PROTOCOL OF A THESIS FOR PARTIAL FULFILLMENT OF MASTER DEGREE IN RADIODIAGNOSIS

Title of the Protocol:

The Role Of MRI In BIRADS Grading Of Postoperative Breast Cancer Patients

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What is already known on this subject? AND
What does this study add?

Postoperative breast cancer patients are commonly followed up using mammography and ultrasound to monitor for local recurrence or newly developed lesions. However, conventional imaging modalities often face significant limitations in the postoperative breast, where scarring, fibrosis, architectural distortion or co-existing benign lesions can create equivocal findings. As a result, a considerable number of lesions are classified as indeterminate or high suspicion for malignancy. These uncertain findings frequently lead to unnecessary biopsies, which impose physical, emotional, and financial burdens on patients. Although breast MRI, particularly contrast-enhanced MRI (CEMRI) and diffusion-weighted imaging (DWI), is known for its higher sensitivity and specificity in breast cancer detection, its focused application for downgrading equivocal postoperative lesions has not been fully established. Previous studies have highlighted the general superiority of MRI in breast imaging, but data specifically targeting post-operative lesion reclassification remain limited ***(Lee et al., 2020)***.

This study will specifically evaluate the role of MRI, combining DWI and CEMRI, in grading suspicious lesions initially detected on mammography or ultrasound in postoperative breast cancer patients. It will provide evidence on the diagnostic accuracy of MRI in distinguishing benign postoperative changes from malignant recurrence, potentially reducing unnecessary biopsies and enhancing patient care.

1. INTRODUCTION/ REVIEW

Breast cancer remains the most common malignancy among women worldwide, and its early detection and effective management have significantly improved survival rates. However, even after successful surgical treatment, breast cancer survivors are at risk of local recurrence or new primary cancers, necessitating close imaging surveillance. Standard postoperative follow-up often relies on mammography and ultrasound, but these modalities can be limited in the postoperative breast due to architectural distortion, scar tissue, and complex changes resulting from surgery and radiation therapy. Consequently, interpreting imaging findings can be challenging, frequently leading to equivocal or suspicious lesions categorized as BI-RADS 3 or more, causing patient anxiety and prompting unnecessary biopsies ***(Li et al., 2024)***.

Magnetic resonance imaging (MRI) has emerged as a superior imaging modality for breast evaluation, particularly for postoperative surveillance. Due to its excellent soft tissue contrast, functional imaging capabilities, and ability to detect even small lesions, MRI offers valuable information that can clarify equivocal findings **(Rahmat et al., 2022**). Thus, incorporating MRI into the surveillance protocol can enable downgrading of suspicious lesions initially detected by mammography or ultrasound, thereby reducing the number of

unnecessary biopsies and alleviating patient stress ***(Xie et al., 2022)***.

The **rationale** behind this study is rooted in the **clinical challenge of over-diagnosis and over-intervention** in breast cancer survivors. Many lesions flagged as suspicious on conventional imaging ultimately prove to be benign; however, the current standards often mandate biopsy due to the fear of missing a recurrence. There is a pressing need for more **specific, reliable imaging tools** that can distinguish benign postoperative changes from true malignancy without subjecting patients to invasive procedures. MRI offers a promising solution to this dilemma by providing additional functional information beyond morphological assessment ***(Moraes et al., 2022)***.

While MRI's role in screening high-risk patients has been widely studied, its specific impact on postoperative surveillance, lesion downgrading, and avoidance of unnecessary biopsies remains underexplored ***(Hernández et al., 2021)***. By evaluating how MRI can change lesion categorization, this study aims to provide evidence that could refine follow-up imaging protocols and improve patient management after breast cancer surgery ***(Mohamed et al., 2024)***.

Therefore, we will perform this study to assess the effectiveness of MRI in grading BIRADS suspicious lesions identified on mammography and ultrasound during postoperative surveillance. We aim to determine the diagnostic performance of enhanced MRI and evaluate its ability to reduce unnecessary biopsies. Ultimately, the goal is to enhance diagnostic confidence, improve patient outcomes, and propose a more cost-effective, patient-friendly surveillance strategy for breast cancer survivors**.**

AIM/ OBJECTIVES

This study aims to evaluate the role of MRI , particularly diffusion-weighted imaging (DWI) and contrast-enhanced MRI (CEMRI) in the grading of suspicious BIRADS lesions initially detected by conventional imaging modalities such as mammography and ultrasound during the postoperative follow-up of breast cancer patients.

