THERMOGRAM CLASSIFICATION IN BREAST CANCER DETECTION

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Abstract: One of the co-effects of breast cancer growth in its early stage is neovascularisation. There are a few techniques to detect these changes and one of them is to watch an image of surface thermal field using infrared thermography. Thermography is non-invasive and is not limited by high density of breasts tissue of young women.

Our research effort should help utilize these advantages and to define thermal infrared imaging as a diagnostic tool in early breast cancer detection, which can be used as a complementary modality to traditional X-ray mammography and ultrasonography.

There are several thermopatological features which could be used to thermogram classification by a physician. This way of classification is very subjective and it leads to high false positive rate of the method. Many publications concerning with an effort to make the classification objective employing digital thermogram processing and classification appeared in last several years. Our approach consists in pattern classifier design.

Introduction

The breast cancer is the second most often cancerous cause of death among women and the second most frequent type of cancer at all. Nevertheless it is proved that early stages of breast cancer are well treatable. That is why the early detection is so important. Thermography is non-invasive and has proved ability to detect physiological changes caused by early cancer growth [2][3].

The cancer consists of metabolically active tissue which doesn't serve its purpose. It is more or less fast growing and needs a lot of blood and oxygen supply. To achieve this goal, it produces chemical substances, which causes angiogenesis - new blood vessels grow in the area near the tumour [1]. And these blood vessels can be thermographically seen if they are near enough to the surface. Some researchers believe that these veins and arteries are one of the first sign of the cancer - they can be apparent some 5 to 10 years before the cancer itself. Even more important is that dangerous, aggressive, fast-growing cancer needs more blood supply and this increases the prognostic value of thermography.

Unfortunately the situation is not so simple - there is not normal thermal pattern. Each man and woman has its own specific thermal pattern which is as characteristic as fingerprints. Normally, if no abnormalities are present, is this pattern laterally symmetrical - it means the pattern of the left and the right breast should be nearly symmetrical. The analysis of thermograms is therefore the analysis of symmetry between the image of the right and the left breast. The problem is the word nearly - nobody is perfectly symmetrical and only certain asymmetry is pathological.

There are many actual publications concerning thermography in breast cancer diagnostics. Most of them follow one of three trends – IR image enhancement or segmentation ([5][6]), definition of thermo-pathological features and subsequent design of decision support systems ([8][9][10]) or numerical modeling of generation of surface temperature field [7].

Our approach consists in complete design of thermal pattern classifier with respect to breast cancer occurrence. Several ways of different approach to semi-automatic (a)symmetry evaluation based on the pattern classification methods are presented in this work.

Materials and Methods

Our main task is to classify patients to at least two classes - positive (have breast cancer) and negative (don't have) according to their thermograms. This decision can hardly be made directly from the image - we separate it into five steps: sensing, image pre-processing, features extraction, features selection, classification. Sensing is represented by thermogram acquisition and is described in subsection *Data* at the end of this section. The other four steps are explained in following subsections.

Image Pre-processing: First step of thermogram analysis is selection of regions of interest (ROI). It is covering whole area of the left and right breast in our case. Selection is performed manually by defining suitable number of edge points and its subsequent interpolation by spline curve. We have tried to employ several semi-automated methods of ROI selection based on edge detectors but none of them proved to be robust enough to work in cases where the anatomical surface incurvation doesn't provide visible edges in IR image.

A hot spots and veins should be detected in the image, so it seems to be a good idea to enhance significant thermal gradients (edges) in the image. This

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operation may be practically realized by derivation. We are not interested in the direction of the edge, so an isotropic version of derivation was devised. We have tested set of directional convolution masks, Laplace operator and sharpening mask performing addition of Laplace filter and original image. Other pre-processing methods such as averaging (to suppress details and noise) or edge extraction didn't prove to be valuable.

Second pre-analysing adjustment we use for some of the methods consists in re-sampling of region of interest to polar coordinates. The reason is that most of used analysis methods evaluate symmetry of ROIs and some of them need ROIs to be registered and with the same number pixels in compared areas. Re-sampling converts symmetry evaluation problem to similarity evaluation.

