Original Article

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The Effectiveness of 1.5 Tesla MRI in Predicting Axillary Lymph Node Metastasis in Cancer Patients with Breast-conserving Surgery

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Abstract:

Objective: Assessing axillary lymph node metastasis accurately before breast-conserving surgery is essential for guiding surgical decisions and improving diagnostic performance. The study aimed to determine the accuracy of breast magnetic resonance imaging (MRI) in assessing axillary lymph node metastasis in cancer patients undergoing breast-conserving surgery.

Material and Methods: A cross-sectional descriptive study was conducted on 76 breast cancer patients with indications for conservative surgery at the Vietnam National Cancer Hospital from June 2020 to May 2021. Patients were assessed for axillary lymph node metastasis using a 1.5 Tesla MRI machine through analysis of parameters of size and morphology on conventional sequences and Diffusion-Weighted Imaging (DWI) sequences. Data were analysed by descriptive statistics and T-test with IBM Statistical Package for the Social Sciences (SPSS) 25.0 software.

Results: Short-axis length, short/long axis ratio, cortical thickness, loss of fatty hilum, and eccentric cortical thickening were the parameters with statistically significant differences between the two groups of metastatic and non-metastatic lymph nodes (p-value-value<0.05). The Apparent diffusion coefficient (ADC) index was statistically significant between the two groups, with area under the curve (AUC) values higher than the AUC values of the parameters on conventional magnetic resonance (AUC: 0.874, with the optimal threshold of 1.046×10^{-3} mm^2/s for sensitivity of 78.6%, specificity of 85.5%) (p-value<0.05).

Conclusion: Conventional MRI combined with DWI sequences can assess axillary lymph node metastasis in patients undergoing breast-conserving surgery with high sensitivity and specificity. Therefore, to improve treatment quality, it is necessary to assess axillary lymph node metastasis before breast-conserving surgery.

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Introduction

In 2022, the world recorded 2.3 million new breast cancer diagnoses and 670,000 deaths. Breast cancer is the second most common cancer in the world and the most common cancer in women. Breast cancer occurs in women of all ages after puberty; however, the rate increases in later stages of life[1]. In Vietnam, there are approximately 21,555 new cases of breast cancer each year, and breast cancer accounts for 25.8% of cancer cases in women[2].

Breast-conserving surgery removes the tumor along with 1–2 cm of the surrounding mammary tissue, ensuring tumor-free margins while preserving the breast's natural shape. Currently, breast-conserving surgery is increasingly indicated to replace total mastectomy in certain groups of patients, because it removes the tumor while still ensuring aesthetic results. However, it is necessary to have a method to accurately determine the size and characteristics of the tumor before prescribing accurate conservative treatment[3].

Patients undergoing breast surgery are often treated with additional therapies such as partial radiation and chemotherapy. In these cases, the status of axillary lymph node metastasis is a crucial prognostic factor that must be evaluated. Accurate prediction of axillary lymph node metastasis helps to plan appropriate treatment for breast cancer patients[4]. In addition, the presence of metastasis in the axillary lymph nodes is also considered the most important predictor of long-term survival in patients with primary breast cancer[5].

Clinical examination, mammography, and ultrasound (US) have been used to predict axillary lymph node metastasis. However, the diagnostic accuracy of predicting axillary lymph node metastasis remains unsatisfactory[6]. The reported sensitivity and specificity of axillary US range from 45.2–100% and 50–89%, respectively[7]. The axillary US with US-guided fine needle aspiration (FNA) has become an accepted method for preoperative assessment as a means of diagnosing metastases[8]. However, FNA is an invasive method, and the sensitivity of US-guided FNA is relatively low (39.5–86%), despite its high specificity (95.7–100%)[9].

Recently, breast magnetic resonance imaging (MRI) has been used for preoperative staging in patients undergoing breast-conserving therapy, helping to differentiate benign from malignant breast lesions in a short imaging time, thanks to its high sensitivity in detecting multifocal, multicentric lesions as well as its ability to assess the extent of the lesions[8]. Several recent studies have shown different sensitivities (53.8–94.7%) and specificities (77–91.7%) of the 1.5 Tesla MRI for axillary lymph node metastases[6,10]. Therefore, the 1.5-T breast MRI is a useful noninvasive modality for assessing axillary lymph node metastases.

