Evaluating automated density maps for local breast density assessment

By Dr A Oliver

In this article we summarize our recent study where we evaluated the consistency of the spatial glandular volumetric tissue distribution provided by Volpara software. To that end, we used repeated pairs of mammograms, which were acquired in a slightly changed position of the breast. We found that the Volpara Density Maps tool is reliable in estimating the local glandular tissue distribution, being robust to small variations of the acquisition angle and in the beam energy, although divergences may arise due to different breast compression conditions.

INTRODUCTION

Volumetric breast density has been shown to have a high correlation with the risk of the development of breast cancer [1, 2]. This has motivated the investigation of strategies for the stratification of women in screening programmes based on breast density [1]. Several software tools have been developed to estimate breast density from X-ray mammographic images, including systems from Volpara [2], from Hologic (Quantra) [3] and from the University of Toronto, Canada (CumulusV) among others.

Global density measures provided by the Volpara system have been validated against MRI [3] and CT images [4]. The reliability of the system has also been investigated in a favorable comparison versus a standard two-dimensional area-based reference method [5].

In contrast to global measures, local density measures aim to provide localized information of the parenchymal distribution. Although as yet there is no clear clinical application, it is expected that this kind of measurement will provide a better risk assessment and local characterisation of disease development and parenchymal changes [6, 7].

The software from Volpara which has recently been approved by the FDA was originally described by Highnam *et al.* [8]. Intuitively, Volpara starts by looking for the region of lowest intensity in the inner area of the mammogram, which is considered as a region where no dense pixels have been traversed in the acquisition. Subsequently, knowing the intensity of the rest of the mammogram and applying some physics of light acquisition, the software is able to provide the thickness of the glandular tissue at each point of the mammogram, obtaining what is known as a density map [Figure 1]. To generate the map, some key acquisition parameters (e.g. kVp, X-ray tube anode material, filter material, compressed breast thickness located in the DICOM header) need also to be extracted from the meta-data of the image [9]. The validation of the spatial distribution of the glandular tissue identified by local measures is a challenging task. Several factors, such as the breast compression or temporal changes (aging, involution, hormonal interactions) [10], can modify the appearance of the mammogram as well as the automatic density measures. In our work [11], we evaluated the repeatability of the glandular tissue measures provided by Volpara Density Maps. Specifically, we used repeated mammograms for quantitative assessment of the variation of the density maps. To our knowledge, our study was the first to analyze the results of Volpara Density Maps using mammograms of the same breast acquired in a short period of time (only a few minutes). In such a case, there is no change in the glandularity of the breast.

EVALUATION OF THE DENSITY MAPS

To evaluate the similarity of the density maps we used 99 pairs of mammograms (198 FFDMs in total), comprising 56 pairs of CC and 43 pairs of MLO projections. Each image pair corresponded to mammograms that had been repeated due to a suspicious area prompting the radiologists to slightly change the position of the breast. Since the mammograms were acquired within a very short time interval, we assume that the only changes in the mammograms are due to the acquisition itself, e.g. different anode/cathode material, different breast compression, and different position of the breast (the breast can be a bit rotated

