Joint Analysis of Multiple Mammographic Views in CAD Systems for Breast Cancer Detection

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Abstract. In screening X-ray mammography two different views are captured and analysed of both breasts. In the four X-ray images some special signs are looked for. First the individual images are analysed independently, but good result can be achieved only if joint analysis of the images is also done. This paper proposes a simple procedure for the joint analysis of the breast's two views. The procedure is based upon the experiences of radiologists: masses and calcifications should emerge on both views, so if no matching is found, the given object is a false positive hit. First a reference system is evolved to find corresponding regions on the two images. Calcification clusters obtained in individual images are matched in "2.5 D" provided by the reference system. Masses detected in individual images are further examined with texture segmentation. The proposed approach can significantly reduce the number of false positive hits both in calcification and in mass detection.¹

1 Introduction

Breast cancer is the most frequent cancer and the leading cause of mortality for women. Evidences show that the chance of survival is significantly increased with early diagnosis and treatment of the disease. X-ray mammography is the only reliable screening method that can be used in masses for early detection. [1] The nationwide screening projects result in enormous amount of mammograms to be analysed in each year. To ease and assist the work of overburdened radiologists computer aided diagnostic (CAD) systems are developed.

During X-ray screening two different views are captured of each breast: a CC (cranio-caudal) from above and a leaning lateral view, the MLO. The two most important symptoms are microcalcifications and masses. Microcalcification clusters have a higher X-ray attenuation than the normal breast tissue and appear as a group of small localized granular bright spots in the mammograms. Masses appear as areas of increased density on mammograms.

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Several algorithms searching for pathological abnormalities on a single mammogram were developed within a combined CAD project of Budapest University of Technology and Economics and of Semmelweis Medical University [2], [3]. The main feature of these algorithms is that the positive cases are found with large probability – a hit rate is about 90-95% – but the number of false positive hits per picture is too high. Similar results can be found in the literature like: [4], [5].

A method is needed to decrease the number of false positive hits, which will not or will barely decrease the number of true positive ones. This paper presents a relatively simple new way of this. The method sets off from the fact that the images of calcifications and masses have to appear on both views (MLO and CC). To be more precise they must be on positions of the two views that correspond to each other. In practice a 3-D reconstruction of the breast would be needed. But the full 3-D reconstruction is impossible, because only two views of the breast are available, and because these two views are the “2-D” projections of the differently compressed breast. Therefore instead of a full 3-D reconstruction we suggest a relatively simple procedure which we call “2.5-D” correspondence.

Due to the different characters of the two pathological abnormalities the joint analysis of the two views is done differently for calcifications and masses, although the base of both methods is to restrict the examined picture to a region corresponding to a region on the other view. As tissues with calcifications and normal breast tissues are rather similar in texture for the regions of calcification clusters only the 2.5-D matching method is used. However, for masses texture segmentation could be developed to further refine their assignment.

Boundary detection and image segmentation were necessary preliminary steps of asymmetry analysis and correspondence assay. Although there are many algorithms for detection of edges in images, here – based on its previous successful applications in the field of computer aided diagnostics [6] – Edgeflow algorithm [7] was selected. The results of Edgeflow algorithm were used to find the high intensity gradient of the pectoral muscle (one element of the reference system for the “2.5-D” matching) and at texture segmentation as well.

In Sect. 2. Edgeflow algorithm is briefly described. The building of a reference system is presented in Sect. 3., while the texture segmentation is described in Sect. 5. The use of the reference system on calcification clusters is examined in Sect. 4., while Sect. 6. describes how the reference system and the texture analysis can combine. The performance of the joint analysis is evaluated in Sect. 7., and conclusions are drawn in Sect. 8.

2 Edgeflow

Image segmentation is beset with difficulties. In fact edge detection and segmentation are ill-posed problems, since it is usually undefined what we regard as an edge or one segment. The strength of EdgeFlow is that the refinement of the segmentation can be adjusted with a so-called scale parameter (σ).

Intensity edges: The EdgeFlow algorithm is based on a differential filtering when edges are defined as local gradient maxima. The differential filter used here is the derivative of the 2D Gaussian function: $G_\sigma(x, y)$.

The filtering results in the edge energy:

$$E(s, \theta) = \left| \frac{\partial}{\partial \vec{n}} \right| = \left| \frac{\partial}{\partial \vec{n}} [I(x, y) * G_\sigma(x, y)] \right| \quad (1)$$

where $s = (x, y)$ is a pixel, $I(x, y)$ is the image value at (x, y) pixel, and $\vec{n}$ represents the unit vector in the θ direction.

