## Original Research

# Evaluation of Role of Diffusion Weighted MRI Imaging in Assessment of Nuclear Grade of Breast Carcinoma at a Tertiary Care Hospital

Gaurav Balpande[1], Mallika Jain Singhai[2], Kanchan Choubey[3]

[1]Assistant Professor, Department of Radiodiagnosis, LN Medical College & Research Center, Bhopal, Madhya Pradesh, India.
[2]Assistant Professor, Department of Radiodiagnosis,Gandhi Medical College, Bhopal, Madhya Pradesh, India.
[3]Assistant Professor, Department of Radiodiagnosis, LN Medical College & Research Center, Bhopal, Madhya Pradesh, India.

**Corresponding Author:**
Dr. Kanchan Choubey
Assistant Professor, Department of Radiodiagnosis, LN Medical College & Research Center, Bhopal, Madhya Pradesh, India. Email: dr.kanchan_07@yahoo.com

**Received Date: 15 March, 2024** **Accepted Date: 28 April, 2024**

**Abstract**
**Background:** Mammography has emerged as a standard screening method for breast cancer. MRI serves as an adjunctive diagnostic modality to mammography and ultrasound in the assessment of breast cancer, particularly in younger women with dense breast tissue. Hence; the present study was conducted for evaluation of role of diffusion weighted MRI imaging in assessment of nuclear grade of breast carcinoma at a tertiary care hospital.
**Materials & Methods:** 40 patients with histopathologically proven breast carcinoma were included. MRI examinations were performed within 2 weeks before surgery. All patients were scanned. Prior to the administration of contrast media, axial bilateral fat-suppressed T2-weighted fast spin-echo and diffusion-weighted imaging (DWI) series were obtained. The ADC values of the lesions were measured. All 40 participants who underwent breast MRI subsequently had surgical intervention. Histopathological and immunohistochemical analyses of the surgical specimens were conducted to identify prognostic factors. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software.
**Results:** Restricted diffusion on DWI was seen in all the patients. 62.5 percent of the patients were of T2 stage of TNM staging. In ROC curve analysis in which grade I was compared with grade II and III, the minimum ADC cut-off value was calculated as $0.77 \times 10^{-3}$ $mm^2/sec$ with 87% sensitivity and 82% specificity. Significant results were obtained while correlating ADC values with tumor grading.
**Conclusion:**MRI studies employing DWI are capable of detecting the biological heterogeneity present within tumor tissue, with ADC values exhibiting considerable variation based on the biological characteristics of breast cancer.
**Key words:**Breast Cancer, Mammography, MRI.



## INTRODUCTION

Carcinogenesis is defined by six principal hallmarks and has the potential to occur in any cell, tissue, or organ, resulting in pathological changes that can lead to a wide array of cancers. The key mechanisms facilitating its advancement include the evasion of programmed cell death, an unlimited capacity for cellular division, increased formation of blood vessels, resistance to inhibitory growth signals, the generation of self-sustaining growth signals, and the ability to metastasize.[1, 2] This process is multifactorial, primarily driven by genetic predispositions alongside environmental factors. The annual rise in cancer-related mortality is alarming, positioning cancer as one of the leading causes of death globally. While many cancers do not invariably lead to fatal outcomes, they considerably diminish quality of life and impose substantial economic burdens.[3]

Mammography has emerged as a standard screening method for breast cancer. Its most significant efficacy is noted among women aged 50 to 69 years. Traditional mammography exhibits a sensitivity range of 75 to 95%

and a specificity between 80 and 95%. For women who are at risk of hereditary breast cancer, magnetic resonance mammography serves as an alternative screening tool. In instances where mammography reveals a suspicious lesion, a subsequent ultrasound examination is conducted, and if warranted, a core needle biopsy is performed, followed by a histopathological analysis of the tumor.[4, 5]

MRI serves as an adjunctive diagnostic modality to mammography and ultrasound in the assessment of breast cancer, particularly in younger women with dense breast tissue. The sensitivity and specificity of Dynamic Contrast Enhancement (DCE)-MRI for breast cancer detection are reported to be approximately 85-99% and 72%, respectively. When Diffusion Weighted Imaging (DWI) is incorporated, sensitivity rises to between 85-100%, while specificity ranges from 37-88%.[6- 8]

Hence; the present study was conducted for evaluation of role of diffusion weighted MRI imaging in assessment of nuclear grade of breast carcinoma at a tertiary care hospital.