In Vietnam, breast-conserving surgery is commonly used for patients with newly diagnosed early-stage breast cancer. However, preoperative assessment of regional lymph node metastasis by breast MRI is still new and controversial, while MRI is the most sensitive method for detecting regional lymph node metastasis[11]. In addition, there are few studies evaluating the effectiveness of MRI in determining regional lymph node metastasis for patients indicated for breast-conserving surgery.

Therefore, this study was conducted to determine the value of breast MRI in assessing axillary lymph node metastasis in cancer patients undergoing breast-conserving surgery.

Material and Methods

Study design

A cross-sectional descriptive study was carried out on 76 newly diagnosed breast cancer patients who came for examination and treatment at the Vietnam National

Cancer Hospital (Tan Trieu Establishment) from June 2020 to May 2021. The study was conducted following the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement (https://www.strobe-statement.org/).

Participants

All patients were indicated for breast-conserving surgery and had breast MRI, surgery, and post-operative histopathology performed at the Vietnam National Cancer Hospital (Tan Trieu Establishment).

Inclusion criteria: 1) patients who came for examination, newly diagnosed with breast cancer by pathology; 2) had no contraindications to general MRI and underwent breast MRI; 3) were indicated for breast-conserving surgery; 4) had post-operative pathology results or biopsy/cytology results for comparison; 5) agreed to participate in the research group.

Exclusion criteria: Patients were excluded if they had previously been treated for breast cancer and/or received pre-operative adjuvant chemotherapy, had not undergone surgery, or lacked histopathological results.

1.5 Tesla MRI protocol Technical parameters: Using the 1.5 Tesla Echelon (Hitachi Medical Corporation, Tokyo, Japan), the Ingenia (Philips Healthcare, Best, Netherlands), and the 1.5 Tesla GE SIGNA Pioneer (GE Healthcare, Chicago, IL, USA) MRI machines with pulse sequence parameters, including turbo spin-echo T1- and T2-weighted sequences. Pulse sequence parameters included:

+ Axial T2-weighted sequence with Repetition Time/Echo Time (TR/TE) 4300/80, FOV 320 mm, image matrix 224 x 192, and slice thickness 4 mm. This sequence is for identifying some benign lesions with a strong signal increase on T2 images, such as cysts and mucinous adenomas. In addition, T2 images also help evaluate lymph node morphology.

+Pre- and post-injection axial T1-weighted sequence with TR/TE 6.2/3, field-of-view (FOV) 320 mm, image matrix 256 x 152, and slice thickness 2 mm. This sequence is for evaluating the morphology and graph of the drug absorption of lesions, helping to differentiate benign and malignant lesions. Images were taken pre-injection, 2 minutes post-injection (early phase), and 4 minutes post-injection (late phase). Drug absorption graphs were constructed with ROIs placed at the most suspected drug washout location on the drug washout map, constructed by software. ROI area was from 10-20 mm^2.

+ Axial (diffusion-weighted imaging) DWI sequences with b values of 0 and 800 s/mm^2, TR/TE is 7000/80, FOV equal 320 mm, image matrix of 128 x 128, and slice thickness of 4 mm. This sequence evaluates tumor and lymph node cell density and helps determine tumor borders and adjacent inflammatory reactions.

Apparent diffusion coefficient (ADC) map is constructed from the DWI image by software, while the ADC value is measured using the Region of Interest (ROI) tool, the area from 10-20mm^2, placed in the area with the lowest signal on ADC map and corresponding to the strong enhancement area on the T1 - (dynamic contrast enhanced) DCE image (for tumor) or the area of thickened lymph node capsule (for lymph node).

1.5 Tesla MRI Screening procedure: Patients underwent preoperative breast MRI with conventional (T1 and T2) and diffusion-weighted (DWI) sequences. The patient was placed in the prone position, maintaining the same positioning as in the conventional MRI scan, with the head probe used.

Evaluation of axillary lymph node results by MRI

Two radiologists with more than 15 years of experience in mammography performed breast MRI interpretation and prepared the report. Axillary lymph node metastasis was assessed by morphology and size on T2-

weighted and T1-weighted contrast-enhanced sequences, and cell density was assessed by axial DWI sequences.

Nodes were selected for study if they had one of the following features on T2 images: loss of fatty hilum, eccentric or round cortical thickening. If multiple nodes had suspicious features, the node with the largest short-axis diameter was selected. In the ADC map, ROIs were placed in the most diffuse-limited part of the node cortex (after comparison on T2 and DW images).