Edge flow vector: The traditional edge detection approach uses a threshold. If the edge energy falls above this value for a given pixel, this pixel is considered as a point of an edge. EdgeFlow also uses thresholding but only after an energy propagation trick with which edge energies are shifted and accumulated during iterative steps. The direction of this propagation is based on probabilities. $P(s, \theta)$ gives the probability of finding an edge in the direction θ within the distance $d = 4\sigma$:

$$P(s, \theta) = \frac{Error(s, \theta)}{Error(s, \theta) + Error(s, \theta + \pi)}, \text{ where} \quad (2)$$

$$Error(s, \theta) = |I_\sigma(x, y) * DOOG_{\sigma, \theta}(x, y)| \quad (3)$$

is a kind of predictive coding error in direction θ at scale σ , and

$$DOOG_{\sigma, \theta}(x, y) = G_\sigma(x', y') - G_\sigma(x' + d, y') \quad (4)$$

$$x' = x * \cos(\theta) + y * \sin(\theta), \quad y' = -x * \sin(\theta) + y * \cos(\theta) \quad (5)$$

The edge flow vector $\vec{F}(s)$ is derived from $E(s)$ and $\Theta(s)$. Its magnitude is proportional to the edge energy, and its phase is directed towards the nearest edge on the given scale σ . (Summing up probabilities instead of finding the maximum reduces the effects of noises.)

$$\vec{F}(s) = \sum_{\theta(s) \leq \theta < \theta(s) + \pi} E(s, \theta) * \exp(j\theta) \quad (6)$$

$$\Theta(s) = \arg \max_{\theta} \left\{ \sum_{\theta(s) \leq \theta' < \theta(s) + \pi} P(s, \theta') \right\} \quad (7)$$

Edge flow propagation and boundary detection: Edge flow vectors are propagated with an iterative algorithm proposed by Ma and Manjunath [8].

1. $n = 0$, $\vec{F}_0(s) = \vec{F}(s)$
2. $\vec{F}_{n+1}(s) = 0$
3. for every s' neighbour of s if $\vec{F}_n(s) \cdot \vec{F}_n(s') > 0$ where dot denotes inner product then $\vec{F}_{n+1}(s') = \vec{F}_n(s') + \vec{F}_n(s)$

The iteration stops when no change occurs. Edge detection ends with the usual thresholding for the magnitudes of the edge flow vectors. According to [6], [7] and our experiments a fixed value can usually be found for this purpose, there is no need for any kind of analysis of the resulting image.

3 Reference System

For single view analysis three landmarks are named in publications [6]: the pectoral muscle, the nipple and the boundary of the breast. These landmarks segment the breast to its anatomical regions.

Many complex algorithms tried to establish 3-D reconstruction [8] of breast segments. With 3-D reconstruction the shape of the mass, microcalcification distributions and matching objects can be determined, which help to distinguish between malignant/benign cases and to reduce false positive cases. Because of the difficulties of 3-D reconstruction our main aim was only to build a simple “2.5-D” positioning system, which can find the approximate corresponding region to a region on the other view, thus it is able to help joint analysis of the CC and MLO views. The system works similar in concept to the procedure a radiologist applies at comparing the two pictures.

CC and MLO are two-dimensional projections of the three dimensional object. Therefore a stripe will correspond to a region on the other image. The reference system is to calculate the position of this stripe. The algorithm is founded on three simple hypotheses:

1. The position of the nipple can be estimated by laying a tangent on the breast border parallel with the pectoral muscle.
2. The pectoral muscle on a CC image is assumed to be the vertical axis.
3. The distance covered from the nipple perpendicular to the pectoral muscle on MLO approximately corresponds to the distance measured up on the horizontal axis from the nipple on CC.

The first step of the algorithm is to find the angle enclosed by the pectoral muscle and the horizontal axis on MLO views. With the angle a tangent is laid on the breast border marking the nipple. The distances of the observed region from the tangent (u and v) – are measured. The same distances are measured up on the perpendicular line to the tangent from the nipple of the other view. The two points and the angle of the tangent mark out the stripe. (See Fig. 1.)

The correctness of the reference system was tested by a statistical analysis. Cases with $400\mu/\text{pixel}$ resolution ($600*400$ pixels) from the DDSM database [9] were selected indiscriminately, where these contained only one pathological growth on each views according to the radiologists’ assessments. Therefore it could be assumed, that those two masses or calcification clusters correspond to each other on the two views. The pixel corresponding to the centroid of the growth on the MLO was determined, and the deviation of the result from the centroid of the growth on the CC was measured in pixel. The results (See Fig. 2.) show that the assumption of the hypotheses was correct though there is some variance caused by the failures of the algorithm, wrong radiologist assessment or the flaw of the hypotheses (because of breast deformation) for a few cases. To compensate the effect of variance the width of the stripe can be increased by a constant or by a number relative to the width of the stripe to counteract the deviation of the algorithm.