## MATERIALS & METHODS

The present study was conducted in the Department of Radiodiagnosis, LN Medical College & Research Center, Bhopal, Madhya Pradesh (India) for evaluation of role of diffusion weighted MRI imaging in assessment of nuclear grade of breast carcinoma from February 2023 to January 2024. Study population included women diagnosed to have breast carcinoma by histopathological study of the biopsy specimen and underwent breast MRI before any therapeutic interventions. For the acquisition of the MRI images, patients were placed in the prone position in a 1.5 T scanner (Achieva; Philips Medical Systems, Best) with a dedicated breast coil. 40 patients with histopathologically proven breast carcinoma were included. MRI examinations were performed within 2 weeks before surgery. All patients were scanned. Prior to the administration of contrast media, axial bilateral fat-suppressed T2-weighted fast spin-echo and diffusion-weighted imaging (DWI) series were obtained. Isotropic diffusion-weighted images were reconstructed for each b value. For the quantitative analysis of the DWI data, apparent diffusion coefficient (ADC) maps were generated automatically using software provided by the MRI system manufacturer, utilizing two b values (50 and 800 s/mm²). Subsequently, dynamic axial bilateral breast images were acquired using fat-suppressed high-resolution T1-weighted 3D fast gradient-echo imaging (VIEWS) at baseline and at 60, 120, 180, 240, and 300 seconds following the administration of the contrast medium. The ADC values of the lesions were measured. All 40 participants who underwent breast MRI subsequently had surgical intervention. Histopathological and immunohistochemical analyses of the surgical specimens were conducted to identify prognostic factors. All the results were recorded in Microsoft excel sheet and were subjected to statistical analysis using SPSS software.

**Table 1: MRI breast protocol**

| **Machine and patient's position** |
|---|
| • Obtained images of both breasts while patient is in a prone position using a breast dedicated coil in 1.5T Philips MRI system |
| **Imaging plane** |
| • Axial plane was obtained in all the imaging sequence. |
| **Pulse sequence** |
| • T2-weighted images |
| • Pre-Contrast<br>▪ Axial Bilateral Fat-Suppressed T2-Weighted Fast Spin-Echo (T2W FSE)<br>▪ Diffusion-Weighted Imaging (DWI) series<br>▪ Isotropic diffusion-weighted images<br>▪ b-values: 50 and 800 s/mm²<br>▪ Apparent Diffusion Coefficient (ADC) maps generated |
| • Post-Contrast<br>▪ Dynamic Axial Bilateral Breast Images<br>▪ Fat-Suppressed High-Resolution T1-Weighted 3D Fast Gradient-Echo Imaging (VIEWS)<br>▪ Time points:<br>- Baseline<br>- 60 seconds<br>- 120 seconds<br>- 180 seconds<br>- 240 seconds<br>- 300 seconds |

| **Considerations when evaluating imaging quality** |
|---|
| • Water content should be well separated in T2-weighted images |
| • Contrast enhanced T1-weighted images should be taken by fat suppression technique or should include subtraction images Contrast-enhanced T1-weighted images should include images taken between 60 and 120 seconds after contrast injection and images taken after 4 minutes |
| • The slice thickness of contrast enhanced T1-weighted images should be less than 3 mm and should not have gaps |
| • The spatial in-plane resolution of contrast enhanced T1-weighted images should be less than 1 mm², should be less than 1.5 mm² |
| • Temporal resolution of contrast enhanced T1-weighted images should be less than 120 seconds. |

## RESULTS

The mean age of the patients was 55.9 years. Lesions were on the right side in 60 percent of the patients while it was present on the left side in the remaining 40 percent of the patients. The maximum and minimum size of the lesions were 7.9 cm and 1.9 cm respectively. enhancement at DCE-MRI was seen in all the patients. Among them, 80 percent of the patients had type III enhancement while type II enhancement was seen in the remaining 20 percent of the patients. Restricted diffusion on DWI was seen in all the patients. 62.5 percent of the patients were of T2 stage of TNM staging. Using b values of 50 and 850 s/mm$^2$, in ROC curve analysis in which grade I was compared with grade II and III, the minimum ADC cut-off value was calculated as $0.77 \times 10^{-3}$ mm$^2$/sec with 87% sensitivity and 82% specificity. Significant results were obtained while correlating ADC values with tumor grading.