Features extraction: The principal aim of our research is to define thermo-pathological features and find the suitable image analysing methods to extract them. As mentioned above, the differences in vascular pattern and in hot (cold) spots appearance between left and right breast are the most significant thermo-pathological features. It represents symmetry evaluation of pairs of pictures from our point of view.

There are two possible techniques how to get appropriate features - non-topological (statistical) and topology-based methods. Commonly used subjective analysis performed by experienced physician is topology-based1, but it is not easy to be automated. We do not use any pure topological method, but most of used methods combine both approaches.

Statistical features: Since the cancer creates a new vascular pattern, the overall skin temperature of the affected breast may be higher. The metabolic activity of the cancer tissue is higher, what also increases the overall temperature. The simplest criterion is therefore to compute average temperatures of ROIs and use the absolute value of their difference as a feature. We can get similar results by using median instead of average. The maximum was tested, too. We also compute standard deviation (expected to be higher for breast with vascular pattern) and so called Index 90, which is the "90%th" member of ordered set (similarly the median may be called *Index 50*).

Histogram: Histogram is commonly used technique in image analysis. Two normalized histograms are constructed, one for each breast's ROI. Such histograms should normally be the same for both sides and their difference histogram should have zero values. We extract four features from difference histogram – absolute value of its maximum, number of columns exceeding threshold t ($t=0.01$ in our case), energy and number of zero crosses. We also compute cross correlation coefficient of the both histograms and we use difference of areas under its positive and negative part as a feature.

Co-occurrence matrix: Co-occurrence matrix in its basic concept is method used for texture classification. We can think of thermal pattern as sort of texture and use this method to obtain corresponding features.

The concept of this method is not commonly known so we will briefly explain it. Let's have a real matrix (or any two-dimensional shape) M. The co-occurrence matrix is matrix X (with elements $x_{k,l}$), where each row and each column represent a bin number. Let's assume the bins on both axis are the same B_i, $\forall i \in \overline{1,M}$. Let's take a pair of pixels (let's name the pixels a and b and their values m_a and m_b) from the M with some (usually spatial) relationship (Fig. 1). The co-occurrence matrix X includes in individual elements the counts of such pairs, where a belongs to the corresponding "row" bin and b to the "column" one. Expressed mathematically, we may write

$$x_{k,l} = count\{(a,b) \mid m_a \in B_k \cap m_b \in B_l\} \qquad (1)$$

In deed, we can calculate any number of these matrixes - there are many different relationships between the pair of pixels a and b possible. In the special case where a and b are identical, we obtain a diagonal matrix and the elements on main diagonal form the histogram of the M. The b-pixel is shifted 5px to the right under angle of 45° in our case.

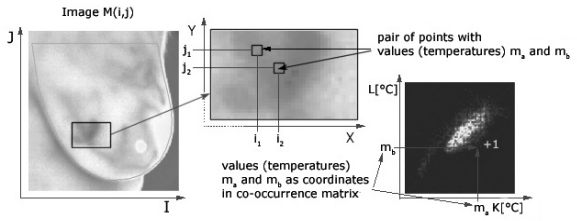

Figure 1: Concept of co-occurrence matrix

The cross co-occurrence matrix is defined the same way, but we have two overlapping matrixes (or shapes) M and N and pixel b is taken from the second matrix N instead from the same matrix (Fig. 2). Only the special case with zero offset was used, so we may say pixels a and b are on the corresponding place in both shapes. If the shapes of M and N are not the same, only overlapping region must be used, or they must be registered (we solved this by re-sampling to polar coordinates). The matrix is normalized by the number of pixels of overlapping region before feature extraction, so the sum of whole matrix is equal to one.

There are many possibilities how to extract features from co-occurrence matrix. Let's briefly resume the equations of used features. They are the same for both modification of co-occurrence matrix, their interpretation naturally differs.

Homogeneity of co-occurrence matrix is defined by equation:

$$G = \sum_k \sum_l \frac{x_{k,l}}{1+|k-l|} \qquad (2)$$

The interpretation of this feature is that it is the sum of co-occurrence matrix values weighted by the inverse

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of the distance from the axis - point more distant from the axis has less weight. Since negative thermograms have non-zero elements closer to diagonal, they would have higher *homogeneity*.

