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Optimal protocols for quantitative assessment of breast density using magnetic resonance imaging

Rooa Sindi, Zhonghua Sun

Discipline of Medical Radiation Sciences, School of Molecular and Life Sciences, Curtin University, Perth, Western Australia, 6845, Australia

Editorial

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Corresponding Author:
Prof Zhonghua Sun
Discipline of Medical Radiation Sciences, School of Molecular and Life Sciences, Curtin University, Perth, WA, 6845, Australia
Email: z.sun@curtin.edu.au

ABSTRACT

Breast density, a measure of dense fibroglandular tissue relative to non-dense fatty tissue, has been confirmed as an independent risk factor of breast cancer. Although some research has been carried out on the quantitative assessment of breast density using breast MRI, there has been no report about the optimal MRI approach in this regard. This editorial highlights key findings reported by a recently published systematic review and meta-analysis through analysing the current methods for quantifying breast density using MRI. Cluster analysis was applied to identify the statistical similarities within and between groups based on a Nearest Neighbour/Single Linkage. The analysis found that the non-contrast-enhanced T1-weighted acquisition is one of the most common MR breast-imaging protocols. Also, the fuzzy c-means clustering is the most widespread used algorithm among all breast density segmentation/measurement methods.

Key Words
Breast density, fibroglandular-tissue, magnetic resonance imaging, non-contrast-enhanced T1-weighted, segmentation, fuzzy c-mean clustering

Implications for Practice:

1. What is known about this subject?
Magnetic resonance imaging (MRI) provides excellent details of soft tissue contrast that can be used reliably to differentiate between fibroglandular and fatty tissues through detection of slight changes in density. However, there has been little agreement on what the optimal approach to assess breast density using MRI.

2. What new information is offered in this editorial?
Use of non-contrast-enhanced T1-weighted acquisition and fuzzy c-means clustering algorithm can allow for accurate assessment of breast density. This editorial analyses the current literature by demonstrating the usefulness of using non-contrast-enhanced T1-weighted images and fuzzy c-means clustering algorithm for the quantitative assessment of breast density.

3. What are the implications for research, policy, or practice?
3D printing techniques can be used to design a patient-specific 3D printed breast phantom to develop the optimal MR breast-imaging protocols. An important implication of this is the possibility of quantifying the amount of fibroglandular-tissue, thus simulating the risk factor of breast cancer.

Introduction

Breast density, a measure of dense fibroglandular tissue relative to non-dense fatty tissue, is an independent risk factor for breast cancer.[1-3] This finding confirms the association between breast density and breast cancer as women with dense breasts their likelihood of developing breast cancer is greater than those with fatty breasts.[4,5] Clinically, the assessment of breast density is performed qualitatively using the American College of Radiology (ACR) Breast Imaging-Reporting and Data System (BI-RADS) atlas, according to which density has different classification based on the amount of fibroglandular tissue.[6] The main limitation of the BI-RADS atlas, however, is the inter- and intra-reader variability, as a result many methods are proposed in the literature regarding the quantification of breast density using MRI data.[7,8] Most of these methods are interpreted as measurements with a semi-automatic thresholding and segmentation approach, to date (and to the best of our knowledge), no consensus has been reached about the optimal approach to quantify breast density. This has been confirmed by our recent systematic review and meta-analysis on the quantitative assessment of breast density using MRI.[9] This editorial attempts to summarize some key findings from the current methods used for the quantitative assessment of breast density using MRI and highlight future research directions.

Quantitative assessment of breast density based on MRI protocols and segmentation/measurement methods

The methodological approach taken in this review is a mixed methodology based on *"metamean"* function in the R system, Version 3.4.1 (http://www.r-project.org/) and cluster analysis using the SPSS Statistics software V 25.0. A total of 38 studies were eventually included in the systematic review and meta-analysis.[1-3,5,9] A wide range of MR breast-imaging protocols were identified to differentiate between fibroglandular and adipose tissues, with the non-contrast-enhanced T1-weighted either with 2D spin echo or 3D gradient echo being one of the protocols most often used. Regarding breast density segmentation/measurement methods of the studies, 20 studies (51.28 per cent) used FCM clustering algorithm, 7 studies (17.95 per cent) FCM and N3 algorithm, 4 studies (10.26 per cent) interactive thresholding algorithm, 4 studies (10.26 per cent) in-house software, and one study (2.56 per cent) manual software, whilst two studies did not mention this information. However, because of the heterogeneity nature of the study, the included studies were categorized into different clusters based on their statistical similarities using Euclidean distance and nearest neighbour agglomeration method. Eligibility criteria required individual studies to have independent study sample size, mean, and standard deviation. As a result, only 20 studies fulfilled the inclusion criteria of clustering analysis (Figure 1).[9]

