Registration and matching of temporal mammograms for detecting abnormalities

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Abstract. Our aim is to establish accurate correspondences between temporal mammograms in order to improve the detection of tumours. We propose a method for detecting abnormalities after aligning a pair of mammograms using thin-plate spline interpolation based on corresponding points on the breast boundary. We also suggest a method for the automatic detection of landmarks within the breast tissue. We show how using suitable boundary points yields reasonable results whilst finding internal landmarks is difficult and using points on the pectoral muscle unreliable.

1 Introduction

The reliable diagnosis of abnormalities from a single mammogram is very difficult [1], and so it is increasingly the case that a pair of mammograms is compared. This is particularly important in view of the fact that second round screening results are frequently becoming available. If mammograms are available from an earlier date, radiologists will compare them to the current ones in order to detect abnormalities on the basis of significant differences. This process can be especially important for those women at high risk of developing breast cancer since baseline mammograms are often taken. Our aim is to automate the comparison of temporal mammograms.

Comparison of a mammogram with a previous one is made more difficult by differences in compression of the breast at the two time instances, and the likely differences in the imaging conditions. The effects of these differences, which from now will be described as temporal changes, consist of a non-rigid transform in the image plane due to difference in compression, and a non-rigid transformation in the intensity of the images due to differences in the imaging conditions. In addition, normal expected changes during female adult life (e.g. weight gain or loss, involution) as well as affects of HRT (hormone replacement therapy) and Tamoxifen, usually introduce more changes in the architecture of a mammogram. The only reliable method for normalising (and thus compensating for the variability in imaging conditions) digitised mammograms, is based on the h_{int} representation of interesting (non-fatty) tissue, developed by Highnam and Brady [1]. On the other hand, variability in breast compression remains a significant problem for registration of temporal mammograms. However, Highnam and Brady [1] have shown that the non-rigid part of the transformation induced by differential compression can be characterised as a divergence of the parenchymal tissue plus a change in some curvilinear structures (vessels). Tumours, and other high-density tissues can be an exception to that smooth motion under differential compression as they can move more and in a non-regular way.

In this paper we start by considering a mammogram registration technique based only upon boundary points to undo the effects of different imaging conditions and compressions. We then consider how to improve that matching by using internal points before presenting results in the form of difference images and a discussion.

2 Methods used

2.1 Registration, unwarping and difference analysis

The basic method that we use for image registration is thin-plate spline interpolation to align temporal mammograms using a set of landmarks from the breast boundary. The utilisation of thin-plate spline interpolation as a way of recovering deformations in medical images was introduced by Bookstein [2]. The calculated interpolating function $f(x, y)$ for the vertical or the horizontal direction is smooth and deforms the image in such a way that the bending energy is minimised, while the landmarks are matched. The bending energy is given by (1):

$$I_f = \iint_{R^2} \left(\left(\frac{\partial^2 f}{\partial x^2} \right)^2 + 2 \cdot \left(\frac{\partial^2 f}{\partial x \partial y} \right)^2 + \left(\frac{\partial^2 f}{\partial y^2} \right)^2 \right) dxdy \qquad (1)$$

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The basis function U, is a fundamental solution of the biharmonic equation $\Delta^2 U = 0$. This method is efficient at recovering local deformations; but special care is needed in the selection of the landmarks. Bowyer and Sallam [3], and Karssemeijer and te Brake [4] have presented work on registration of bilateral mammograms using thin-plate splines for the automatic detection of abnormalities through visual examination of the difference images after registration. Breast asymmetry is the main characteristic that can be assessed with that method. However, both techniques use points evenly spaced along the breast boundary, along the chest wall, and include points from the boundary between the breast and the pectoral muscle. In addition, the method for the automatic detection of corresponding points presented in [3] cannot be robust, since in most cases it is impossible to establish point-to-point correspondence in a bilateral pair of mammograms. We contend that special care is needed in order to decide which points should be used in mammogram registration and this issue is addressed in the discussion.