Research Question:

Can MRI effectively grading of suspicious BIRADS lesions identified by mammography and ultrasound in postoperative breast cancer patients, thereby reducing the need for unnecessary biopsies while maintaining high diagnostic accuracy?

Research hypothesis:

MRI can accurately grading of suspicious BIRADS lesions detected by mammography and ultrasound in postoperative breast cancer patients, significantly reducing the number of unnecessary biopsies without compromising the detection of true malignant recurrences.

3. METHODOLOGY:

- **Type of study:** A Prospective study.
- **Study Setting:** Radiology Department, Ain Shams University Hospital.
- **Study Period:** 6 to 12 months.
- **Study Population:**

Women who are categorized as BI-RADS 3 or more on prior mammography and/or ultrasound examinations in postoperative follow up.

- **Selection criteria for cases:**

Inclusion Criteria:

- Female patients who are surgically treated by breast conservative surgery after at least 6 months from the operation.
- Prior imaging study (mammography or ultrasound) performed within one month before MRI , classified as BI-RADS 3 or more .

Exclusion Criteria:

- Contraindication to mammography e.g. pregnant women.
- Any patient with absolute or relative contraindications to MRI examination e.g. :
    - Presence of pacemakers or non-removable metal objects contraindicating MRI.
    - severe claustrophobia may not be able to tolerate an MRI scan
- Any patient with contraindications to contrast media e.g.:
    - Patients having contrast allergy
    - Patients with elevated kidney functions or lowered eGFR (eGFR< 30 ml/min/1.73m^2)
- **Elimination of detection bias:**

To minimize detection bias, all imaging evaluations will be performed by experienced radiologists. Breast MRI images will be interpreted independently according to standardized

BI-RADS criteria. Radiologists will be only aware of the initial mammography and ultrasound findings.

- **Sample Size Justification:** the study will include all female patients diagnosed with breast cancer who are categorized as BI-RADS 3 or more on prior mammography and/or ultrasound examinations in postoperative follow up who attend the radiology department for follow up and meet the inclusion and exclusion criteria within six months (30 patients).

- **Study Procedures:**

Protocol approval:

Before the beginning of the study and in accordance with the local regulation followed, the protocol and all the corresponding documents will be declared for ethical and research approval by the council of Faculty of Medicine, Ain Shams University according to the WMA Declaration of Helsinki.

Then, all participants will be subjected to a detailed clinical assessment including: a detailed history, general, abdominal and local examinations.

- **History taking**:
  - Personal history, age, menopausal, medical history,
  - Detailed history of previous breast operation & duration.
  - History of received therapy (radiation, chemo or hormonal)
  - New complaint concerning ipsilateral or contralateral breast (e.g., lump, mastalgia, nipple discharge).
  - Ask about any possible contraindication to perform the study
- **Clinical examination**: of both breasts & axillary regions by experienced clinicians.
- **Investigations:** including pre-operative & therapeutic as well as the follow up imaging studies to evaluate the lesions and assign an initial BIRADS category.
- MRI is performed then follow up sono-mammography after 6 months to validate the MRI result by comparing imaging findings to those obtained during the initial assessment

prior to the MRI, analyzed any changes in BIRADS categorization based on the updated imaging and correlated these findings with previous results to assess progression, stability, or resolution of suspected lesions. Biopsy will be taken when needed.

Patient Preparation:

- Detailed explanation of the procedure.
- Obtaining an informed consent.
- Check the patient's recent renal function tests

Ultrasound :

- Using a GE LOGIQ P9 with a linear 3–12 MHz transducer.
- Patient position: Patient supine, Elevated the side being scanned with a wedge under the shoulder. Raised the ipsilateral arm over the patient's head.
- The breast and axilla was examined for any lesions according to ultrasound lexicon.
- Color Doppler is applied for any lesions to assess the vascularity.

Mammography

- Patients were guided to do mammography (GE Prestina Senographe Hologic's Selenia Dimensions system, France). Patient's breast is positioned on the mammography table to obtain the two standard mammographic views, for the medio-lateral oblique view, the breast was placed on the image receptor which lies parallel to the pectoralis muscle. The compression paddle compressed the breast from the superomedial direction.
- For the cranio-caudal view, the nipple was positioned midline and the length of the PNL(posterior nipple line) was about 1 cm from that of the MLO view, the image receptor was positioned beneath the breast and compression was applied superiorly.
- Mammography will be reviewed according to mammography lexicon.

the suspicious sonomammographic leasions in postoperative breast cancer patients:

- Post operative scar.
- Focal asymmetry.
- Radiation induced skin and parenchymal changes (increased skin thickening and breast density)
- Lesion with indistinct margin.
- Amorphous calcification.
- Fat necrosis and fibrosis (may be seen as an ill-defined and irregular, speculated mass, associated calcification can be present, which can mimic malignancy).

