DETECTION OF MICROCALCIFICATION CLUSTERS IN SCREENING MAMMOGRAPHY

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Abstract: Breast cancer is one of the most common forms of cancer among women. Currently mammography (X-ray examination of the breast) is the most efficient method for early detection of breast cancer. In screening X-ray mammography some special signs of cancer (mainly microcalcifications and masses) are looked for. In this paper methods for automatic microcalcification detection are presented. Because of the high variability of the parenchymal tissue and the size and type of the microcalcifications several methods were developed and tested independently. The basic idea is that if the individual solutions are accurate and diverse, the combined result can be better, than the result of any individual algorithm.

Introduction

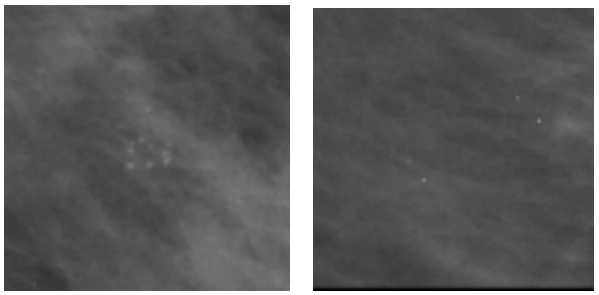
Breast cancer is the most common form and the second major cause of cancer among women. The chance of effective treatment is rather large if the signs of breast cancer are detected as early as possible. For early detection of breast cancer currently screening mammography is the most effective way [1].

In screening X-ray mammography some special signs of cancer (mainly microcalcifications and masses) are looked for. This paper deals only with microcalcification detection. Detection of calcifications is a challenging task because of the high variability of the mammographic images and the features that have to be checked. The chances of detection are increased by the fact that diagnostically important microcalcifications occur in clusters. Microcalcifications have higher X-ray attenuation than the normal breast tissue and a microcalcification cluster appears as a group (cluster) of small, localized granular bright spots in the mammograms.

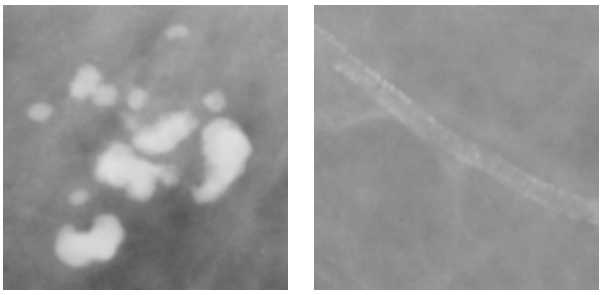
Several methods were developed and tested for the microcalcification detection subtask of the diagnosis. Because a precise (or even an approximate) mathematical description of the microcalcification clusters is not possible, no direct solution is available. Two main types of algorithms were investigated: transform-based methods mainly using wavelet transform and heuristic approaches. From both approaches promising results can be obtained, but until now heuristic algorithms has better final performance. In this paper manly heuristic algorithms are presented, but a short summary of the transformation approaches will also be given.

Microcalcification detection

A simple but characteristic property of calcificates is that they are local intensity peaks in the images (Figures 1.a, 1.c). Formally: the first derivative is (nearly) zero inside the calcification and high on the boundary, and the second derivative is less than a given bound inside calcificate positions in every direction. Unfortunately this property is required but not sufficient, beacause it can hold for other objects too (e.g. noise, calcificated blood-vessels; see Figures 1.b, 1.d). The separation of calcificates from these irrelevant objects needs additional knowledge.



a.) microcalcification b.) impulse noise



c.) macrocalcification d.) calcificated blood vessel

Figure 1: Some examples of bright spots in a mammographic image.