**Table 2: Correlation of ADC values with grading**

| Grading | Mean ADC value (x$10^{-3}$ mm$^2$/sec) | p-value |
|---|---|---|
| **Grade I** | 0.99 | 0.0072 (Significant) |
| **Grade II** | 0.71 | |
| **Grade III** | 0.60 | |

**Table 3: Correlation of ADC values with lympho-vascular invasion**

| Invasion | Mean ADC value (x$10^{-3}$ mm$^2$/sec) | p-value |
|---|---|---|
| **Present** | 0.73 | 0.674 |
| **Absent** | 0.79 | |

**Table 4: Correlation of ADC values with axillary lymph node status**

| Status | Mean ADC value (x$10^{-3}$ mm$^2$/sec) | p-value |
|---|---|---|
| **Positive** | 0.69 | 0.449 |
| **Negative** | 0.73 | |

## DISCUSSION

In India, breast cancer has emerged as a significant health concern, particularly among women. According to the Indian Council of Medical Research (ICMR), the average lifetime risk of a woman being diagnosed with breast cancer in India is approximately 8.6% (Age-Standardized Rate: 25.8 per 100,000). This rising trend is attributed to factors like increasing life expectancy, lifestyle changes, and genetic predisposition. Notably, breast cancer accounts for nearly 27% of all cancer cases among Indian women. This positions breast cancer as the second most prevalent cancer among women in the country, following skin cancer. The development of breast cancer is influenced by a multifaceted array of risk factors, which include a personal history of the disease, a positive family history, obesity, taller stature, smoking habits, alcohol intake, early onset of menstruation, late onset of menopause, a sedentary lifestyle, nulliparity, and the use of hormone replacement therapy. Conversely, certain factors are linked to a reduced risk of developing breast cancer, such as having multiple pregnancies, a history of breastfeeding, engaging in regular physical activity, and achieving weight loss. The rising incidence of breast cancer, which has been observed to increase by approximately 0.5% annually, can be correlated with a national trend of increasing body weight and declining fertility rates. Breast cancer predominantly affects females, with a significantly lower incidence in males. Additionally, the risk of breast cancer is closely associated with age and race, with White females exhibiting the highest incidence rates, followed by Black, Asian, and Hispanic females. Women who have a first-degree relative diagnosed with breast cancer face a two- to three-fold increased likelihood of developing the disease themselves.[9- 11]

Diffusion-weighted magnetic resonance imaging (DW MRI) is a rapid and readily accessible imaging modality that does not require contrast enhancement and has demonstrated potential in the detection and characterization of breast malignancies. The phenomenon of restricted or impeded diffusion of water molecules within breast tissue results in hyperintense signals on high b-value DW MRI, accompanied by lower apparent diffusion coefficient (ADC) values compared to normal tissue or benign lesions. Recent studies suggest that DW MRI may serve as a valuable component of a multiparametric or non-contrast-enhanced strategy for the local staging of breast cancer in female patients.[12, 13] Hence; the present study was conducted for evaluation of role of diffusion weighted MRI imaging in assessment of nuclear grade of breast carcinoma at a tertiary care hospital.