The technique for MRI:

All patients will undergo a standardized breast MRI examination on a 1.5 Tesla MRI scanner (Philips) using a 7-channel dedicated breast coil.

- **Patient position**
  - The patient should be centred over the bilateral breast coil symmetrically with the sternum overlying the centre bar.
  - The patient lowers herself (in a prone position) into the dedicated breast coil, the technologist's hand over the patient's back guides the patient into the coil. The other hand smooths out any inferior breast skin folds by pulling down toward the patient's feet, maintaining tension as the breast drops into the coil.
  - A visual check is performed to see that the breast is centred from top to bottom and from left to right. The steps to check each breast position include smoothing out the inframammary folds from the lateral view, checking the breast position from the top down, smoothing out the medial folds, then the same steps to check the other breast.
  - Make sure that the breasts are fixed in this position
- **The imaging protocol will include:**
  - Pre-contrast sequences: Axial T1-weighted imaging (T1WI) , axial T2-weighted imaging (T2WI) , Axial short T1 inversion recovery (STIR) with slice thickness 2mm, matrix 307-512 and field of view (FOV) 300-360 mm
  - Diffusion-weighted imaging (DWI).
  - 3D gradient-echo dynamic contrast-enhanced MRI (DCE-MRI) using gadolinium-based contrast with a dose of 0.2 m-mol/kg using an automated injector at a rate of 3–5 ml/s through a 18–20 gauge intravenous cannula inserted in an ante-cubital vein and this was followed by a bolus injection of saline (total of 20 ml at 3–5 ml/s). Dynamic study consists of one pre-contrast and 5 post contrast series.
  - Dynamic images were transferred to a workstation and post-processed. Subtracted images, MIP (maximum intensity projection) and MPR (multi-planar reconstruction) functions were obtained and studied in cine loop.
  - Post-processing that showed signal intensity changes in a given point of space in time, the region of interest (ROI) was selected, and a dynamic curve was obtained

Image Interpretation

- All imaging interpretations will be conducted by experienced radiologists
- STIR images are examined to detect edema, postoperative seroma and hematoma. T1WI was also examined to detect fat within the lesion
- Lesions will be categorized according to **BI-RADS criteria** based on morphological and kinetic features on MRI.
- BIRADS grading will be based on DWI combined with CEMRI findings.
- **Benign feature of MRI in post-operative changes not necessitating biopsy:**
    - Post-surgical scar : appears as a low in T1 with no enhancement.
    - Symmetrical skin thickening.
    - Fat containing lesion.
    - Absence of suspicious enhancement (as heterogeneous enhancement)
    - kinetic curves: type I curve (progressive or persistent enhancement pattern)
    - Facilitated diffusion.

- **Outcome Measures**:

Primary outcome:

- Comparison of BI-RADS categorization between sono-mammography, DCE-MRI, and DWI sequences.
- Evaluation the concordance between the MRI findings with follow up sono-mammography after 6 months and or biopsy (as standard reference).

Secondary outcome:

- Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for:
    - Sono-mammography alone.
    - CE-MRI and DWI imaging.
    - Analysis of interobserver agreement between radiologists using kappa statistics.
- **Ethical considerations:**

Informed consent:

Before being admitted to the clinical study, the patient must consent to participate after the nature, scope and possible consequences of the clinical study have been explained in a form understandable to her.

Confidentiality:

Only the patient initials will be recorded in the case report forms, and if the patient's name appears on any other document, it will be kept in a secured place by the investigators.

The investigator will maintain a personal patient identification list (patient initials with the corresponding patient names) to enable records to be identified.

The right to withdraw:

Participation in research is voluntary, and participants should be made aware of their right to withdraw from the study at any point without feeling an obligation to continue. The participants don't need to provide a reason for leaving the study. This should be discussed prior to consent and reiterated after the research session. In most instances, withdrawing from the study will also mean that the data collected from the participant is also deleted.

- **Data management and analysis**:

The collected data will be coded, tabulated, and statistically analyzed using IBM SPSS statistics (Statistical Package for Social Sciences) software version 22.0, IBM Corp., Chicago, USA, 2013.

Descriptive statistics will be done for quantitative data as minimum & maximum of the range as well as mean±SD (standard deviation) for quantitative normally distributed data, median and 1st& 3rd inter-quartile range for quantitative non-normally distributed data, while it will be done for qualitative data as number and percentage.

Differential analysis will be done.

4. REFERENCES

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