In 7 series of temporal mammograms that we have experimented with, we have observed that a good initial alignment can be achieved using only five characteristic points along the breast boundary. These points are the nipple, the two points at either end of the breast boundary near the chest wall, and the two points located centrally along the breast boundary between the nipple and the two ends. The intensity histogram of a mammogram is bimodal, and the breast boundary can be approximated by automatically selecting a threshold in the valley of the histogram. Once we've calculated the interpolating function, we can produce unwarped images by forcing every point (x, y) in a mammogram to take the intensity value of the point where the interpolating function maps the (x, y) point of the previous mammogram. Bilinear interpolation can be used to calculate intensities outside the pixel grid [3]. After image unwarping, we can produce difference images and search for regions of large intensity differences. These regions can be either new growths (e.g. a cancer), changes due to involution, or they can be due to local inaccuracy in registration. The registration can be improved if we are able to automatically detect landmarks inside the breast tissue. In the next section, we propose a method for the automatic detection of internal landmarks.

2.2 Proposed method for matching internal points

Matching a pair of mammograms of the same patient acquired at different times, is a process in which we look for image primitives (points, regions or contours) that are present in both images. In other words, we use a similarity measure to match important features across the two images. Kok-Wiles, Brady, and Highnam [5], developed an algorithm for matching regions defined in temporal or bilateral mammograms. Their algorithm uses heuristics to model the non-rigid transformation and matches iso-intensity contours corresponding to salient regions of the image. This is done after removing the curvilinear structures of the breast (ducts and vessels) that change significantly under the different compressions. The technique can be applied, with advantage, to h_{int} images. On the other hand Vujovic and Brzakovic [6], select intersections of image structures such as ducts and blood vessels as potential control points which subsequently they match between the temporal mammograms. Although their algorithm is successful in detecting such points even in predominantly radio-opaque mammograms, we have observed that the vessel and duct structure appearance is very susceptible to temporal changes, because of the difference in compression [1, Chapter 9].

Our new approach to detecting internal landmarks is based on their geometrical and textural characteristics. Like [5], we assume that even though tissue structures are deformed differently between temporal images there must be points and regions (which may be part of the reason we perceive architectural similarity) with similar geometrical and textural characteristics. For that reason we calculate 1-dimentional local maximum and minimum points and use them as potential control points. A point is classified as maximum (minimum) if the intensity of n previous pixels increases (decreases) monotonically (in the horizontal or vertical direction) and decreases (increases) for the next n pixels. In that way we significantly reduce the number of points to be matched to a very significant, in terms of information, subset of the 1-dimentional maximum and minimum points. For each of these points in the first image (x_i, y_i), we search for candidate matches in a fixed window around (x_i, y_i) in the second image and the closest point in feature space is assigned as the match of (x_i, y_i). The features consist of texture measures based on co-occurrence matrix (e.g. entropy, homogeneity and contrast). We also take into consideration the difference in the distance of a candidate pair and the mean distance of previous matches, thus imposing a smoothness constraint.

3 Results

In figure 1 (a) and (b) we see an example of an interval cancer. Figure 1 (c) is the second image unwarped in the co-ordinates of the first, while 1 (d) shows the difference image after registration. The difference image can be used for the automatic detection and segmentation of the cancer using a one-tailed t-test on the pixel intensities inside the pre-calculated breast boundary (figure 1 (e)). In that way we avoid segmenting the bright line of misregistration along the boundary. Since the segmented cancer has been transformed to the co-ordinates of the first mammogram we can estimate the region of future development of cancer in the first, “normal” mammogram by superimposing the boundary of the transformed cancer region (figure 1 (f)). Figure 2, illustrates that registration using the pectoral muscle can be severely in error, especially if landmarks from the inside of the breast have not been included in the interpolation scheme. Since the pectoral muscle is currently being used in mammogram registration ([3], [4]), we return to this issue in the discussion. Finally, in figures 3 (c) and (d), we show calculated matches (maximum points) superimposed on the images shown in figure 3 (a) and (b), which are “similar” parts of a temporal mammogram pair. The brighter points belong to the first image. We hope to improve the results further by including internal points in the registration process, but we haven't yet included them since the registration method we used so far does not allow any errors in the localisation of the landmarks.

