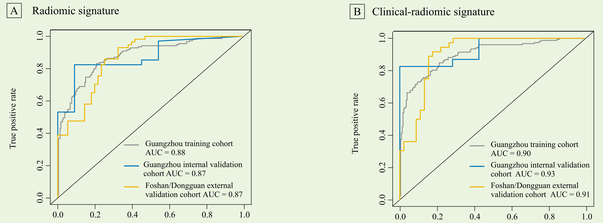

## Patients and methods


1,090 eligible early-stage invasive breast cancer patients from 4 institutions were enrolled in this multicenter retrospective diagnositc study. Key radiomic features extracted from intratumoral and ALN regions were selected by machine learning and used to develop the radiomic signature for ALN metastasis prediction in 803 patients from Sun Yat-sen Memorial Hospital and Sun Yat-sen University Cancer Center (Guangzhou training cohort). Clinical-radiomic siganture was constructed by combining radiomic signature and significant clinic-pathological risk factors. The performance of the signatures was validated in patients from prospective phase 3 trials [NCT01503905] (Guangzhou internal validation cohort, n=106), and Shunde Hospital of Southern Medical University and Tungwah Hospital of Sun Yat-Sen University (Foshan/Dongguan external validation cohort, n=181). This study is registered with ClinicalTrials.gov, number NCT04003558, and Chinese Clinical Trail Registry, number ChiCTR1900024020.


## Results


The radiomic signature for predicting ALN status consisted of intratumoral and ALN features showed AUCs of 0.88, 0.87, and 0.87 in the Guangzhou training cohort, Guangzhou internal validation cohort, and Foshan/Dongguan external validation cohort, respectively (Figure 1A). The clinical-radiomic signature achieved the highest AUCs of 0.90, 0.93 and 0.91 in the Guangzhou training, Guangzhou internal validation and Foshan/Dongguan external validation cohorts, respectively (Figure 1B). In addition, the clinical-radiomic signature could successfully discriminate high- from low risk patients in entire cohort, and the high-risk patients had significantly shorter DFS (HR 0.43, 95% CI 0.21-0.86; P=0.014; Figure 2). The clinical-radiomic signature also performed well in discriminating ALNM patients with 1, 2, and 3 positive nodes (AUC of 0.88, 0.89 and 0.92 in the Guangzhou training cohort; AUC of 0.79, 1.00 and 0.93 in Guangzhou internal validation cohort; AUC of 0.97, 0.93 and 0.87 in the Foshan/Dongguan external validation cohort). The decision curve analysis (DCA) demonstrated that if the threshold probability in clinical decision was > 5%, the patients would benefit more from the clinical-radiomic signature than the radiomic signature or radiologists' diagnosis (Figure 3).


**Figure 1. ROC curves of signatures for ALN metastasis prediction.**




A.Radiomic signature for ALN metastasis prediction; B. Clinical-radiomic signature for ALN metastasis prediction

**Figure 2. Kaplan-Meier survival analysis discriminated high- from lowrisk patients in entire cohort.**

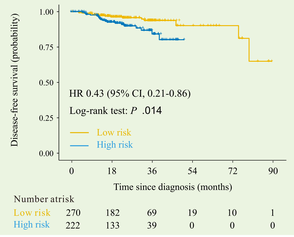
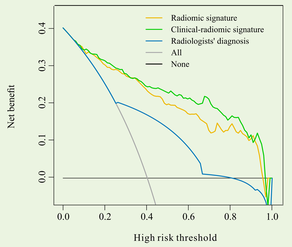



**Figure 3. Decision curve analysis for ALN metastasis prediction in the radiomic signature, clinical-radiomic signature, and radiologists' diagnosis.**




## Conclusion

We developed a clinical-radiomic signature incorporated the intratumoral and ALN radiomic features and clinical risk factors, which could serve as a non-invasive tool to evaluate ALN status for guiding surgery plans of early-stage breast cancer patients and benefit patients with negative ALN by avoiding unnecessary SLNB and the associated complications.

## Acknowledgments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## Conflict of Interest Disclosures

The authors have no conflicts of interest to declare.


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