Further difficulties of detection of microcalcification clusters come from the great variability of the type of the parenchymal tissue and the size, form and brightness of the microcalcifications (Figure 1. a - c). To solve these problems several different algorithms were

ISSN: 1727-1983

developed and tested. The development work is based on a large mammography database, DDSM, that containes more than ten-thousand images [2]. The main feature of these algorithms is that their sensitivities are quite good - all algorithms have larger than or around 90% sensitivity values - , but at the same time the number of false positive findings are rather high – this value is in the range of 0,5-5,3/image for all algorithms. These methods use at least partly different approaches, and the results of these approaches are also different. This means that most of the true positive cases can be found by all or at least most of the algorithms, while the false positive cases are rather different from algorithm to algorithm. Based on this result a combined approach is proposed: a modular architecture that will form a weighted sum of the results of the individual microcalcification detection algorithm. The basic idea is that if the idividual solutions are *accurate* and *diverse*, the combined result can be better, than the result of any individual algorithm [3].

In the whole mammography CAD system five different approaches are used for microcalcification detection. Here the main features of these approaches are summarized.

Common ideas of the microcalcification detectors

During the mammographic session four X-ray images are taken; two from the left breast and two from the right one (one top view, called craniocaudal (CC), and one roughly side view, called mediolateral oblique (MLO)). Human experts always evaluate a set of four images in two steps: they evaluate the individual images and at the same time all images are looked at parallel to check if a suspicious area can be found in the corresponding other view. These two phases of detection are also applied in our mammographic CAD system, however this paper deals only with the first one: the detection of microcalcification clusters in individual images. The problems of the second step and a proposed solution are presented in an accompanying paper [4].

The image-level detection of this structure can be decomposed into three steps:

1) Detection of individual calcificates
2) Finding calcificate clusters
3) Verification of the clusters

Therefore the different algorithms are embedded in the same processing scheme shown in Figure 2.

Currently 3 steps are individual in the different algorithms (marked in Fig. 2), the detection pixels of bright spots (microcalcification candidates), the clustering of these spots and the cluster classification. The images and the resulting masks have the same size and format in all algorithms, therefore the algorithms can be combined in several ways.

The case-level detection of microcalcifications (that is, what human experts do) can be modelled as image-level detection followed by a joint analysis, where the two views of a breast are compared. This step effectively decreases the number of false-positive findings [4].

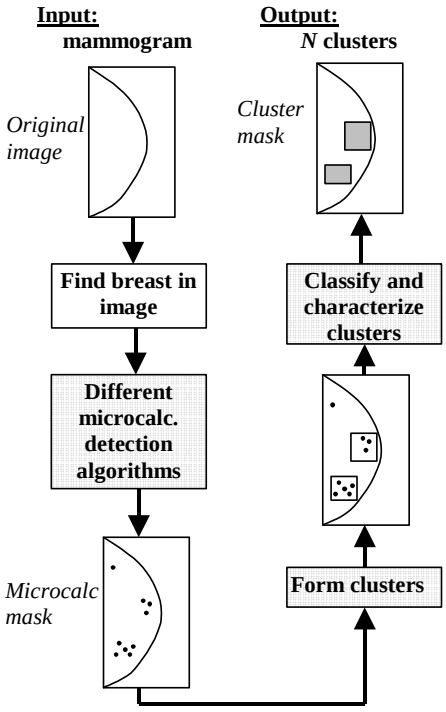


Figure 2: The main steps of microcalcification cluster detection

The rule-based microcalcification detector

At each pixel position (x, y) the calcificate detector assesses calcificate boundary in eight directions. Various constraints are applied for center intensity value, boundary intensity values and boundary distances to separate calcificates from normal tissue and irrelevant objects. If any constraint is violated then the pixel in position (x, y) is considered as a negative one.

Normal positions can be processed very fast in this way if the constraints are evaluated in a good order.

The rules:

R1) If the current pixel is located outside the breast, then it is a negative pixel.
R2) If the current pixel is located inside the pectoral muscle, then it is a negative pixel.
R3) If the intensity of the current pixel (*Intensity*) is less than the local average intensity (*AvgIntensity*) plus a *Bias*1 parameter, then the current pixel is negative.
R4) If *Intensity* is less than a *MinIntensity* parameter, then the current pixel is negative.

After the evaluation of these constraints calcificate boundary points are validated in eight directions (vertical, horizontal and both diagonal directions). The search is performed in a ring specified by a *MinRadius* and a *MaxRadius* parameter. Boundary intensities are subtracted from center intensity to get directional contrast values ($DirContrast_i$).