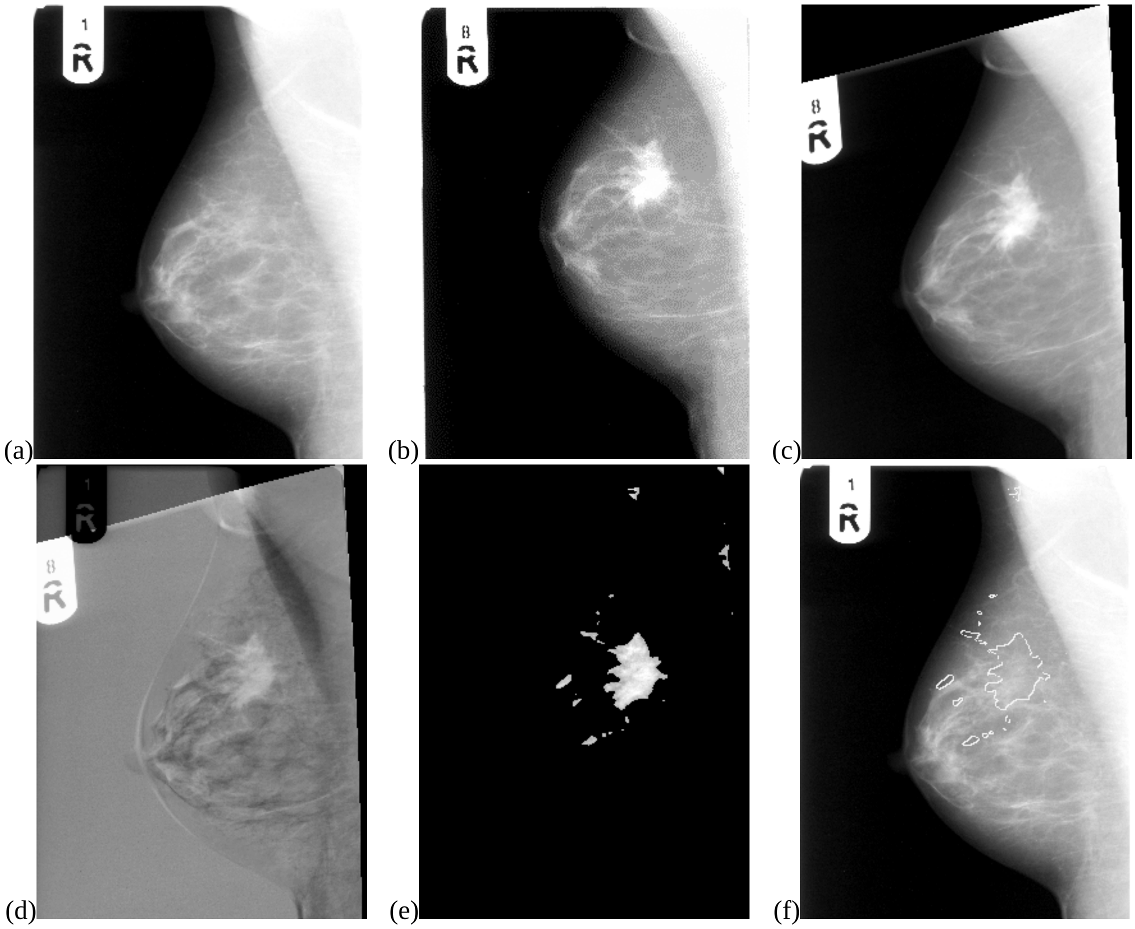

Figure 1. (a): Before cancer developed, (b): A clear cancer has developed, (c): Mammogram (b) unwarped in the co-ordinates of mammogram (a), (d): Difference image after registration, (e): Cancer segmented from (d), (f): The transformed boundary of the cancer superimposed on the “normal” mammogram (a), indicates the region of the future development of cancer.