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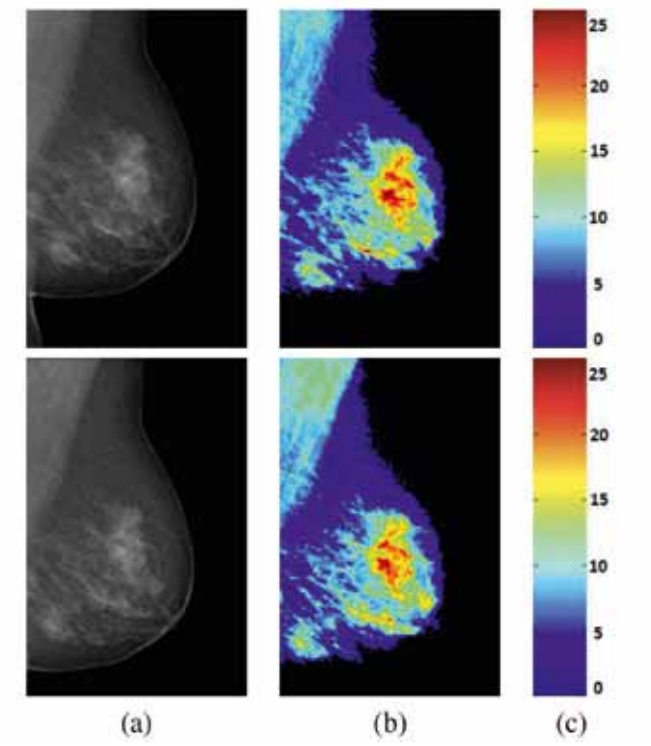
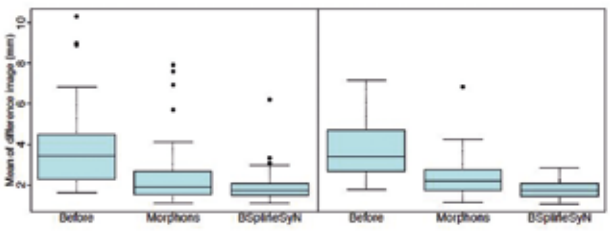


Figure 1. First column (a) shows an example of a mammogram pair studied in the work. The mammograms are very similar, although there are small changes due to differences in compression and patient's placement between the two acquisitions. The second column (b) corresponds to the respective density maps, being blue the less dense areas and red the densest parts of the breast. The color scale (c) shows the amount of glandular tissue in millimetres.

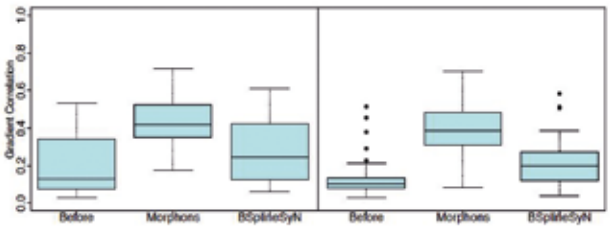
between the two explorations). Therefore, this dataset allows a quantitative evaluation of the robustness of density maps generated by the software.

A common way to assess the similarity between two images is to subtract them, so that the same structures in the same position cancel each other. In contrast, small variations in location result in a repeated presence of the structure (i.e. the positive and the negative location). Our dataset inherently corresponds to the second case, i.e. where the structures do not necessarily appear in the exact same position in both density maps. In order to minimise such differences we needed to use a deformable registration algorithm that allows local deformation of the images, making them more similar. For this, we used the morphons [12] and the B-Spline SyN [13] algorithms. Once the density maps were registered, the similarity between them was analyzed by statistics, namely the mean and the standard deviation computed on small regions extracted from the difference image on the one hand and on the other, the correlation between gradients of the two density maps. In this latter case, the gradient images were obtained convolving each image with a Sobel filter and the statistic using the normalised cross-correlation. These statistics allowed us to evaluate the structural similarity of the local tissue distribution: the more similar, the lower the measures. This allowed us to objectively measure the glandular tissue deformation: the closer the similarity, the higher the gradient correlation.

We analyzed the similarity of the density maps according to different parameters. We mainly evaluated how differences in anode/filter and breast thickness affected the results. Figure 2 shows the mean of the difference image and the gradient correlation results before and after registration according to the anode/filter used. Significant differences were found between the use or not of the registration algorithm. However a similar behavior was observed independently depending on whether the anode/filter was changed or not in the second acquisition. There was a difference in the behavior of the registration algorithms, in that B-Spline SyN outperformed the morphons algorithm with the intensity-based measure while the reverse was true with the gradient-based measure. This shows the necessity of using different deformable registration algorithms. On the other hand, Figure 3 shows the similarity of the obtained density maps depicted for different breast thickness between acquisitions. It can be seen that in this case, when no registration algorithm was used , there was a relationship between breast thickness and the mean of the difference image. The larger the differences in compression, the larger the mean difference, which indicated a bigger difference in the local glandular tissue (in the density map). Notice, however, that when using either morphons or B-Spline SyN registration, the final result was almost independent of the breast compression. A similar trend was observed in the gradient correlation, although, for this measure, the use of morphons registration again provided better results than using the B-Spline SyN combination. Additionally, we also analyzed the effect of the angle of view and end point energy. No significant differences were found in both cases, although mammograms pairs had