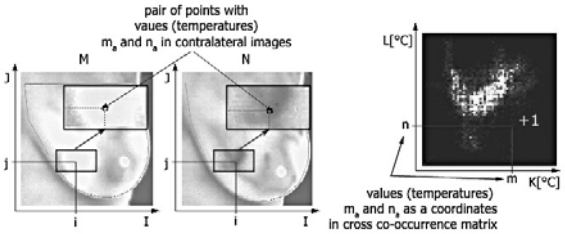

Figure 2: Concept of cross co-occurrence matrix

The co-occurrence matrix *energy* is defined similarly to histogram energy as the sum of squares of normalized co-occurrence matrix values

$$E = \sum_{k}\sum_{n} x_{k,l}^{\ 2} \tag{3}$$

The co-occurrence matrix values should be for negative patients around the diagonal axis, so axis moments of different orders should be good features. The axis moment of the p^{th} order is defined as *axis moments*:

$$m_p = \sum_{k}\sum_{l} (k-l)^p x_{k,l} \tag{4}$$

The m_0 is always one; the absolute values of moments from m_1 to m_4 are used as features.

Other useful features are *contrasts* (there are two possible definitions)

$$C = \sum_{k}\sum_{l} |k-l| x_{k,l} \tag{5}$$

$$C' = \sum_{l}\sum_{k>l} |k-l| \left| x_{k,l} - x_{l,k} \right| \tag{6}$$

and *symmetry*:

$$S = 1 - \sum_{l}\sum_{k>l} \left| x_{k,l} - x_{l,k} \right| \tag{7}$$

It's clear that that perfectly symmetrical matrix has the *symmetry* of one, all non-symmetric matrixes smaller. Negative patients would have, therefore, higher *symmetry* then positive ones.

Mutual information and Joint entropy: There is a statistical parameter, which describes statistical (in)dependence of two (or more) sets of data, it is called *Mutual Information* (*MI*). It can be used for evaluation of the similarity of the left and the right breast pattern. It is small for completely independent (or non-similar) sets of data - positive patients would have small values of *MI*. Similarly the joint entropy *H* represents the relationship between two sets of data - the negative value of joint entropy is taken as feature, since entropy is always negative. The mutual information can be calculated by the equation.

$$MI = HL + HR - H \tag{8}$$

where *HL*, *HR* and *H* are entropies of left and right side and the joint entropy defined

$$H_L = -\sum_{\forall k} p_L(k) \log_2 p_L(k) \tag{9}$$

$$H_R = -\sum_{\forall l} p_R(l) \log_2 p_R(l) \tag{10}$$

$$H = -\sum_{\forall k}\sum_{\forall l} p_{LR}(k,l) \log_2 p_{LR}(k,l) \tag{11}$$

where:

$p_R(l)$ . . . . is the probability density that the random value *R* equals *l*,

$p_L(k)$ . . . . is the probability density that the random value *L* equals *k*, and

$p_{LR}(k,l)$ . .is the probability density that the random value *R* equals *k* and value *R* equals *l*.

These probabilities may be estimated from cross co-occurrence matrix according following equations

$$p_{LR}(k,l) = \frac{x_{k,l}}{\sum_{\forall k,l} x(k,l)} \tag{12}$$

$$p_L(k) = \sum_{\forall l} p_{LR}(k,l) \tag{13}$$

$$p_R(l) = \sum_{\forall k} p_{LR}(k,l) \tag{14}$$

Moments Analysis: Set of raw moments of ROIs transformed to polar coordinates is computed. The raw moments are defined by equation:

$$m_{pq} = \int_{-\infty}^{\infty}\int_{-\infty}^{\infty} x^p y^q f(x,y) dx dy \quad p,q = 1,2,3... \tag{15}$$

Moment m_{00} is basically only an integral over the whole area. Negative patients should have similar left and right breast and their difference should be small and with varying sign. The moments m_{01} and m_{10} are proportional to coordinates of centre of gravity (COG). The distance of COG from the geometrical centre of breast is another feature, which seems to be very promising for classification. Patients with breast cancer

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have small distance of COG from the centre. This is probably caused by the fact that negative patients have usually some part of breast a little bit warmer or colder and this causes the move of COG, while the positive patients with strong vascular pattern have often the difference of temperature oscillating around zero - the COG remains approximately at the centre.