Fig. 1. The corresponding stripe on the CC of a selected region on the MLO

Fig. 2. Histogram of pixel errors, number of cases 1159

Finding the angle of the pectoral muscle on the MLO view: Pectoral muscle is a roughly triangular region with high intensity and is located at the upper corner of the MLO mammogram. It has a higher intensity than the surrounding tissues therefore its border appears as a sharp intensity change, as an edge. Therefore boundary detection - Edgeflow - is the first step of finding the pectoral muscle, then the elimination of weak edges with cutting at a threshold.

Secondly, a region of interest (ROI) containing the pectoral muscle is obtained according to the commendation of paper [6]. Five control points are used. P1: top-left corner pixel, P2: top-right pixel of the breast boundary, P5: lowest pixel on the left of breast boundary, P3: 2/3 between P1 and P5, P4: completes a rectangle with P1, P2 and P3 and forms the ROI. (See Fig. 3(a).)

As the whole line of the pectoral muscle is not needed, just an approximation of the angle enclosed by the pectoral muscle and the horizontal axis, the iteration processing the lines diverges from paper [6]. Like the deletion of line segments disturbing the angle finding is allowed. The pseudo code of the algorithm is:

1. $n = 0$, $BW_0 = ROI$
2. $L_n =$ longest object on BW_0
3. L_n is divided to parts with uniform length along the vertical axis
4. $L_{bad_n} =$ objects which enclose $< 40^\circ$ or $> 90^\circ$ angles with the horizontal axis
5. $L_{good_n} = L_n - L_{bad_n}$, $BW_{n+1} = BW_n - L_{bad_n}$
6. – if $BW_{n+1} == BW_n$
– then iteration stops, the pectoral muscle is the object L_{good_n}
– else $n = n + 1$ and go to Step 2.

The steps 3, 4 and 5 are used to increase the robustness of the algorithm for cases, where a mass or blood vessel deflects the edge of the pectoral muscle. (See Fig. 3.) With the deletion of segments that cannot be part of the pectoral muscle the angle is better approached.

Finding the nipple and transformation in the reference system: The nipple is marked out by a tangent parallel to the pectoral muscle laid on the breast border. With the knowledge of the nipple position and the angle of pectoral muscle

Fig. 3. (a) ROI selection (b) BW_0 , (c) L_0 , (d) $L_0 + Picture$, (e) L_{bad_0} , (f) L_{good_1} , (g) BW_1 , (h) $L_1 + Picture$

Fig. 4. (a) Original image, (b) Strip on other view

Fig. 5. Figure showing the process of matching

connection between the two views is provided by simple coordinate transformations. (See. Fig 4.)

4 Application of 2.5-D Reconstruction on Microcalcification Clusters

The probability accompanied to a calcification cluster is modified with the area ratio of the stripe corresponding to it and of other calcification clusters found on the other view. Fig. 5. represents such a matching. 5(a) shows the result of the calcification detection algorithm on a CC view. Two ROIs were found where the brightness (intensity) values of these regions are proportional to the “probability” of finding a calcification cluster. The Fig. 5(b). image shows the corresponding stripes on the MLO view, while Fig. 5(c). shows the result: the “probabilities” are changed according to the matching rations.

5 Texture Segmentation

For masses a more sophisticated joint analysis can be done because they have a distinctive texture that makes it possible to do a texture-based pairing in the stripe. Since the given mass detecting algorithms are fairly characteristic in size and shape of the identified mass, a good segmenting algorithm is needed.

The first question arising when trying to apply EdgeFlow is the selection of the proper scale. After running it for a wide variety of mammographic images and range of scales, scales 1, 2 and 3 seem to be useful. Since the EdgeFlow algorithm itself only detects edges, some further steps are necessary to create a segmentation from its output: line segments should be linked creating continuous borders and closed segments. With some basic morphological operations (removing isolated pixels, dilation, removing disjointed line segments) one can get a practically good segmentation.

However, the result is sometimes too detailed, or may also contain unduly small segments. Computing some texture features and using clustering for the segments based on them can solve these problems. Note that in this case the number of clusters is not equal to the numbers of segments created after merging the members of each cluster, since these members may form more isolated groups on the image. With about 100 isolated areas the resulting segmentation is adequate for our aims. By binary search for the number of clusters needed this number can be approximated in 2-3 steps. (The number of segments on the original segmentation varies from about 80 up to even 300. Small regions are forced to merge even if we have less than 100 segments.)

The texture features used are as follows: mean of intensity, variance of intensity, mean and variance of co-occurrence values, mean and variance of grey-level differences. (Co-occurrence matrix and grey-level differences are image features used with great success for mass detection in the project. Reviewing these features of this article, but one can find descriptions in [9].) For clustering four methods have been tested: single linkage hierarchical-, k-means, fuzzy k-means and subtractive clustering [10], [11], [12]. Reasoned by our experiments the first two ones have been chosen for their simplicity and reliability.

