

ORIGINAL RESEARCH

A Prospective Study of Predicting the Nuclear Grade of Breast Cancer Using Diffusion Weighted Imaging: An Institutional Based Study

¹Tushar Prabha, ²Jawahira Chisti, ³Mahendra Kumar Yadav, ⁴Kartikeya Jain

¹Associate Professor, ³Junior Resident (IIIrd year), ⁴Junior Resident (Ist year), Department of Radio-Diagnosis, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

²Assistant Professor, Department of Obstetrics and Gynaecology, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

Correspondence:

Tushar Prabha

Associate Professor, Department of Radio-Diagnosis, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India

Email: prabha.tushar@gmail.com

ABSTRACT

Introduction: As it has to aware that the breast cancer is the commonest cancer among women around the globe. Diffusion Weighted Imaging (DWI) helps to evaluate the physiological and functional environment of the lesion by observing the random motion of water molecules, tissue cellularity, fluid viscosity, membrane permeability and blood flow pattern that could be measured quantitatively by Apparent Diffusion Coefficient (ADC) values.

Materials and Methodology: A total of 70 patients with histo-pathologically proven breast carcinoma form the study sample in the study (3 patients had bilateral malignancy). MRI examinations were performed within 2 weeks before surgery. All the 70 participants who had done breast MRI underwent surgery. Statistical analysis was performed using SPSS (Statistical package for social science version 16.0 for windows). Students T test and Analysis of Variance (ANOVA) were used to study the difference in ADC between two groups.

Results: Out of all the total 70 breast lesions, 53 lesions were (76%) single, while 9(13%) were multifocal carcinoma and 8 (11%) were multicentric multifocal breast carcinoma. Histological types included invasive ductal carcinoma no special type (65) invasive lobular carcinoma (1) mucinous carcinoma (2) papillary carcinoma (1) medullary carcinoma (1). The ADC value was correlated with pathological grading of the tumour ($r = -0.497$, $P < 0.001$).

Conclusion: DWI usually takes short acquisition time and post-processing time and does not require any administration of contrast dyes and provides a real-time quantitative functional parameter for evaluating the tumour aggressiveness.

Keywords: Breast Carcinoma, DWI, MRI, Prognosis, Imaging.

INTRODUCTION

Worldwide, breast cancer is a multivariate disease.¹ The most crucial that are determining its prognosis include histological grade (Elston-Ellis modification of Bloom-Richardson histologic grading system or Nottingham combined histologic grading system), histopathological type of cancer, Estrogen Receptor/Progesterone Receptor(ER/PR) status, Human Epidermal Growth Receptor (HER2) Neu status, lymph node status, and tumour size.^{2,3} Lympho-vascular invasion and perineural invasion were the other factors that helps in

prognosis status.^{4,5} MRI seems as a complementary diagnostic tool to mammogram and ultrasound in assessing the prognosis breast cancer, especially in young women with dense breast.⁶ The sensitivity and specificity of Dynamic Contrast Enhancement (DCE)-MRI in analysing the breast cancer that is approximately 85-99% and 72%.^{7,8} Moreover, Diffusion Weighted Imaging (DWI), the sensitivity increases to 85-100% and specificity to 37-88%.^{1,2} As it has to aware that the breast cancer is the commonest cancer among women around the globe.⁷ In India the incidence rate of breast cancer is reported to be less. But the mortality rate is almost equal with that reported in western countries. Also, the Indian women usually have tumours (use - tend to have) 10 years much earlier than western population with the presence of more aggressive tumours.⁸

Diffusion Weighted Imaging (DWI) helps to evaluate the physiological and functional environment of the lesion by observing the random motion of water molecules, tissue cellularity, fluid viscosity, membrane permeability and blood flow pattern that could be measured quantitatively by Apparent Diffusion Coefficient (ADC) values.² Earlier studies have reported that lower apparent diffusion coefficient values for malignant breast lesions than for benign lesions and normal breast tissue.³⁻⁵ In addition to differentiation of benign and malignant lesions, DWI is identified to have a broader role in detecting the prognosis of breast carcinoma.⁴ In the current study, it has been attempted to correlate the ADC values with the histopathological prognostic factors that helps in predicting the tumour aggressiveness preoperatively and thereby assisting in treatment planning.

MATERIALS AND METHODOLOGY

Present study was conducted in Department of Radio-diagnosis, Mahatma Gandhi Medical College and Hospital, Jaipur, Rajasthan, India. Informed consents were taken from all the study participants. Study population included women diagnosed to have breast carcinoma by histopathological study of the biopsy specimen and underwent breast MRI before any therapeutic interventions during a period of 2 years. The exclusion criteria that have been followed in this study include those patients with motion artifacts on DWI, prior neoadjuvant chemotherapy, excision biopsy, those with in situ ductal cancer, and those with small invasive focus detected only in histopathology are duly excluded from the study.

A total of 70 patients with histopathologically proven breast carcinoma form the study sample in the study (3 patients had bilateral malignancy). MRI examinations were performed within 2 weeks before surgery. All the 70 participants who had done breast MRI underwent surgery (either breast conservation or modified radical mastectomy). The histopathological and immunohistochemical analysis of the surgical specimen was done to determine the prognostic factors like histopathological type of tumour, grade of the tumour, ER, PR status, Her 2Neu status, lympho-vascular, and perineural invasion. The tumour size and axillary lymph-node status were also assessed.

