Influence of Fat-sat and Non-fat-sat Imaging Sequences, Spatial Resolution, and Breast Morphological Types on Density Measurements

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Purpose: Mammographic density is a strong risk predictor for breast cancer development. However, using mammography, a 2-dimensional projection modality, to measure 3-dimensional volumes encounters several issues, which includes gross overestimation of true volumetric density and variability due to patient positioning [1]. MRI, on the other hand, acquires 3-dimensional images and has been demonstrated as a promising alternative for characterizing breast density as well as the parenchymal distribution patterns. Currently the American College of Radiology (ACR) in the US recommends using fat-suppressed (fat-sat) images for direct lesion detection; while European Society of Breast Imaging (EUSOBI) recommends the use of subtraction images generated from non-fat-sat images. Though MRI-based density no longer suffers from the tissue-overlapping issue, the different imaging sequences and different acquisition parameters (leading to different spatial resolution) may affect the measured density. If the density from multiple centers using different protocols were to be combined, the impact of these factors needs to be evaluated first. Furthermore, downsampling to reduce spatial resolution is commonly used in image processing to decrease the processing time. In this work we examined the density measurements on fat-suppressed (fat-sat) and non-fat-suppressed (non-fat-sat) T1-weighted sequences, at the original and reduced spatial resolution generated by downsampling. As the density measurement is based on image segmentation, which may have different performance in breast that presents as the central pattern (dense tissue inside surrounded by fatty tissue outside) vs. the intermingled pattern (mixed dense and fatty tissues), we also examined these two groups separately.

Methods: A total of 38 normal breasts from 38 women (age 28-82, mean 48) were scanned with a 3T Phillips MRI scanner. Fat-sat and non-fat-sat images were acquired before the injection of contrast agents. The breasts were categorized according to parenchymal distribution into either central type (N=17, **Figure 1**) or mixed type (N=21, **Figure 2**). Breast density was analyzed with a software package previously developed by our group [2], which uses a fuzzy c-means segmentation algorithm with b-spline curve fitting to first segment the breast from the rest of the body, and then to segment fibroglandular tissue from breast adipose tissue. Breast density was first measured at original resolution. In-plane resolution was then downsampled by a factor of two with bicubic interpolation, and density parameters calculated again for all subgroups. Intra-rater reliability was assessed by analyzing all 38 breasts three times at two-week intervals, based on the coefficient of variation.

Results: When plotting the fat-sat measurements on the y-axis and non-fat-sat measurements on the x-axis, the Sperman's Rho correlation shows a strong correlation for all three parameters with $p<0.001$. The best-fit line passing through the origin shows a slope of 1.0019 for breast volume (BV), 1.0276 for fibroglandular tissue volume (FV), and 1.0247 for percent density (PD). Therefore, the results indicate that the measurements of BV are consistent on these two sequences, but the results of FV and PD are slightly higher on fat-sat than on non-fat-sat images. **Figure 1** and **Figure 2** show 2 case examples. The original fat-sat and non-fat-sat images, downsampled images, and the segmentation results are illustrated. Overall, the segmentation quality is excellent on all images without obvious errors. The intra-operator reproducibility was analyzed on all 38 cases. The coefficient of variation obtained from 3 separate analysis sessions is in the range of 3-4% for the whole group of 38 subjects. Within the central pattern subtype or the intermingled pattern subtype, the coefficient of variation for each measured parameter maybe higher or lower, but also in the vicinity of 3-4%. The mean difference in the fibroglandular tissue volume analyzed on fat-sat compared to non-fat-sat sequence is in the order of 5 cm^3, which is approximately 5% higher (over the mean fibroglandular tissue volume of 100 cm^3). For the percent density, the difference is also in the order of 5%. We have tried to investigate whether there is a systematic difference. The segmentation results based on fat-sat and non-fat-sat images were placed side-by-side, and scrolled through slice-by-slice for inspection, but revealed no definitive explanation for the underlying differences. The 5% difference is very small, and a subtle difference on several slices can easily add up to a 5% difference. Given the intra-operator variation within 3-4%, the 5% difference in the density parameters measured on fat-sat vs. non-fat-sat sequences is only slightly higher than the intra-operator uncertainly. The comparison of segmentation results based on the original and downsampled images revealed a small, yet significant, difference in breast volume, fibroglandular volume, and breast density. On the downsampled low spatial resolution images, the breast volume was increased by 2%, and the fibroglandular volume was decreased by 5%. Although the matched pair analysis shows that the difference is significant, yet visual inspection by scrolling through all slices cannot pick up this subtle difference. The difference may be explained by the partial volume effect.