Statistical analysis

Data were analyzed using SPSS 20.0 software. Categorical variables were described by frequency and percentage (%), while continuous variables were described by mean and standard deviation. T-test was used to describe the continuous variables and compare the two groups with and without axillary lymph node metastasis. The test was considered statistically significant when the p-value was <0.05. Receiver operating characteristic (ROC) curve was used to compare the diagnostic value of the variables, to predict the value of conventional magnetic resonance and diffusion magnetic resonance in axillary lymph node metastasis, and to calculate the optimal threshold, according to the Youden index.

Ethical consideration

The study was carried out after being approved by the Ethics Committee in Biomedical Research of Vietnam National Cancer Hospital (Tan Trieu Establishment) with number 36/GCN-BVKHN, 13 March 2020, before being conducted. All participants and legal representatives were instructed regarding the purpose and the benefits of the study. Patients signed a voluntary commitment to undergo a contrast-enhanced breast MRI. The personal information of the research subjects was kept confidential. All information collected was for research purposes only, contributing to diagnosis and treatment, for the benefit of the patient's health, and was not used for any other purpose.

Results

Participants' characteristics

Among the 76 patients participating in the study, most were between 40 and 60 years old (73.7%), and 61.8% were still menstruating. Sixty (78.9%) patients had no clinically palpable tumors.

Table 1 Participants' characteristics (n=76)

Contents	n	%
Age		
20–40	18	23.7
>40–60	56	73.7
>60	2	2.6
Menstrual status		
Still menstruating	47	61.8
Premenopause	18	23.7
Menopause	11	14.5
Clinical features of tumors		
Palpable	16	21.1
Not palpable	60	78.9

Effectiveness of the 1.5 Tesla MRI in predicting axillary lymph node metastasis

Table 2 shows that 14 (18.4%) patients had axillary lymph node metastasis, and 62 (81.6%) patients had no axillary lymph node metastasis on pathology. However, among the continuous variables, short-axis length (p-value=0.03), short/long axis ratio (p-value=0.03), cortical thickness (p-value=0.02), and ADC index (p-value<0.001) have statistically significant differences between the metastatic and non-metastatic groups. The mean ADC index in the metastatic lymph node group (0.894×10^{-3} mm^2/s) was significantly lower than that in the non-metastatic group (1.228×10^{-3} mm^2/s) (see Table 2).

Based on the AUC index, the ADC value was the most valuable variable in predicting lymph node metastasis

(AUC=0.874). With the optimal threshold taken as $1x10^{-3}$ mm^2/s, according to the Youden index, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were 78.6%, 85.5%, 55.0%, and 94.6%, respectively. Capsule thickness was also a good predictor of lymph node metastasis, with an optimal cutoff of 3.35 mm (AUC 0.783, sensitivity 85.7%, specificity 72.6%, PPV 41.4%, NPV 95.4%). In contrast, the long-axis length of the lymph node was not able to differentiate benign/malignant characteristics well. Six (42.9%) of 14 metastatic lymph nodes had a loss of hilar fat structure, and 58 (93.5%) of nonmetastatic lymph nodes had hilar fat structure (see Table 3).

For lymph node morphology, eccentric capsule thickening was also a statistically significant parameter in the malignant lymph node group; specifically, 7 (50%) metastatic lymph nodes had eccentric capsule thickening morphology, while only 4 (6.5%) benign lymph nodes had this morphology (see Table 4). A specific case was seen in Figure 1 (see Figure 1).

Table 2 Features of axillary lymph nodes on the 1.5 Tesla MRI

Features	Mean±S.D.	Range	p-value
Short axial length (mm)			0.03
Benign	6.12±1.44	3.7 - 10.5	
Malignant	8.59±3.76	4.1 - 15.8	
Long axial length (mm)			0.23
Benign	10.89±3.38	4.8 - 18.9	
Malignant	12.11±3.89	6.9 - 20.9	
Short/long axis ratio			0.03
Benign	0.59±0.14	0.36 - 0.89	
Malignant	0.70±0.14	0.49 - 0.93	
Capsule thickness (mm)			0.02
Benign	3.00±0.84	1.7 - 5.6	
Malignant	4.20±1.55	2.1 - 8.3	
ADCa index (x10-3 mm^2/s)			<0.001
Benign	1227.96±266.13	753.4 - 2210.0	
Malignant	893.51±216.56	551.5 - 1234.8	

