The Value of Radiomic Features of Primary Breast Tumor in STIR Sequences in Predicting Axilla Metastasis

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ABSTRACT

Background: Detection of axillary metastases in breast cancer is critical for treatment options and prognosis. The aim of this study is to investigate the value of radiomic features obtained from short tau inversion recovery (STIR) sequences in magnetic resonance imaging (MRI) of primary tumor in breast cancer in predicting axillary lymph node metastasis (ALNM).

Methods: Lesions of 165 patients with a mean age of 51.12 ±11 (range 28-82) with newly diagnosed invasive breast cancer who underwent breast MRI before treatment were manually segmented from STIR sequences in the 3D Slicer program in all sections. Machine learning (ML) analysis was performed using the extracted 851 features Python 3.11, Pycaret library program. Datasets were randomly divided into train (123, 80%) and independent test (63, 20%) datasets. The performances of ML algorithms were compared with area under curve (AUC), accuracy, recall, precision and F1 scores.

Results: Accuracy and AUC in the training set were in the range of 57 % -86 % and 0.50-0.95, respectively. The best model in the training set was the catBoost classifier with an AUC of 0.95 and 84% accuracy. The AUC, accuracy, recall, precision values and F1 score of the CatBoost classifier on the test set were 0.92, 84 %, 89%, 85 %, 86 %, respectively.

Conclusion: Radiomic features obtained from primary tumors on STIR sequences have the potential to predict ALNM in invasive breast cancer.

INTRODUCTION

Axillary lymph node metastasis (ALNM) is one of the most important prognostic factors determining survival in breast cancer.1 The status of the axilla determines the need for axillary lymph node dissection (ALND), axillary radiotherapy, neoadjuvant or adjuvant chemotherapy.2 Accurate determination of the axillary status before treatment is critical in determining individualized treatment options.3 Age, tumor size, tumor quadrant, multifocality, histological grade, pathological type, receptor status, molecular subtype are associated with ALNM.4-9

Radiomic analysis aims to contribute to diagnosis, treatment and follow-up processes by extracting specific quantitative information about diseases that the human eye cannot perceive from medical images. With radiomic analysis, the aim is to maximize the information obtained from images by obtaining quantitative data about signal intensities and spatial distribution of inter-pixel relationships.10

Recently, radiomics has attracted considerable attention in the medical field, especially in oncology.
Successful results were also obtained in the diagnosis, treatment and classification of breast cancer. Also, promising results were acquired in the differentiation of malignant and benign breast masses, in the estimation of the grade and receptor status and subtypes of malignant tumors using radiomic features extracted from magnetic resonance imaging (MRI). This method is also promising in the prediction of neoadjuvant chemotherapy response in breast cancer. In studies performed with MRI, it was found that radiomics successfully helped even in the prediction of recurrence of breast cancer. 

Radiomics features of axillary lymph nodes from T2W MR images were not successful in predicting ALNM. However, ALNM could be predicted with radiomic features obtained from T2-weighted (T2W), diffusion-weighted (DW) and T1+C images of the primary tumor. 

Our aim in this study was to investigate the performance of radiomic features obtained from short tau inversion recovery (STIR) sequences of primary tumor in predicting axillary metastasis.

**METHODS**

**Participants**

Patients diagnosed with invasive breast cancer by core biopsy between August 2017 and February 2023 were evaluated retrospectively. Patients who underwent sentinel lymph node biopsy (SLNB) or ALND and patients who underwent MRI before treatment were included in the study. Patients who received neoadjuvant chemotherapy, or had unknown pathology, another malignancy, a recurrent disease, or artifacts in MRI images were excluded from the study.