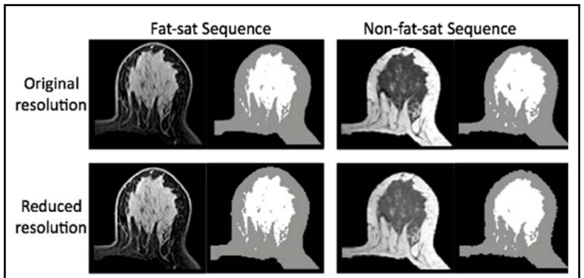

Figure 1: An example on a "Central" type breast, showing confined dense tissue inside surrounded by fatty tissue outside. The contrast between fibroglandular tissue and fatty tissue is strong on both sets of images. There are some subtle differences on the segmented dense tissues, but the quality is acceptable on both sets of images without obvious errors. The downsampled image with reduced resolution is slightly blurred. The measurement results are listed in Table 1.

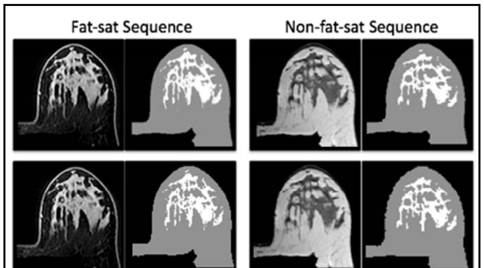

Figure 2. An example on an "Intermingled" type breast, showing mixed dense tissue and fatty tissue. The segmented quality is acceptable on both sets of images without obvious errors. Compared to the original image, the downsampled image is blurred, yet the contrast remains very strong for segmentation, and the results are similar. The measurements are listed in Table 2.

Table 1. The measurements of Figure 1 case

	BV(cc)	FV(cc)	PD(%)
	Original resolution		
Fat-sat	714	152	21.2
Non-fat-sat	725	162	22.3
	Reduced resolution		
Fat-sat	725	146	20.2
Non-fat-sat	736	155	21.1

Table 2. The measurements of Figure 2 case

	BV(cc)	FV(cc)	PD(%)
	Original resolution		
Fat-sat	914	140	15.4
Non-fat-sat	910	141	15.5
	Reduced resolution		
Fat-sat	924	134	14.6
Non-fat-sat	915	130	14.2

Discussion: We have conducted a thorough study to compare the measurement of breast volume, fibroglandular tissue volume, and percent density based on fat-sat and non-fat-sat images of the same women. The intra-rater variability was analyzed using all cases on both sequences, which was in the range of 3-4%. Similar variations were seen on central and mixed type breasts, therefore the parenchymal pattern does not affect the measurement consistency. The matched-pair comparison indicates that fibroglandular tissue volume and percent density analyzed on fat-sat and non-fat-sat sequences show 5% differences, which although significant, but only slightly higher than the intra-rater uncertainty. Analysis based on images at original and reduced spatial resolution showed a small yet significant difference, indicating the potential influence of partial volume effect on density measurements. In future multi-center studies from different datasets, the impact of pulse sequence and acquisition parameters needs to be evaluated before the data can be pooled together. Our results show that with a careful standardization, combined analysis is feasible.

References: [1] Kopans. Radiology 2008;98(17):1204-14. [2] Nie K, et al. Medical Physics 2008;35(12):5253-5262.