Statistical analysis was performed using SPSS (Statistical package for social science version 16.0 for windows). Students T test and Analysis of Variance (ANOVA) were used to study the difference in ADC between two groups. A P value < 0.05 was considered as statistically significant.

RESULTS

The age of the patients ranged from 30 to 80 years. 33 had lesion on the right side, 36 had lesion on the left side and 6 had bilateral invasive breast carcinoma. The maximum size was 7.3 cm and minimum size was 0.8 cm. All the 70 index lesions showed enhancement at DCE-MRI, out of which 54 (77.6%) had type III enhancement kinetics and 16 (22.4%) had type II enhancement kinetics. All the index lesions reported to exhibit restricted diffusion on DWI.

Out of all the total 70 breast lesions, 53 lesions were (76%) single, while 9(13%) were multifocal carcinoma and 8 (11%) were multicentric multifocal breast carcinoma. Histological types included invasive ductal carcinoma no special type (65) invasive lobular carcinoma (1) mucinous carcinoma (2) papillary carcinoma (1) medullary carcinoma (1). The minimum and maximum size of the tumours in HPE were 0.6 cm - 7.8 cm respectively. On post hoc analysis, there was significant difference in the ADC values (both minimum and mean ADC values) of tumours of grade I and II ($P < 0.001$) as well as grade I and III ($P < 0.001$) and insignificant difference between grade II and III (P value - 1.0). The ADC value was correlated with pathological grading of the tumour ($r = -0.497$, $P < 0.001$).

Table 1: Statistical analysis of ADC values with prognostic factors

Parameters		Number of lesions (n=70)	Mean ADC ($\times 10^{-3}$ mm ² /sec)	P - value
Grade	Grade – I	15 (21)	0.96 ± 18	<0.001
	Grade – II	36 (51.3)	0.82 ± 0.13	
	Grade – III	19 (27.2)	0.75 ± 0.15	
ER	Positive	52 (74.5)	0.81 ± 0.19	0.72
	Negative	18 (25.5)	0.82 ± 0.09	
PR	Positive	49 (70)	0.81 ± 0.19	0.68
	Negative	21 (30)	0.82 ± 0.11	
HER 2 NEU	Positive	36 (52)	0.83 ± 0.11	0.18
	Negative	33 (48)	0.79 ± 0.22	
Lympho-vascular invasion	Positive	39 (55.5)	0.79 ± 0.13	0.29
	Negative	31 (44.5)	0.82 ± 0.21	
Perineural invasion	Positive	16 (22.9)	0.85 ± 0.08	0.43
	Negative	54 (77.1)	0.79 ± 0.18	
Axillary nodes	Positive	36 (52)	0.78 ± 0.14	0.21
	Negative	34 (48)	0.83 ± 0.19	

DISCUSSION

This technique diffusion weighted imaging (DWI) is a functional imaging process that analyses the early changes at the molecular level, cellularity and cell membrane permeability which directly correlate with tumour biology.⁹ There are chances that diffusion weighted imaging and ADC values would possibly identify the tumours with highly malignant potential and helps in preoperative prognostication and treatment planning. In this study, both minimum and mean ADC values were separately analysed for all lesions using a 3T MRI system. It can acquire high-resolution images while retaining high signal to noise ratio.^{10,11}

Tumour grade of breast cancer is the very important prognostic factor which could easily predicts the invasive behaviour of tumour and its consequences in long-term prognosis. In this study, the grade I carcinoma was reported to have significantly higher ADC values than grade II and grade III. There was no significant difference in ADC values between grade II and grade III. In a study done by Kizildagyirgin et al cut off of 1.05×10^{-3} mm²/sec was adopted for differentiating grade I from higher grade tumours.¹² This value is observably higher as compared to the cut off derived in our study. A statistically significant inverse correlation between ADC values and tumour grading was reportedly observed in few other earlier studies.^{9,12,13} But studies by Park et al and Martincich et al seemed to have no statistically significant difference between ADC values and grade of tumour.^{14,15}

It is aware that HER2-positive cells have a higher cell proliferation rate, rapid invasion and metastasis. Therefore, ADC values of HER2-positive Intra Ductal Carcinoma (IDC) are reported to be lower because of its increased cellularity. In our study, on the contrast, the

mean ADC values of lesions with HER-2-NEU positive were more than that of lesions with HER2-NEU negative cases, but they were statistically not significant. This can be greatly explained by the increased angiogenesis thus greatly suppressing diffusion restriction.¹⁷ This result is consistent with other studies done by Martincich et al and Park et al.^{14,15}

Lympho-vascular invasion denoted that increased risk of axillary lymph node involvement and distant metastasis in node negative cancer.⁸ No significant relation was observed between the lympho-vascular invasion and ADC values in our study which is similar to that reported by Guvenc et al.¹¹ Perineural invasion is observed to be in coincidence with lympho-vascular invasion and thereby confounding its significance as an independent prognostic factor.⁷ In this study no statistically significant relation is noted between the ADC values and perineural invasion.

CONCLUSION

The biological heterogeneity of the tumour tissue and ADC values can be detected easily using MRI studies using DWI technique. DWI usually takes short acquisition time and post-processing time and does not require any administration of contrast dyes and provides a real-time quantitative functional parameter for evaluating the tumour aggressiveness.

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