**MRI Acquisition Protocol**

MRI examinations were performed with a 1.5 T MRI device (Philips Ingenia, Philips Healthcare, Best, The Netherlands) using a dedicated 16-channel phased array breast coil. Non-fat-saturated turbo-spin-echo T1 (Field of View (FOV): 302x302 mm, Matrix: 199x203, Flip Angle (FA): 90 deg, Repetition Time (TR): 547 ms, Echo Time (TE): 8 ms, Slice thickness: 3.00 mm, Slice gap: 3.30), spin-echo STIR (FOV: 341x341 mm, Matrix: 263x223, FA: 90 deg, TR: 4040 ms, TE: 65/175.000 ms, Slice thickness: 3.00 mm, Slice gap: 3.30), three dimensional fat-saturated ultrafast spoiled gradient-echo dynamic (FOV: 342x342 mm, Matrix: 342x340, FA: 10 deg, TR: 5 ms, TE: 3 ms, Slice thickness: 2 mm, Slice gap: 1 mm) images were obtained. Dynamic sequences were acquired at 90, 142, 194, 246, and 298 seconds after contrast injection. A single dose of 0.1 mmol/kg body weight gadolinium chelate was administered to the patients with an automatic injector.

**Segmentation and Feature Extraction**

STIR sequences in DCOM format were transferred to the 3D Slicer program (version 4.10.2; https://www.slicer.org ). Resampled images (size: 1x1x1 mm) were acquired and normalized. Manual segmentation was performed independently by two radiologists with 8 and 10 years of experience in breast imaging, blinded to the axillary condition of the patients. Segmentation was performed from all axial STIR sequences with tumor. A total of 851 texture features, including first-order, second-order and wavelet-based features were extracted with Slicer-Radiomics (PyRadiomics v3.0.1) (Figure 1). One month later, 30 randomly selected patients were independently segmented by the same two radiologists and radiomic features were extracted again. Thus, interobserver agreement was evaluated.

**Figure 1.** Workflow for extraction of radiomic features from STIR sequences and machine learning analysis

**Machine Learning Analysis**

Python 3.11 (Jupyter Notebook, Pycaret Library) was used for data processing and machine learning analysis. The synthetic minority oversampling technique (SMOTE) was used to avoid imbalanced data sets. Data normalization was performed before model development.

The data sets were randomly divided into training and independent testing sets. We used 10-fold cross validation of the trained models to avoid data overfitting.

Overall, 15 machine learning (ML) algorithms were used. The area under the curve (AUC), accuracy, recall, precision and F1 scores were compared with the performances of the ML algorithms. The best model for accuracy and AUC was selected and evaluated on the test set. AUC, accuracy, recall, precision, and F1 scores were given
by the confusion matrix. The best model was tuned and finalized.

**Statistical Analysis**

The data were analyzed by the Statistical Package for Social Sciences (SPSS) version 25.0.0.0 software (IBM Corp., Armonk, N.Y., USA). Percentage, mean, and standard deviation were used to present descriptive results. The one-sample Kolmogorov–Smirnov test was used to see if the groups have a normal distribution. Continuous variables with a normal distribution were shown as mean (± standard deviation [SD]). Interobserver agreement was evaluated using ICC values. Features with an ICC value >0.7 were further checked with ML.

**RESULTS**

In this study, 421 patients were evaluated retrospectively. Overall, 106 patients who did not undergo MRI before treatment, 48 patients whose SLNB or ALND data were not available, 52 patients who received neoadjuvant chemotherapy, 6 patients with recurrent disease, 3 patients with concurrent malignancy and 41 patients with artifacts were excluded from the study. Thus, 165 patients with a mean age of 51.12 ±11 (range 28-82) were included in the study. While 92 (55.76 %) patients had axillary metastases, 73 (44.24 %) did not have axillary metastases. The mean lesion size was 24.78 ± 15 (6-120) mm.

Altogether, 667 features with ICC values above 0.7 were evaluated with ML. Wavelet filtered texture features, maximum 3D diameter, skewness kurtosis and maximum signal features showed a high correlation with ALNM. The features selected by ML algorithms and their importance are presented in Figure 2.

The accuracy and AUC of ML algorithms on the training set were in the range of 57%-86% and 0.50-0.95, respectively (Table 1). Among the ML algorithms, the best model was CatBoost classifier (AUC:0.95, accuracy: 84%). The ROC curve showing the success of the CatBoost classifier in predicting ALNM is presented in Figure 3.

**Table 1.** Performance of machine learning models in differentiating those with axillary metastases from those without axillary metastases in patients with invasive breast cancer in the training set from STIR sequences.

