MALIGNANT BREAST TUMOURS: ROLE OF MRI IN PREDICTING HISTOPATHOLOGICAL GRADING.

Thesis
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By

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Abstract

Purpose: To evaluate the correlation between dynamic MRI parameters and ADC values with histological grading in breast cancer.

Patients and methods: Thirty patients with BIRADS V lesions on mammography were included in the study. MRI examination included conventional sequences; diffusion weighted imaging and dynamic contrast enhanced magnetic resonance imaging. Morphological features, dynamic parameters, and ADC values were recorded and correlated with with the histological grades.

Results: A statistically significant inverse correlation between ADC value and histological grade was found. Tumors with higher grade showed lower ADC value compared with those of lower grade (p= 0.001). The mean ADC values of grade I, II and III were $0.96 \pm 0.09 \times 10^{-3}$ mm^2/s, $0.89 \pm 0.11 \times 10^{-3}$ mm^2/s and $0.76 \pm 0.07 \times 10^{-3}$ mm^2/s, respectively. Also, high grade tumors (grade III) were more associated with washout dynamic curve compared to those with lower grades (grades I and II) (p= 0.04). However, no correlation was found between the maximum relative enhancement and the grade.

Conclusion: DWI using ADC mapping is the most reliable technique to differentiate between different histological grades of breast carcinoma.

Keyword: Histopathological, Lcis, Dce-Mri, Adc

List of Abbreviations

ACR: American College of Radiology

ADC: Apparent diffusion coefficient

BI-RADS: Breast Imaging Reporting and Data System

CAD: Computer Aided Detection

CC: Cranio- caudal

DCE-MRI: Dynamic contrast enhanced magnetic resonance imaging

DCIS: Ductal carcinoma in situ

DWI: Diffusion weighted imaging

ER: Estrogen receptor

FOV: Field of view

HER-2: Human epidermal growth factor receptor 2

IDC: Invasive duct carcinoma

ILC: Invasive lobular carcinoma

LCIS: Lobular carcinoma in situ

MIP: Maximum intensity projection

MLO: Medio-lateral oblique

MRI: Magnetic resonance imaging

NCI: National cancer institute

PR: Progesterone receptor

RF: Radio frequency

ROI: Region of interest

SI: Signal intensity

SNR: Signal to noise ratio

STIR: Short time inversion recovery

T2 WI: T2 weighted image

TDLU: Terminal ductal lobular unit

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Introduction

Magnetic Resonance Imaging (MRI) is an established supplemental technique to mammography and ultrasonography for evaluation of breast lesions **(Macura et al, 2006).**

Dynamic contrast enhanced breast MR imaging is currently accepted as the most sensitive imaging technique for diagnosis of breast cancer. It provides important information not only on the morphology of the lesion but also on the functional aspect reflected by the pattern of uptake of the contrast medium. Integration of both kinetic and morphological features is important for accurate diagnosis **(Macura et al, 2006).**

However it provides no direct information about tumour cellularity, which is known to be an important index of tumour grade. Consequently, there has been an increasing interest in the development and the use of diffusion-weighted breast imaging for its potential to improve the diagnosis of breast lesions at the cost of a small increase in the examination time **(Woodhams et al, 2011).**

Diffusion-weighted MR imaging (DWI) has recently been integrated into the standard breast MRI in addition to images obtained from dynamic contrast enhanced MRI. It is a non-invasive technique that has a high sensitivity for detection of changes in the local biological environment, without the need for intravenous contrast material injection **(Woodhams et al, 2011)**.

DWI is quantified using the Apparent Diffusion Coefficient (ADC) value which is the measurement of the mean diffusivity of water in tissues along three orthogonal directions. ADC value can be affected by cellularity of the tissue, fluid viscosity, and membrane permeability. Several potential applications for DWI and ADC value have been suggested and studied; including detection, characterization, and differentiation of breast lesions **(Petralia et al, 2011).**

Aim of work

The aim of this study is to investigate the relationship between DWI findings (represented by ADC values) and the dynamic contrast enhanced MRI findings (including functional parameters and morphological criteria) with the histopathological grade of malignant breast tumours, as grade is one of the important prognostic factors of breast cancer.

I-Breast MRI

Magnetic resonance (MR) imaging, when used in conjunction with mammography and ultrasonography, can be a powerful tool for breast imaging. MR imaging provides key information that can affect diagnosis, management, and follow up of breast cancer **(Kuhl, 2007).**

The main indications of breast MRI

- Preoperative staging.
- Malignant axillary lymph nodes with unknown primary.
- Postoperative assessment after conservative breast surgery.
- Evaluation of therapeutic response after neoadjuvant chemotherapy.
- Inconclusive findings after conventional imaging.
- Screening in high risk patients. **(Rankin, 2002)**

Contraindications of breast MRI

General contraindications of MR imaging:

- Cardiac pacemakers.
- Implantable devices that are not MRI compatible.
- Cochlear implants.
- Marked obesity.
- Severe claustrophobia.
- Contraindications related to gadolinium-based contrast media due to allergy, pregnancy, or compromised renal function **(Kuhl, 2007).**

Specific contraindications for breast MR imaging:

- Immediately post irradiation therapy of the breast.
- Patients with clinically obvious inflammatory lesion.
- Imaging during the second half of the menstrual cycle.
- Immediately after hormone therapy in postmenopausal women.