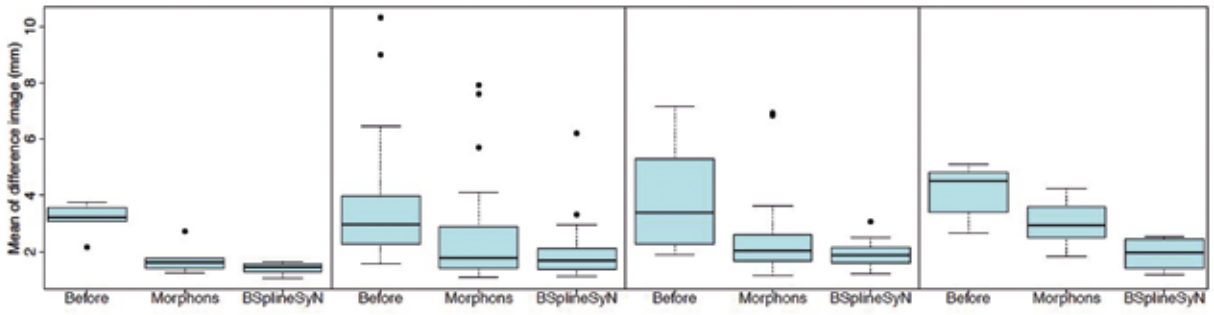


(a) Mean of Difference Image.

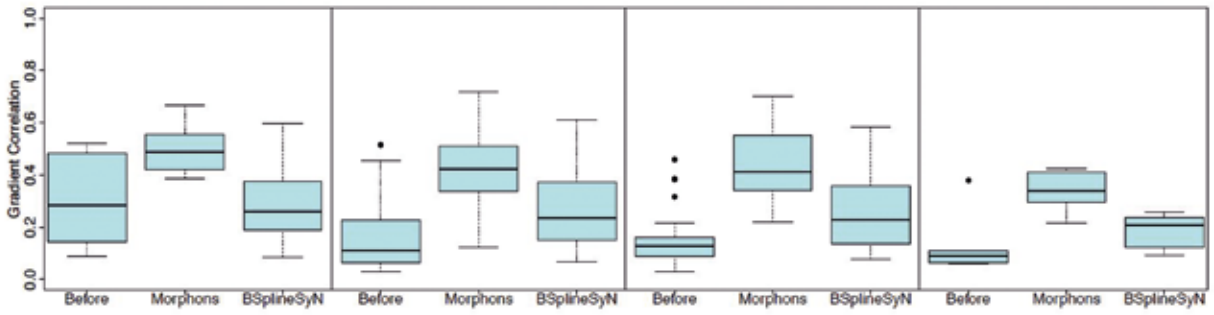


(b) Gradient Correlation.

Figure 2. (a) Mean of the difference image and (b) gradient correlation between density maps without registration and after use of the morphons and B-Spline SyN registration algorithms for different breast thicknesses between acquisitions. The left box shows the results obtained when both density maps came from images acquired with the same anode/filter composition whilst the right box shows the result when the anode or the filter changed between acquisitions.



(a) Mean of Difference Image.



(b) Gradient Correlation.

Figure 3. (a) Mean of the difference image and (b) gradient correlation between density maps. The first box (left) corresponds to the reference level (0 - 1 mm). The rest of them are: small (2 - 5 mm, centre-left), medium (6 - 10 mm, centre-right) and large (10 - 19 mm, right) difference.

differences in angle acquisition from 1 to 3 degrees and in end point energy of the spectrum between 1 and 4 keV.

DISCUSSION

In this work, the objective was to evaluate the repeatability of the local glandular tissue density map generated by the Volpara Density Maps software. An ideal dataset for such an evaluation would consist of duplicate mammograms with totally identical acquisition conditions. However, obtaining such an ideal dataset would involve (i) ensuring that the patient's positioning was exactly the same and (ii) subjecting the patients to an extra dose of radiation purely for data quality purposes.