4 Discussion and conclusions

Special care should be taken when selecting landmarks for the alignment of mammograms. Points in the line of the chest wall (first column of the image) can be used with some certainty in cranio-caudal view mammograms, but this might not be the case for medio-lateral mammograms where we usually observe different chest wall portions in the first column of the image. Additionally, since the duct patterns of the breast converge to the nipple they will not match if the nipple is not used as a landmark. This can affect the adequacy of the method for asymmetry detection in bilateral mammogram registration. Nevertheless, the position of the nipple is difficult to calculate automatically, so equally spaced points in the boundary can be used as an alternative, as in [3] and [4]. However, if such a method is to be used in clinical practice, the trade-off between automatic registration with the nipple misaligned and semi-automatic with the nipple aligned, should be decided by the radiologist. Moreover, as is illustrated in figure 2, trying to align the pectoral muscle without including landmarks from the inside of the breast (like in [4]), leads to an increase in the error of registration. In fact, the difference image 2 (f) reveals that although the pectoral muscles are aligned, the fibroadenoma present in both images is further away than in the unregistered images. We have observed from differential compression mammography [1], that the pectoral muscle seems to move independently of the breast tissue under different compression and this might be a possible explanation. For that reason, further investigation is necessary to clarify if the pectoral muscle should be taken into consideration in mammogram registration.

On the other hand, matching points inside the breast is difficult due to temporal changes and depends upon the extent to which the architecture (or topology of the surface) is preserved. This method provides many good matches, but insignificant and multiple matches are unavoidable. Thus the next step should be to locate more reliably "topographic" features of the intensity surface for calculating internal landmarks more robustly and use a registration method that takes into consideration the localisation uncertainty of internal landmarks.

In conclusion, previous work on matching temporal mammograms [5], has concentrated on defining regions inside the mammograms as a basis for matching. That work ignores the breast boundary. Here, we demonstrate the considerable redundancy that is available in matching breast images by showing that those good results can be obtained using *only* the breast boundary. Future work will combine the two sources of information in order to develop a robust matching technique. In addition, our work will be focused on combining normalisation (using the h_{int} representation) and registration of temporal mammograms. Since the imaging conditions can vary over time, even if a temporal pair is very accurately aligned, the intrinsic differences in the intensity of corresponding points remain, diminishing the value of the difference image. We therefore believe that the h_{int} representation can improve the quality of the resulting difference image.

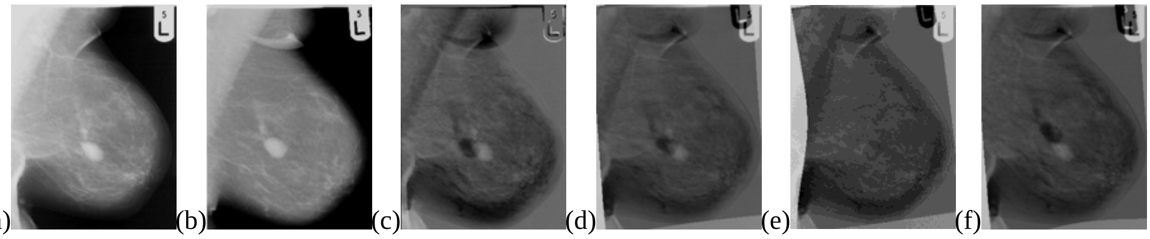

Figure 2. (a),(b): A temporal pair of mammograms with a fibroadenoma present, (c): Difference image before registration, (d): After registration using five points in the boundary the difference image indicates that we have compensated for some (but not all) of the tissue deformations, (e): By manually adding two internal landmarks, registration is improved, (f): If we use two points from the line of the pectoral muscle instead, although we align the pectoral muscle, the mass is further displaced than in the unregistered difference image 2(c).

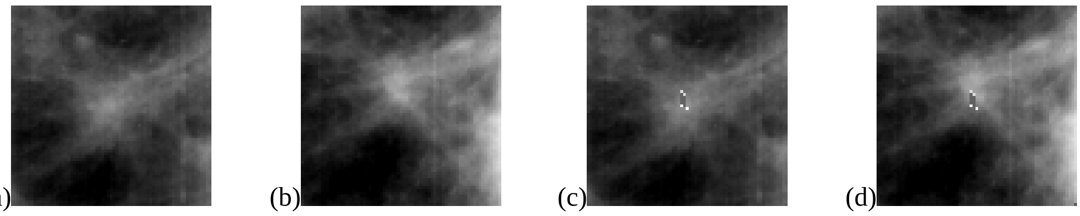

Figure 3. Matches in (c), (d) are superimposed on the original temporal images (a) and (b)

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