<table>
<thead>
<tr>
<th>Model</th>
<th>Accuracy</th>
<th>AUC</th>
<th>Recall</th>
<th>Prec.</th>
<th>F1</th>
</tr>
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<tr>
<td>CatBoost Classifier</td>
<td>0.8391</td>
<td>0.9518</td>
<td>0.9288</td>
<td>0.8197</td>
<td>0.8675</td>
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<tr>
<td>Extra Trees Classifier</td>
<td>0.8391</td>
<td>0.9517</td>
<td>0.8981</td>
<td>0.8326</td>
<td>0.8618</td>
</tr>
<tr>
<td>Light Gradient Boosting Machine</td>
<td>0.8696</td>
<td>0.9510</td>
<td>0.9212</td>
<td>0.8632</td>
<td>0.8870</td>
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<tr>
<td>Gradient Boosting Classifier</td>
<td>0.8652</td>
<td>0.9480</td>
<td>0.9058</td>
<td>0.8687</td>
<td>0.8834</td>
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<tr>
<td>Random Forest Classifier</td>
<td>0.8522</td>
<td>0.9461</td>
<td>0.9058</td>
<td>0.8447</td>
<td>0.8720</td>
</tr>
<tr>
<td>Extreme Gradient Boosting</td>
<td>0.8652</td>
<td>0.9379</td>
<td>0.9141</td>
<td>0.8626</td>
<td>0.8842</td>
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<tr>
<td>Ada Boost Classifier</td>
<td>0.8261</td>
<td>0.8644</td>
<td>0.8679</td>
<td>0.8406</td>
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<td>Logistic Regression</td>
<td>0.8174</td>
<td>0.8479</td>
<td>0.8372</td>
<td>0.8478</td>
<td>0.8299</td>
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<tr>
<td>Quadratic Discriminant Analysis</td>
<td>0.8261</td>
<td>0.8427</td>
<td>0.7045</td>
<td>0.9798</td>
<td>0.8091</td>
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<tr>
<td>Decision Tree Classifier</td>
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<td>0.8338</td>
<td>0.8449</td>
<td>0.8654</td>
<td>0.8479</td>
</tr>
<tr>
<td>Linear Discriminant Analysis</td>
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<td>0.7738</td>
<td>0.7660</td>
<td>0.8083</td>
<td>0.7820</td>
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<tr>
<td>K Neighbors Classifier</td>
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<td>0.7348</td>
<td>0.8263</td>
<td>0.7443</td>
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<td>Naive Bayes</td>
<td>0.5739</td>
<td>0.5393</td>
<td>0.8641</td>
<td>0.5767</td>
<td>0.6897</td>
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<td>Dummy Classifier</td>
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<td>0.5000</td>
<td>1.0000</td>
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<td>Ridge Classifier</td>
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<td>0.8212</td>
<td>0.8274</td>
<td>0.8116</td>
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</tbody>
</table>
Figure 3. Receiver operating characteristics curve of the CatBoost classifier in predicting axillary lymph node metastasis.

CatBoost classifier was evaluated on the test set. After tuning the AUC, accuracy, recall and precision values and F1 score were 0.92, 84 %, 89 %, 85 %, 86 %, respectively. The CatBoost classifier model had a 92.86% sensitivity and 86.36 % specificity in detecting ALNM. The classification report and confusion matrix showing the performance of the CatBoost model are presented in Figure 4.

Figure 4. Confusion matrix (A), classification report (B) for CatBoost classifier in predicting axillary lymph node metastasis.

DISCUSSION
Recently, less invasive treatment approaches for the axilla have been accepted. SLNB is preferred instead of ALND in early stage breast cancer. Determining the condition of the axilla in the preoperative period is important in the development of surgical plans. For individualized and minimally invasive treatment options, it is important to determine the condition of the axilla before treatment. Among the imaging methods, ultrasound (US) is the primary tool in the evaluation of the axilla.
However, approximately 15-20% of patients with negative US findings have metastases in the SLNB. In mammography (MG), 50% of level 1 axillary lymph nodes can be visualized and levels 2 and 3 cannot be evaluated. It has been reported that MRI has similar sensitivity to US, but less specificity in detecting nodal metastases.