Let *MinContrast* be a decreasing function of *AvgIntensity*! Calcificates have to be more conspicuous in darker regions. The purpose of using a function

ISSN: 1727-1983

instead of a constant is to separate true calcificates from random noise. Then further rules can be applied:

R5) (Checking intensity peak property): If $DirContrast_i$ is less than *MinContrast* for any *i*, then the current pixel is negative.
R6) If the current pixel has a bright neighbour (the neighbour's intensity is greater than *Intensity* + *Bias2*), then the current pixel is negative.
R7) (Separation from impulse noise): If min_i $DirContrast_i$ (*Contrast*) is greater than a *MaxContrast* parameter then the current pixel and its neighbourhood is negative.
R8) (Separation from some calcificated blood-vessel components): If max_i $DirContrast_i$ minus Contrast is greater than a *MaxContrastVariance* parameter then the current pixel is negative.
R9) Otherwise the current pixel is positive.

At the end of the processing an additional rule is applied: single-pixel positive regions are removed. The output of calcificate detection is a binary mask that marks the pixels of calcificates. We achieved the best results with the following parameter setting: *Bias*1 = 4, *MinIntensity* = 8, *MinRadius* = 2, *MaxRadius* = 8, *MinContrast* = max {1280/*AvgIntensity*, 8 }, *Bias*2 = 6, *MaxContrast* = 45, *MaxContrastVariance* = 15.

Clustering. Calcium spots may predict cancer only if several of them occur close to each other. Thus a clustering step is needed to find calcificate groups. The substeps of clustering are the following:

1) Identify calcificates (continuous regions) in the calcificate mask. Since the regions are small this can be approximated with a heuristic method faster than region-filling.
2) Remove outliers (isolated calcificates that have no close neighbours).
3) Form clusters by iteratively joining the first pair of clusters that are closer than a given bound (90 pixels proved to be a good choice).

Classification. Although the calcificate detection step tries to separate true calcificates from irrelevant objects it still returns some false positive pixels. Full separation is impossible at object-level. After the clustering step a new, structure-level distinction becomes available between microcalcifications and irrelevant structures.

At first the following structure-level features are computed:

- Number of calcificate pixels (*NPixels*).
- Number of calcificates in the cluster (*NCalcs*).
- Elongation of the minimal bounding rectangle of the cluster (*Elongation*).

Then an "energy" value is assigned to each cluster containing at least 3 calcificates with the following formula:

$$Energy = \frac{NCalcs \cdot NPixels^2}{Elongation} \qquad (1)$$

The classification step returns *MaxHits* clusters, having the highest energy values. Obviously an energy lower bound can be applied to control the sensitivity of the system.

The algorithm was tested on a test subset of 189 cases randomly selected from the DDSM database. No cases were selected for the test that were used in the construction of the algorithm. The algorithm reached 85% sensitivity with 0.4 false positive marks/image.

Hierarchical microcalcification detectors

Two different hierarchical approaches have been developed for microcalcification detection. In the first method the analysis starts with a rather rough resolution image (200μm/pixel) where only some suspicious areas are selected and only the selected regions are analysed further, but here the full resolution (50μm/pixel) image areas are used.

In the second method the full resolution images are analysed from the beginning, however first the whole image is segmented into 350×350 pixel segments. For every segment it is decided whether or not it may contain a calcification cluster. If not this segment will not be processed further. On the other case, if there is a chance that a segment may have a calcification cluster then a more detailed analysis follows.

In both cases the goal of hierarchical processing is to reduce computational complexity and to accelerate the processing while achieving good result.

Hierarchical algorithm using different resolution images. Microcalcifications are rather small bright spots: it may happen that one microcalcification is only 4-5 pixels in the full resolution image. So there is a risk that in the lower resolution images some of them are lost. To avoid this danger the lower resolution image is composed from the original one using a nonlinear sampling method. (From every 4*4 window the brightest pixel is taken, so the smallest bright spots can be seen in the lower resolution image as well.)