The mean age of the patients was 55.9 years. Lesions were on the right side in 60 percent of the patients while it was present on the left side in the remaining 40 percent of the patients. The maximum and minimum size of the lesions were 7.9 cm and 1.9 cm respectively. enhancement at DCE-MRI was seen in all the patients. Among them, 80 percent of the patients had type III enhancement while type II enhancement was seen in the remaining 20 percent of the patients. Restricted diffusion on DWI was seen in all the patients. 62.5 percent of the patients were of T2 stage of TNM staging. Research has demonstrated that apparent diffusion coefficient (ADC) values can effectively differentiate among various tumor grades, proliferation rates, and subtypes. For instance, Costantini et al conducted an analysis of 162 malignant lesions across 136 patients, revealing a notable inverse relationship between ADC values and tumor grade. Specifically, the mean ADC was observed to be higher in less aggressive and in situ cancers compared to more aggressive malignancies. In a more extensive study, Choi et al corroborated the disparity in ADC values between in situ and invasive cancers, additionally noting that lower ADC values were significantly linked to heightened proliferation of the Ki-67 protein, as well as estrogen receptor (ER) and progesterone receptor (PR) positivity, alongside increased microvascular density. Numerous other research teams have also reported associations between lower ADC values and ER positivity.[14-17]

In ROC curve analysis in which grade I was compared with grade II and III, the minimum ADC cut-off value was calculated as $0.77 \times 10^{-3}$ $mm^2/sec$ with 87% sensitivity and 82% specificity. Significant results were obtained while correlating ADC values with tumor grading. Jeong S, et al investigated the imaging findings and visibility of breast invasive lobular carcinoma (ILC) on diffusion-weighted imaging (DWI) and compare quantitative apparent diffusion coefficient (ADC) metrics of ILC and invasive carcinoma of no special type (NST) using a histogram analysis. They performed an observational retrospective study of 629 consecutive women with pathologically proven ILC and invasive ductal carcinoma of NST, who underwent 3-T MRI including DWI. 71 women were allocated to each group. On DWI, 9 (12.7%) lesions of ILC and 4 (5.6%) invasive carcinomas of the NST were not visualized. For the tumor visibility on DWI, tumor size, tumor ADC value, and background diffusion grade were significantly associated with the visibility score in both groups, whereas the mean background ADC value was not significant. The mean ADC, median ADC, maximum ADC, minimum ADC, 90th percentile ADC and 10th percentile ADC were higher in ILC than in invasive carcinoma of NST. Additionally, the ADC difference value of the ILC was higher than that of invasive carcinoma of NST. On DWI, the visibility of ILC was lower compared to invasive carcinoma of NST. ILC showed higher quantitative ADC values and higher ADC difference values.[18] Kim et al evaluated the role of diffusion-weighted imaging (DWI) in the detection of breast cancers and correlated the apparent diffusion coefficient (ADC) value with prognostic factors. Sixty-seven women with invasive cancer underwent breast MRI. Histological specimens were analyzed for tumor size and grade, and expression of estrogen receptors (ER), progesterone receptors, c-erbB-2, p53, Ki-67, and epidermal growth factor receptors. DWI detected breast cancer as a hyperintense area in 62 patients (92.5 %). A statistically significant difference in the mean ADC values of breast cancer and normal parenchyma was detected. There were no correlations between the ADC value and prognostic factors. However, the median ADC value was lower in the ER-positive group than the ER negative group, and this difference was marginally significant. The ADC value was a helpful parameter in detecting malignant breast tumors, but ADC value could not predict patient prognosis.[19]

## CONCLUSION

Magnetic Resonance Imaging (MRI) studies utilizing Diffusion-Weighted Imaging (DWI) have demonstrated the ability to identify and quantify the biological heterogeneity within tumor tissue, providing valuable insights into the complex characteristics of breast cancer. Specifically, Apparent Diffusion Coefficient (ADC) values, which measure the rate of water diffusion within tissues, have been found to vary significantly depending on the biological features of breast cancer. For instance, tumors with higher cellular density and restricted diffusion tend to exhibit lower ADC values, whereas those with necrotic or cystic components display higher ADC values. This variability in ADC values enables researchers and clinicians to non-invasively assess tumor biology, differentiate between various breast cancer subtypes, and potentially predict treatment response. Furthermore, DWI-MRI's sensitivity to tissue microstructure allows for the detection of subtle changes in tumor composition, and more personalized treatment strategies.