A comparison of the two forest plots of cluster 1 (consisted of 9 studies) and 2 (consisted of 8 studies) reveals that the study means (i.e., cluster 1) are heterogeneous (X^2=19.54, P=0.0066), however, the study variances are not heterogeneous (X^2=8.84, P=0.2641), as shown in Figure 2. On the other hand, the study means (i.e., cluster2) are not heterogeneous (X^2=4.77, P=0.6874), whereas the study variances are mildly heterogeneous (X^2=15.54, P=0.0206) as indicated in Figure 3. Overall, there are two likely causes for the heterogeneity within the breast density studies: the used MR breast-imaging protocol and the applied breast density segmentation/measurement method. The evidence presented thus far supports the idea that optimal approach for the assessment of breast density should be established.

Summary and conclusion

The editorial further confirmed the high level of variation within the breast density studies, a possible explanation for these results may be due to the lack of adequate MR breast-imaging protocols and ideal breast density segmentation or measurement methods. A reasonable approach to tackle this issue could be to develop a patient-specific 3D printed breast phantom with different amounts of breast composition to quantify the volume of fibroglandular-tissue. Further, the 3D printed model can be used to develop optimal MR breast-imaging protocols, therefore, simulating the risk factor of developing breast cancer. 3D printing has been increasingly used in different medical fields ranging from orthopaedic surgery to cardiovascular disease and pre-surgical assessment of tumours.[10-13] Use of 3D printing in breast tissue is limited,[14] thus, personalized 3D printed breast models could be a novel approach to overcome current limitations in utilising breast MRI for quantitative assessment of breast density.

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PEER REVIEW

Peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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Figure 1: Scatter plot of the study means versus standard deviations using 6-clusters memberships of the 21 included studies in the subgroup meta-analyses. Legend indicates the number of studies in each cluster, solid fill represents clusters with two or more studies, while open markers represent singleton study. Reprinted with permission under the open access from Sindi et al.[9]

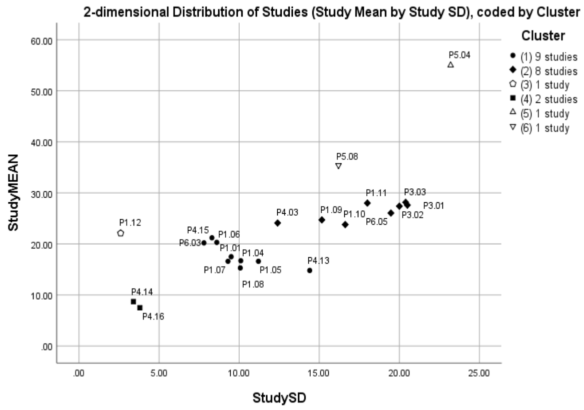

Figure 2: Forest plot of the study means, and 95% confidence limits of the studies in cluster 1 of % breast density. Reprinted with permission under the open access from Sindi et al.[9]

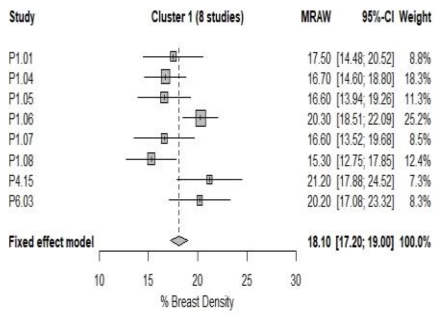

Figure 3: Forest plot of the study means, and 95% confidence limits of the studies in cluster 2 of % breast density. Reprinted with permission under the open access from Sindi et al.[9]