The microcalcification detection in the pixel level uses an adaptive thresholding, because in the brighter (more dense) parenchymal tissue the calcificates cannot cause such a high gradient than in the darker (fatty) tissues. The characterization of the microcalcification-candidate pixel groups is based on the heuristics that we compare the spot to the pixel ring around it. Therefore two rings are formed, the first contains the neighbour pixels, the next is the ring one-pixel distance from the calcification candidate. (In Figure 4 the black pixels belong to the calcification candidate, the dark grey pixels belong to the neighbour ring, the grey pixels to the one-pixel distance away ring.)

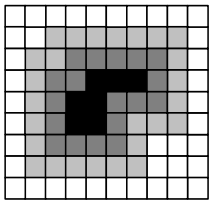


Figure 4: Pixels in microcalcificate-candidate compared to the neighboring pixel rings in the resolution-hierarchical method

ISSN: 1727-1983

The evaluation of the microcalcificate candidates is based on the following parameters:

1) The average brightness of the spot compared to the average brightness of the 2 rings around it,
2) The brightness of the border pixels of the spot compared to the closest ring pixel,
3) The size of the spot,
4) The shape of the spot (characterized by area/perimeter).

The block-scheme of the algorithm is shown in Figure 5.

After that detection step clusters are formed based on the distances between the calcificates. At the end a false-positive cluster-filtering step comes, where the following parameters are checked for every cluster:

1) The number of microcalcifications in the cluster,
2) The size of microcalcifications in the cluster,
3) The contrast of microcalcifications (compared to the background) in the cluster.

Using these 3 parameters a probability-like number is given to each cluster, any cluster is kept only above a limit, and maximum 3 (most probable) clusters are kept.

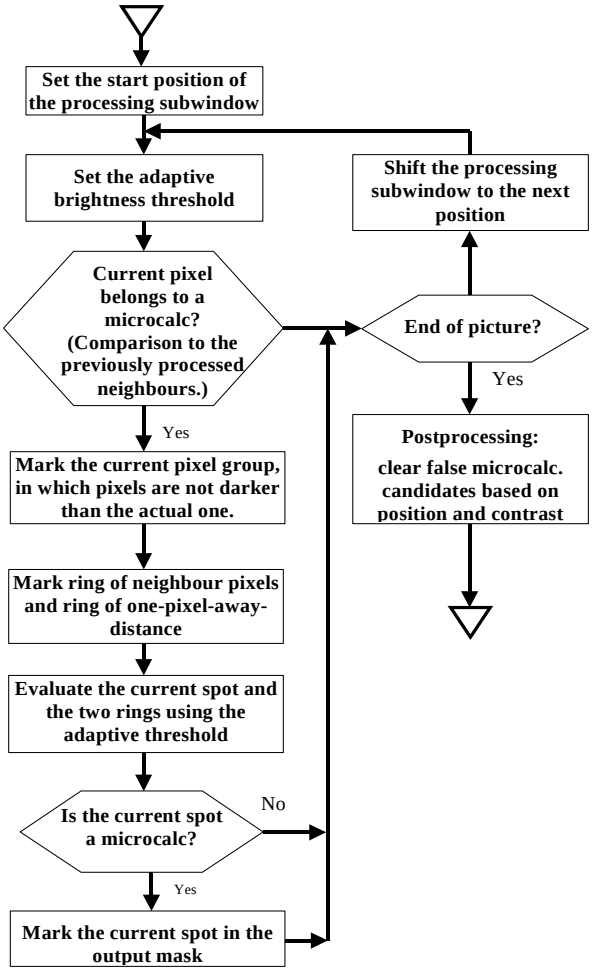


Figure 5: Detection of individual microcalcification-candidates in the resolution-hierarchical method

The same test set was used as in the previous algorithm. In this case 87% sensitivity with 2.3 false positive marks/image were achieved.