## REFERENCES


1. Hanahan D., Weinberg R.A. The Hallmarks of Cancer. Cell. 2000;100:57–70.
2. Sung H., Ferlay J., Siegel R.L., Laversanne M., Soerjomataram I., Jemal A., Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J. Clin. 2021;71:209–249.
3. Duggan C., Dvaladze A., Rositch A.F., Ginsburg O., Yip C., Horton S., Rodriguez R.C., Eniu A., Mutebi M., Bourque J., et al. The Breast Health Global Initiative 2018 Global Summit on Improving Breast Healthcare Through Resource-Stratified Phased Implementation: Methods and overview. Cancer. 2020;126:2339–2352.
4. Amin M.B., Greene F.L., Edge S.B., Compton C.C., Gershenwald J.E., Brookland R.K., Meyer L., Gress D.M., Byrd D.R., Winchester D.P. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J. Clin. 2017;67:93–99.
5. Hayes D.F., Isaacs C., Stearns V. Prognostic Factors in Breast Cancer: Current and NewPredictors of Metastasis. J. Mammary Gland Biol. Neoplasia. 2001;6:375–392.
6. De Boer M., van Dijck J.A., Bult P., Borm G.F., Tjan-Heijnen V.C. Breast Cancer Prognosis and Occult Lymph Node Metastases, Isolated Tumor Cells, and Micrometastases. J. Natl. Cancer Inst. 2010;102:410–425.
7. Bogner W, Gruber S, Pinker K, Grabner G, Stadlbauer A, Weber M, et al. Diffusion-weighted MR for differentiation of breast lesions at 3.0 T: How does selection of diffusion protocols affect diagnosis? Radiology. 2009;253:341–51.
8. Min Q, Shao K, Zhai L, Liu W, Zhu C, Yuan L, et al. Differential diagnosis of benign and malignant breast masses using diffusion-weighted magnetic resonance imaging. World J Surg Oncol. 2015;13:32.
9. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer Statistics, 2021. CA Cancer J Clin. 2021;71(1):7–33.
10. Alkabban FM, Ferguson T. StatPearls; Treasure Island (FL): 2022. Breast Cancer.
11. Abdelwahab Yousef AJ. Male Breast Cancer: Epidemiology and Risk Factors. Semin Oncol. 2017;44(4):267–72.
12. Lee SH, Shin HJ, Moon WK. Diffusion-weighted magnetic resonance imaging of the breast: standardization of image acquisition and interpretation. Korean J Radiol. 2021;22:9–22.
13. Girometti R, Marconi V, Linda A, Di Mico L, Bondini F, Zuiani C, et al. Preoperative assessment of breast cancer: Multireader comparison of contrast-enhanced MRI versus the combination of unenhanced MRI and digital breast tomosynthesis. Breast. 2020;49:174–182.
14. Costantini M, Belli P, Rinaldi P, et al. Diffusion-weighted imaging in breast cancer: relationship between apparent diffusion coefficient and tumour aggressiveness. Clin Radiol 2010; 65:1005–12.
15. Choi SY, Chang YW, Park HJ, Kim HJ, Hong SS, Seo DY. Correlation of the apparent diffusion coefficiency values on diffusion-weighted imaging with prognostic factors for breast cancer. Br J Radiol 2012; 85:e474–e479.
16. Guvenc I, Akay S, Ince S, et al. Apparent diffusion coefficient value in invasive ductal carcinoma at 3.0 Tesla: is it correlated with prognostic factors? Br J Radiol 2016; 89:20150614.
17. Jeh SK, Kim SH, Kim HS, et al. Correlation of the apparent diffusion coefficient value and dynamic magnetic resonance imaging findings with prognostic factors in invasive ductal carcinoma. J Magn Reson Imaging 2011; 33:102–9.
18. Jeong S, Kim TH. Diffusion-weighted imaging of breast invasive lobular carcinoma: comparison with invasive carcinoma of no special type using a histogram analysis. Quant Imaging Med Surg 2022;12(1):9.
19. Kim et al. Diffusion-weighted imaging of breast cancer: Correlation of the apparent diffusion coefficient value with prognostic factors. J. Magn. Reson. Imaging 2009;30:615–20.