MRI=magnetic resonance imaging, S.D.=standard deviation, ADCa=average apparent diffusion coefficient

Table 3 Diagnostic value of continuous variables

Contents	Se (%)	Sp (%)	PPV (%)	NPV (%)	AUC	CI 95%	p-value	Thresh-old	Youden index
Short axial length	50.0	95.2	70.0	89.4	0.698	0.511-0.884	<0.05	8.25	0.552
Long axial length	64.3	61.3	27.3	88.4	0.597	0.432-0.763	0.873	10.85	0.256
Short/long axis ratio	78.6	53.2	27.5	91.7	0.697	0.550-0.844	<0.05	0.602	0.318
Capsule thickness	85.7	72.6	41.4	95.4	0.783	0.628-0.939	<0.001	3.35	0.583
ADCa index	78.6	85.5	55.0	94.6	0.874	0.782-0.967	<0.001	1046.9	0.641

Se=sensitivity, Sp=specificity, PPV=positive predictive value, NPV=negative predictive value, AUC=area under the curve CI=confidence interval

Table 4 Diagnostic value of morphological variations by the 1.5 Tesla MRI

Morphological variations	Se (%)	Sp (%)	PPV (%)	NPV (%)
Loss of fatty hilum	42.9	93.5	60.0	87.9
Eccentric cortical thickening	50.0	93.5	63.6	89.2
Morphological features (loss of fatty hilum or thickened cortex)	64.3	88.7	56.2	91.7

MRI=magnetic resonance imaging, Se=sensitivity, Sp=specificity, PPV=positive predictive value, NPV=negative predictive value

Figure 1 A case of infiltrating ductal carcinoma. MRI revealed an irregularly shaped mass with heterogeneous enhancement (type 3 pattern). Adjacent lobular segments also showed heterogeneous enhancement (type 3 pattern). The patient underwent total left mastectomy, and postoperative pathology confirmed multifocal lesions

Discussion

Breast cancer is the most common malignancy in women; however, early detection and appropriate treatment significantly improve survival outcomes.[12] With the continuous advancement of comprehensive treatments and research on breast cancer, breast-conserving surgery for breast cancer patients is gradually becoming more common. Accurate assessment of primary tumor characteristics to predict axillary lymph node metastasis before breast-conserving surgery is of great significance for breast cancer patients in order to adjust surgical strategies and reduce pain and costs.

Among the routine MRI parameters, cortical thickness was the most valuable parameter for predicting lymph node metastasis (AUC 0.783, optimal threshold 3.35 mm). This result was similar to that in the studies of Kim et al. and Scaranelo et al., with corresponding AUC indices of 0.77 (cortical thickness of 0.37 mm and 0.86 mm), respectively[13-14]. Other size parameters also differed between the metastatic and non-metastatic groups (p-value<0.05); the optimal threshold for short-axis length was 8.25 mm. In the study of He et al., the short-axis length threshold was 5.5 mm[15], while the study of Luciani et al. recorded a short-axis length threshold of 4 mm[16].

Thus, the short-axis length threshold in our study was higher than in the above studies; conversely, the specificity was also higher, reaching 93.5%, which was similar to Kim's study[13]. The short/long axis length ratio also had a significant difference between the two groups, with the optimal threshold being 0.602. This result was similar to the results in the study of He et al., with this ratio being 0.62[15], while the study of Yoshimura et al. showed that this ratio was 0.63[17]. In contrast, Kim's study showed that this difference was not statistically significant (p-value>0.05)[13]. Not only that, our study and some other studies, such as the study of Arslan et al., showed no difference in long-axis length between the two groups[11], while the studies of Kim et al. and Yoshimura et al. gave the opposite result[13,17]. The reason for the unstable values of the size parameters may be that some nodes have only partially invaded the cortex, while some nodes have been completely replaced by cancer cells, causing complete transformation. These results lead to the need for some additional functional parameters to assess the benign/malignant nature of the nodes.

The morphological difference between the benign and malignant groups was also statistically significant (p-value<0.05). Accordingly, both parameters of fatty hilum loss and eccentric cortical thickening had high specificity (93.5%) and were therefore useful in excluding lymph node metastasis. These results were similar to previous studies. Specifically, in the study of Balter et al., eccentric cortical thickening had a specificity of 93.9% and fatty hilum loss had a specificity of 85.7%[18], while in the study of Mortellaro et al., the image of fatty hilum loss on magnetic resonance was highly correlated with positive pathological results[19]. In addition, combining both of these parameters in the diagnosis significantly increased the sensitivity (42.9% to 64.3%), while the specificity did not change much (88.7%).