(Rankin, 2002)

Technique

Equipment

The magnetic field strength most widely used in breast MRI is 1.5 T. There is a linear relationship between magnetic field strength (B0) and signal-to-noise ratio (SNR). With greater B0, the SNR is higher, and images with higher spatial resolution can be obtained in a relatively short acquisition time if appropriate pulse sequences are used. The magnetic field should be homogeneous across the entire field of view, which includes both breasts. With low to intermediate field strengths (ie, less than 1.0 T), a lack of adequate homogeneity may affect fat suppression and may compromise image quality **(Kuhl, 2007).**

Preparation and positioning

Prone positioning with bilateral breast coil is the most commonly used technique (Fig.1). Mild compression may be applied to the breast in the lateral-to-medial direction which decreases the amount of tissue to be imaged in that direction and thereby decreases the image acquisition time. Compression also decreases patient motion during each sequence and between sequences and thus enables the avoidance of signal misregistration on subtracted images **(Sylvia et al, 2003).**

In premenopausal women contrast-enhanced imaging should be performed between days 7 and 14 of the menstrual cycle (day 1 being the day on which menstruation begins) **(Delille et al, 2005)**.

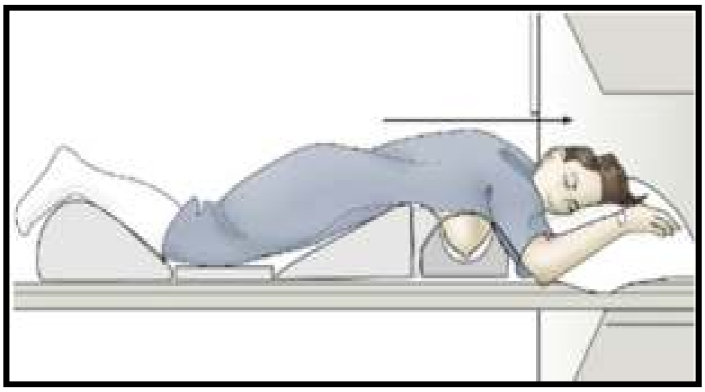

Figure 1: Position of the patient in the MRI (Schnall et al, 2006)

Pre-contrast sequences

Before contrast administration, unenhanced T2-weighted images are acquired using spin-echo, fast spin-echo, and short inversion time inversion recovery (STIR) sequences. This is used to identify cysts (Fig.2) and fibroadenomas which appear bright **(Schnall et al, 2006).**

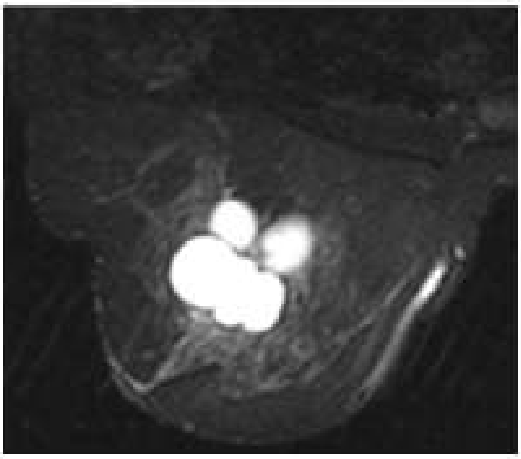

Figure 2: Axial MR image obtained with a short time inversion recovery sequence *shows several areas of uniform high signal intensity in the breast, a finding that signifies one or more cysts* ***(Rausch and Hendrick, 2006).***

Contrast administration

The hallmark of breast MRI is T1-weighted imaging with contrast agent injection **(Hylton, 2006).**

Benign and malignant breast lesions may appear similar on unenhanced MR images, but the sensitivity of breast MR imaging for detection of malignancies is significantly improved with the acquisition of images both before and after the injection of a paramagnetic contrast agent such as a gadolinium chelate (e.g Magnevist) **(Runge and Nelson, 1999)**.

For breast MR imaging in the clinical setting, a gadolinium chelate is injected intravenously at a dose of 0.1– 0.2 mmol per kilogram of body weight. The injections should be administered with a power injector at a rate of 1–2 mL/sec to achieve consistency in the timing of contrast enhancement **(Hylton, 2006).**

Dynamic High-Spatial Resolution Post-Contrast MR Imaging:

The sequence is called ‘dynamic’ because it is first performed before contrast administration and is repeated multiple times after contrast administration. A dynamic sequence demands at least three time points to be measured, that is, one before the administration of contrast medium, one approximately 2 minutes later to capture the peak and one in the late phase to evaluate whether a lesion continues to enhance, shows a plateau or shows early wash-out of the contrast agent (decrease of signal intensity) **(Kuhl, 2007).**