Hierachical algorithm based on image segments. In this approach not the resolution but the area analysed using the different elementary algorithms are reduced. The whole full resolution (50μm/pixel) image is segmented into 350×350 pixel segments where the neighbouring segments are overlapping by 50 pixels. The reason of this segmentation is that in this way local nonlinear intensity adjustments can be applied independently for the different segments. With segmentation a further advantage can be achieved, as using smaller image areas both the required memory and the computing time can be reduced. The first phase of the algorithm uses different classical image processing steps adjusted to the special features of the breast images: intensity gradient calculation for edge detection and morphological processing for cleaning the image.

The second phase of the algorithm is applied only if the result of the first phase indicates that there may be microcalcifications in the selected segment. The steps of the second phase are: reducing the false positive findings by removing black spots, by using a clustering filter and by detecting blood vessels.

Edge detection extracts edges around both high and low intensity spots. To reduce false positive marks after the morphological processing step, such finding, where the intensity is less then in its neighbourhood should be removed.

For microcalcification detection one of the most difficult task is to distinguish real microcalcifications from calcificated blood vessels. A special algorithm is used to detect these blood vessels. Although this does not solve this task in all cases, the result of this algorithm can help to reduce false positive detections. Finally only those marks are left that can form clusters: at least three calcificate candidates should be within a given distance. In Figure 6 a series of images show the intermediate results of the different steps.

Again the algorithm was tested using the same test set. With this algorithm 93% sensitivity could be obtained and 2.6 false positive marks/image.

Experiences gained from these algorithms. From the results of the three heuristic algorithms it can be seen that the price of higher sensitivity is that there will be more false positive findings. It is a trade-off question to find the best parameters of the algorithm. In general it can be said that the sensitivity value is rather good, especially for the third algorithm. At the same time the false positive marks should be reduced.

One way of this reduction maybe to find better parameters of the algorithm, however this is a rather hard task and it needs extensive testing with a large database containing rather different cases.

A better way may be if in addition to the individual image processing the two views of a breast is analysed jointly. The reason behind this idea is that if a suspicious area is found in one view, it should be detected in the corresponding view of the same breast. A correct joint analysis could be done only if the 3D reconstruction of the breast were possible. Unfortunately using the CC and MLO views exact 3D reconstruction is not possible. Instead an approximate reconstruction is applied – it is called 2.5D

ISSN: 1727-1983

reconstruction. The whole approach and the results are presented in [4].

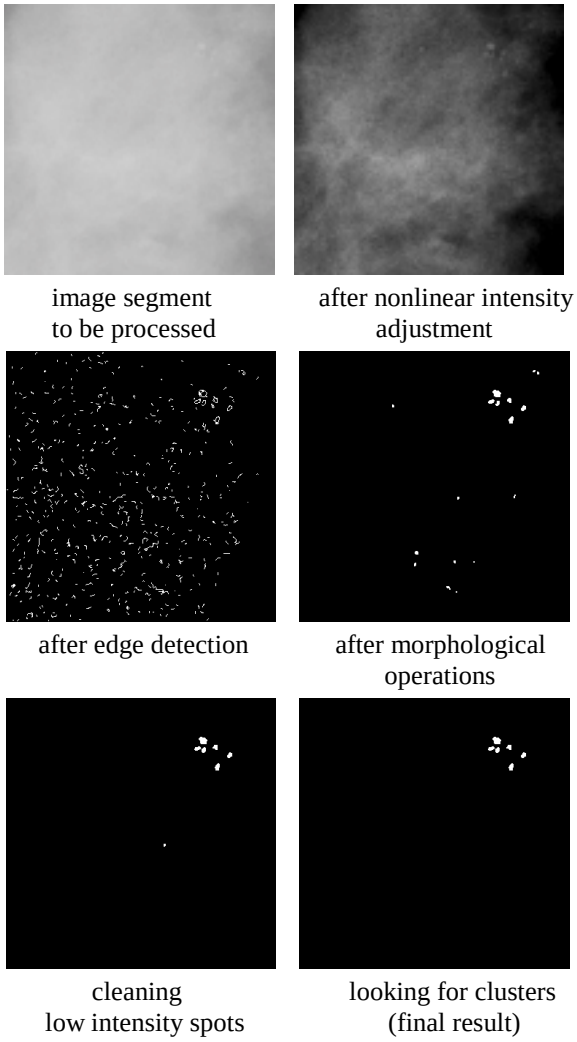


Figure 6: Results of the different steps of the microcalcification detection algorithm based on image segments.