The above results have shown that functional parameters can contribute to the ability of magnetic resonance to predict lymph node metastasis. Axial DWI sequences are a promising option, as they can be performed in addition to conventional magnetic resonance techniques without requiring additional resources and without the need for contrast injection. In our study, the value of the ADC index in distinguishing the benign/malignant properties of lymph nodes was even superior to conventional magnetic resonance parameters (AUC=0.874). With the optimal threshold of $1.046x10^{-3}$ mm^2/s, the ADC index had a sensitivity, specificity, PPV, and NPV of 78.6%, 85.5%, 55.0%, and 94.6%, respectively. Our results are similar to many previous studies, with sensitivities ranging from 53.8 to 94.7% and specificities ranging from 65.8–93%[15,20-24]. At b=1000 s/mm^2, the optimal threshold in the study by Kamitani et al. was $1.05x10^{-3}$ mm^2/s,[20] and the optimal threshold in the study by Junping et al. was $1.04x10^3$ mm^2/s[23]. These results are very close to our study. Meanwhile, there are also studies by Nakai et al. and Heusner et al. that showed that the ADC index had no value in predicting lymph node metastasis[25-26]. There are several reasons for this difference, beyond just technical variability. First, differences in the threshold values, such as the higher threshold, could explain the better specificity observed in our results. A higher threshold often leads to fewer false positives, improving specificity, but this can sometimes come at the cost of sensitivity. Second, the studies by Nakai et al. and Heusner et al. used a b value of 800 s/mm^2, which differs from the b value in our study (1000 s/mm^2), and this may have influenced the ADC measurements[25-26]. Furthermore, the method for placing ROIs may vary: in our study, we combined fat-suppressed T1 images with contrast injection to more accurately place ROIs, ensuring the lymph node area with invasive cancer tissue was correctly identified. This method may have minimized errors due to incorrect ROI placement in the surrounding fat tissue. Other contributing factors may include population differences, scanner models, and slice thickness, all of which could affect the accuracy of ADC measurements. Additionally, subjectivity in ROI placement by radiologists may contribute to variability in ADC values, influencing the results. These factors should be considered when interpreting and comparing the findings across studies.

Therefore, it can be seen that conventional magnetic resonance combined with DWI pulse sequence using the 1.5 Tesla machine is a very promising non-invasive method to predict the status of lymph node metastasis in the group of patients indicated for breast-conserving surgery. However, there have not been many studies comparing the ability of magnetic resonance to diagnose malignant lymph nodes with traditional methods, such as sentinel lymph node biopsy, and there have not been many studies measuring the impact of these results on the 5-year survival rate, as well as the recurrence rate, especially in the group of patients indicated for breast-conserving treatment.

Our study had some limitations. First, we selected the most suspicious lymph node for analysis and assumed that it corresponded to the postoperative lymph node results. However, there is no way to be sure that the lymph node we selected is also the secondary lymph node detected in pathology. Second, due to the limitation of section thickness, we only included lymph nodes with a long axis of more than 4 mm in the study, which may have missed small lymph nodes that had infiltrated with tumor cells, as mentioned above. Third, our method of measuring the ADC index is different from some previous studies: measuring the area with the lowest ADC index, after comparing it with the fat-suppressed T2 image, while Kim et al. used ROI to capture the maximum possible lymph node area[13]. Although this method increases the sensitivity in detecting small metastatic areas in the lymph nodes, it may cause errors due to the partial volume effect. Fourth, our study did not use the enhancement kinetic parameter, which is widely used to assess the benign/malignant nature of primary tumors.

Conclusion

The results of the study show that several parameters of conventional MRI and axial DWI sequences, including short-axis length, short-axis/long-axis ratio, cortical thickness, hilar fat loss/eccentric cortical thickening, and ADC index, were valuable in the assessment of axillary lymph node metastasis in breast cancer patients with indications for conservative treatment. Thus, MRI, especially the ADC index (with the optimal threshold of $1.046 \times 10^{-3} mm^2/s$), is an effective method to assess lymph node metastasis in patients with indications for breast conservation. However, further studies are needed to evaluate the effectiveness of MRI on the final treatment outcome in this group of patients.

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