In previous studies, ALNM could be predicted by the radiomics features of the primary tumor in MRI. Yu et al., on the other hand, successfully predicted axillary lymph node status on T1+C, T2W, DW MRI with a multicomponent signature including radiomics features and clinicopathologic features obtained from lymph nodes and primary tumor. Qiu et al. were successful in predicting ALNM using clinicopathological features, morphological features of lymph nodes from MR images, and radiomics features of the primary mass. Radiomic features obtained from DWI, T2W and T1+C images of the primary mass were successful in predicting ALNM with an AUC value of 0.806. Wang et al. were able to predict axillary metastases with an AUC value of over 0.80 with the radiomics and deep learning features obtained from dynamic contrast-enhanced (DCE) MRI. Chen et al. were able to predict ALNM with the nomogram created by the radiomics and clinicopathological features of the primary tumor obtained from DW and DCE MRI (AUC value in the training set and test set, respectively 0.80, 0.71). Using DCE MRI, Liu and colleagues were able to predict ALNM by tumoral and peritumoral radiomics signature (AUC values in the training and test set were 0.872, 0.863, respectively). Cui et al. predicted axillary lymph node status with radiomic features obtained from second post-contrast images on MRI with an AUC of 0.86 and an accuracy of 89%. However, none of these studies presented the performance of T2W images alone in predicting ALNM.

Dong and colleagues were successful in predicting sentinel lymph node metastasis with radiomic features obtained from fat-suppressed T2W and DW MRI images. With T2W alone, AUC values were 0.847 in the training set and 0.770 in the validation set. With DW MRI, they obtained AUC values of 0.847 in the training set and 0.787 in the validation set. When they combined the features obtained from T2W and DW images, the AUC values were 0.863 in the training set and 0.805 in the validation set. In our study, we predicted ALNM with 0.92 AUC and 84% accuracy in the training and validation set with the radiomic features obtained from STIR sequences by modeling using machine learning analysis. The ML models used except Naive Bayes, Dummy Classifier, SVM - Linear Kernel and Ridge Classifier showed successful performance with at least 0.73 AUC and 74% accuracy. CatBoost Classifier, Extra Trees Classifier, Light Gradient Boosting Machine, Gradient Boosting Classifier and Extreme Gradient Boosting had AUC values above 0.93 and accuracy values above 86%. Among the models CatBoost Classifier, Extra Trees Classifier, Light Gradient Boosting, Gradient Boosting Classifier and Random Forest Classifier had the highest performance with 0.95 AUC values and with 84-86% accuracy values. Among these models, CatBoost Classifier had the highest recall and precision values with 0.93 and 82%, respectively.

Radiomics features derived from T2W sequences detected ALNM with an AUC of up to 0.85. When DWI and DCE were combined with T2W, the AUC value increased to 0.86. In our study, only STIR arrays reached 0.92 AUC. Since STIR sequences are used in routine breast MRI in some centers, they may contribute to the prediction of ALNM. To our knowledge, STIR radiomics have not been used in studies investigating ALNM. STIR sequences stand out compared to other fat suppression techniques by providing more uniform fat suppression without being affected by magnetic field inhomogeneity. Although the signal-to-noise ratio is poor, it is useful because it includes both T1 and T2 contrast.

There is a correlation between tumor size and lymph node metastasis. In our study, the maximum diameter of the tumor and axillary metastases showed a high correlation. Kurtosis and skewness features, which evaluate intralesion homogeniety, were also correlated with ALNM.

Our study has some limitations. Its retrospective nature, small number of patients, and choosing the largest lesion in patients with more than one lesion are among the limitations of our study. Another limitation is that we did not divide the patients according to the number of metastatic lymph nodes.

CONCLUSION
In conclusion, radiomic features obtained from the primary tumor on STIR sequences have the potential to predict ALNM. STIR sequences are noninvasive and are currently used as a routine component of breast MRI in some centers. However, some lesions cannot be segmented since they have signal intensity close to parchyma in STIR sequences.

ETHICAL CONSIDERATIONS
Ethics committee approval was obtained from our institution for this retrospective study (Approve no: 202351425036).

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CONFLICT OF INTEREST
No conflicts of interest exist regarding the publication of the present study.

REFERENCES


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