6 Matching of Masses

Once a good segmenting algorithm and characteristic texture features are given, the accuracy of mass detecting can be increased matching their results on the different views. If pairs can be found on both pictures of the same side, the identifying probability of that mass should be increased. And finding no pair reduces this probability.

The expression *identifying probability* is used since finding a counterpart to a mass merely says that there is something characteristic *in the breast* – because it can be seen from both views – but it might be either malignant or benign. Alike – if no counterpart is found, it says the mass supposed to be recognized on one of the images is only virtual, its appearance is the result of some overlaying

tissues. Note also that this correspondence can solely be done for “clear” breasts. For dense ones even experienced radiologists can rarely find the a mass on both images.

Pairing goes by the following steps:

1. In the beginning results of a mass detection algorithm are given – usually a binary mask covering the mass-candidate area with the probability of that hit (see Fig. 6(b)., 6(d).). (During the matching mass-candidates of one image called *source* are to be paired with mass-candidates of the other one called *target*.)
2. A mass-candidate – in this case the upper one – is chosen from the source image.
3. Based on the reference system described before, a stripe in the target image is determined. In Fig. 6(f). the segmentation can be seen, with the stripe highlighted.
4. Segments overlapped by a mass-candidate are identified, and for each segment the distance – a measure of similarity – is computed from segments overlapped by the corresponding stripe, creating a non-binary mask where nonzero elements cover the paired segments. For each segment the covering values are the reciprocal of the above detailed distance. Thus on Fig. 6(g). intensity is proportional to similarity. (Areas fairly overlapping with the mask or having radically different size or intensity are omitted.) Since one mass-candidate area may overlap more segments, these masks must be added. In fact as EdgeFlow may be run for more scales and for more clustering algorithms, one may also sum along these dimensions as well. (In our experiments 3 scales and k-means segmentation are used.) At the end this non-binary mask is thresholded. The resulting pairs can be seen on Fig. 6(h).
5. Taking the hits on the source image one by one, we examine if its pairs overlap with any of the mass candidates on the target image. If so, the similarity of this pair is the mean of those nonzero elements on the non-

Fig. 6. Steps of pairing for masses based on area and texture matching

binary mask (Fig. 6(h).) that are covered by the given mask pair on the target image.

6. This pairing is done in reverse direction as well. Mass-candidates that are not paired are dropped.

7 Performance

The calcification matching was analysed over 188 cases (376 pairs of mammographic images). 66 of these cases contained malinous calcifications. The original calcification searching algorithm solved 63 of these cases but only 1 (in 122) of the negative ones. As it was previously emphasised the number of false positive hits are enormous. With the combined matching 61 malignant cases and 15 normal cases are solved.

- 12.4% of false positives hits were dropped
- 96.8% of true positive hits were kept
- 3.2% of true positive hits were dropped

The reasons for the loss of positive markers are summarised in the conclusion.

In the case of mass detection the above detailed algorithm has been tested on 363 pairs of mammographic images – with 256 masses – from the DDSM database.

- 90% of true positive hits were kept
- 18% of false positives were dropped

There are 4 main reasons for dropping true positive hits: (i) a mass can be seen on both views but only one of them is marked as mass-candidate (3/18), (ii) the mass can be seen only on one of the images (2/18), (iii) the reference system is not accurate enough (7/18), (iv) miscellaneous errors of the pairing algorithm (2/18). The results of mass-pairing are worse than that of calcification-pairing since the number of mass-candidates per image is higher than the number of calcification-candidates per image.

8 Conclusions

The paper proposed a relatively simple way of combining the results of mass and microcalcification detection algorithms applied for individual X-ray breast images. The joint analysis follows the way applied by skilled radiologists: if a suspicious area can be found in one view, usually its corresponding pair should be detected in the other view of the same breast. The first results – based on a few hundred of cases - show that using this approach the number of false positive detections can be reduced significantly while the decrease of true positive hits is relatively small. The loss of a few true positive cases comes from three problems: (i) the variance of the corresponding distances (Fig. 2), (ii) the lack of detected

microcalcification cluster or mass in one of the corresponding views, (iii) the lack of microcalcification cluster or mass in one of the corresponding views. The variance can be decreased if the different deformation caused by breast compression is taken into consideration. The reason of the second problem is that although there are signs of tumour in both views, the primal algorithms can detect them only in one of the views, in these cases the primal algorithms should be improved. The third problem cannot be solved as in these cases the signs cannot be seen in one of the images even by a skilled radiologist. This means that in such cases other modality like ultrasound should also be used. The proposed joint analysis system is under testing: the whole 2.600 cases of the DDSM data base will be analysed in the near future.

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