To avoid this in practice we obtained images retrospectively from a real clinical scenario, where mammograms were repeated to allow further investigation of suspicious findings. Mammograms which were repeated due to artifacts within the image, a bad placement of the breast resulting in misalignment or even in part of the breast lying outside of the mammogram, were discarded in our study.

Therefore, in the pairs of mammograms we used, both images were in perfect conditions to be studied using the Volpara software. Direct comparison between the density maps obtained from the two acquisitions was not feasible, due to the different positioning and acquisition parameters. We were able to get round this issue by using deformable registration algorithms, which allowed us to artificially move the structures present in the density maps to similar locations, thus obtaining a statistically significant improvement in the similarity. When analyzing the robustness of the density maps according to the acquisition parameters, our results show that the output of the Volpara software was not affected by the change of the anode and filter material, the end point energy, and (small) difference of point of view between the first and second acquisition. However, breast thickness had a clear impact on the glandular tissue distribution. A posterior deformable registration between the density maps showed that discrepancies can be minimized.

REFERENCES

1. N. Boyd, L. Martin, M. Yaffe, S. Minkin, Mammographic density and breast cancer risk: current understanding and future prospects, Breast Cancer Res. 2011; 13 (6): 223.
2. J.J. Heine, P. Malhotra, Mammographic tissue, breast cancerrisk, serial image analysis, and digital mammography: Part1. Tissue and related risk factors, Academic Radiology 2002. 9 (3): 298–316.
3. A. Gubern-Mérida, M. Kallenberg, B. Platel, R. Mann, R. Martí, N. Karssemeijer, Volumetric breast density estimation from fullfield digital mammograms: a validation study, PloS one 2014; 9 (1): e85952.
4. O. Alonzo-Proulx, N. Packard, J. Boone, A. Al-Mayah, K. Brock, S. Shen, M. Yaffe, Validation of a method for measuring the volumetric breast density from digital mammograms, Physics in medicine and biology 2010; 55 (11): 3027.
5. O. Alonzo-Proulx, G. Mawdsley, J. Patrie, M. Yaffe, J. Harvey,Reliability of Automated Breast Density Measurements., Radiology 2015; 275 (2): 366–376.
6. E. Sala, R. Warren, J. McCann, S. Duffy, N. Day, R. Luben, Mammographic parenchymal patterns and mode of detection: implications for the breast screening programme, Journal of Medical Screening 1998; 5 (4): 207–212.
7. J.N. Wolfe, Risk for breast cancer development determined by mammographic parenchymal pattern, Cancer, 1976; 37 (5): 2486–2492.
8. R. Highnam, M. Brady, M. Yaffe, N. Karssemeijer, J. Harvey,Robust breast composition measurement-Volpara, in: IWDM Digital Mammography 2010, Springer, 342–349, 2010.
9. S. V. Engeland, P. Snoeren, H. Huisman, C. Boetes, N. Karssemeijer,Volumetric breast density estimation from full-field digital mammograms, Medical Imaging, IEEE Transactions 2006; 25(3): 273–282.
10. J.J. Heine, P. Malhotra, Mammographic Tissue, Breast Cancer Risk, Serial Image Analysis, and Digital Mammography: Part 2. Serial Breast Tissue Change and Related Temporal Influences, Academic Radiology, 2002; 9 (3) 317–335.
11. E. Garcıa, O. Diaz, R. Martí, Y. Diez, A. Gubern-Mérida, M. Sentís, J. Martí, A. Oliver, Local breast density assessment using reacquired mammographic images, European Journal of Radiology, 2017; 93:121–127.
[12] A. Wrangsjö, J. Pettersson, H. Knutsson, Non-rigid registration using morphons, in: Image Analysis, Springer, 501–510, 2005.
13. N. J. Tustison, B. B. Avants, Explicit B-spline regularization in diffeomorphic image registration, Front Neuroinform 2013; 7: 39.