Microcalcification detection using wavelet transform

In addition of the mentioned approaches two wavelet based algorithms were also used. These algorithms are applied also for 350×350 - pixel segments. Here segmentation is used to reduce computational complexity. The first method - which is based on [5] - applies continuous wavelet transform, while the other is based on wavelet transform modulus maxima (WTMM) [6]. This latter applies Gaussian derivative wavelets and matched filters. These algorithms have been implemented and tested on a small set of cases from DDSM database. Using the first method for 56 images of the DDSM database (from volume C06) a sensitivity of 80,4% is obtained, while the false positive marks/image is rather high: 5.37. As an illustration Figure 7 shows a result of the algorithm.

The second method was tested only in a few images, so although the results are encouraging currently general conclusions cannot be drawn. According to the present state of the wavelet-based method we can conclude only that these approaches can serve as preprocessing steps. However, using them as standalone algorithms both the resulted sensitivity and the false positive marks/images values are inferior to the results of the previously mentioned heuristic approaches.

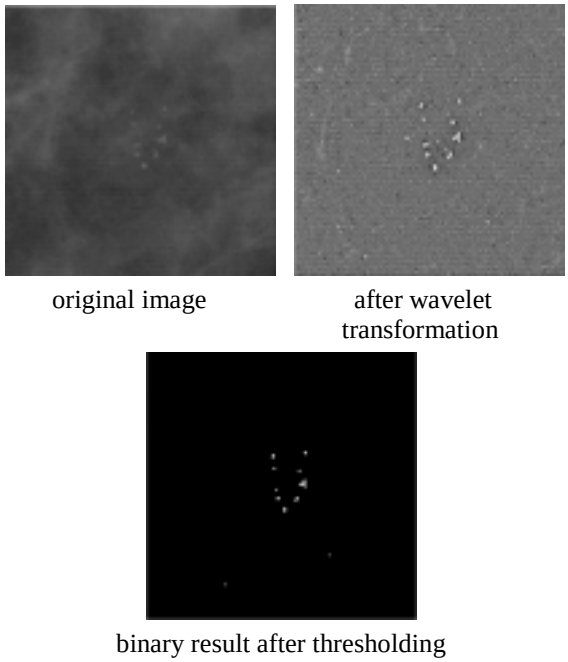


Figure 7: A results of the wavelet-based algorithm

Conclusion

Microcalcification detection in mammographic images is a hard and complex task, but it is very important from the final diagnosis point of view. There is no perfect solution for that problem; all the methods have advantages and disadvantages as well. Therefore the final goal is to use the principle: combination of diverse but as precise as possible methods give better result than the individual ones.

For that purpose several methods were developed and tested, there were two main approaches: heuristic methods and transform-based methods. (Wavelet transform was used in the second category.) Every group contained 2-3 individual algorithms developed and tested. Looking at the sensitivity the heuristic methods reached the level of the human experts (about 90%) but produced too many false positive marks (3-5 false marks/image). The transform-based (wavelet) algorithms (in its present form) performed worse in sensitivity (about 80%) with the highest false positive detections.

From the point of view of calcification detection three main categories of mammographic images can be distinguished: in the first category of images clustered calcifications can be detected by all approaches. These are the easy-to-find cases. In the second category none of the developed algorithms can find microcalcification clusters. This means that if such a case is analysed the result is false negative. In the third category at least one algorithm detects calcification clusters, so some combi-

ISSN: 1727-1983

nation of the results of the individual algorithms should be used to form a final result.

The integration of the results has started and it is under way. Until now the simple majority vote of the microcalcification cluster results was examined on a limited number of cases (40 images were used). It turned out, that the loss of true positive detection was less than 4%., while the combination helped to reduce the false positive findings by around 30%. These results are promising but need confirmation on a larger database. Other current direction of the research is to use more sophisticated combination methods, where the advantages of the individual algorithms are more emphasized than in the simple majority vote.

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ISSN: 1727-1983