Fourier analysis: Fourier spectrum analysis also seems to be good tool for feature extraction, because the warm lines and spots should be visible as higher spatial frequencies in the spectrum. It was computed in polar coordinates too. The mathematical background is commonly known so we can skip it. For extraction of two features we use the difference of absolute values (modulus) of the ROIs spectrums. The features are a value of the *difference maximum* and *distance* of this maximum from the centre.

Feature selection: We have about 40 features now, but not all of them have to necessarily be related to searched thermo-pathology. It is need to find suitable criterion for evaluation of usability of each particular feature.

Each diagnostic method classifies patients into two groups - positive and negative. In reality, they may be again either positive or negative. This fact we usually describe with several parameters - *sensitivity* is the ratio of positively detected patients and all positive patients; *specificity* is similarly ratio of negatively detected patients and all patients. *Negative Prognostic Value* (NPV) is the answer to question "If the method classifies the patient as negative, what is the chance, he/she is really negative?".

All these values are dependent on the decision level (threshold) - which values are supposed to be negative and which positive. Setting the threshold is always finding the compromise between sensitivity and specificity. There are many possible approaches. The simplest is the intersection between sensitivity and specificity plots - this situation is shown in the figure 3.

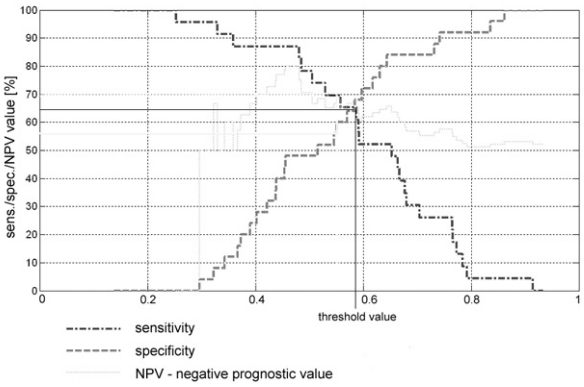

Figure 3: Plot of sensitivity/specificity/NPV values to threshold value

Sensitivity (specificity) value of this intersection can be used as an indication of the efficiency of a classifier respectively of the suitability of the particular feature. We use value 60% as a criterion for acceptance of feature for next processing. This criterion passed 9 of all features computed (see Results Table 2)

Classification: We have 9 features extracted and selected in the previous sections. The next step is classifying images into positive, negative classes according these features. Each of the features individually can do this, sensitivity, specificity plots provide sufficient information for setting the threshold(s) to separate images into the classes. There is, however, one more possibility - combine the best features into one to achieve better results then using each feature individually.

To combine many different features into one, we must first normalize them to have all in comparable range of values. We do this by "normalizing" all features to the range from zero to one.

We proposed four methods of features combination. Two of them are based on relative rank of each patient among other patients; next two were inspired by neural networks [4].

Average Relative Rank: Each patient is in each feature at certain "rank" among other patients. We can express the rank relatively, so the first patient (with the lowest feature value) has "relative rank" *1/N*, the second *2/N* and the last (with highest feature value) *N/N=1*. We obtain for each patient *L* such ranks (for each feature) and the resulting "average relative rank" is obtained as the mean value of them.

The advantages of this method are that we don't need feature normalization and we didn't need the correct classification (except for the evaluation of statistical parameters). The method is, however, quite difficult to use in praxis - if we want to classify new patient, we should add her features to the set of patients (with known diagnoses and with threshold already set) and see, where she falls among others.

Weighted Relative Rank: This method is only a minor modification of the previous one. We include the relative ranks of individual features with weight according their results. The value of sensitivity and specificity for their intersection is used as the weight. The advantages and disadvantages of this method remain unchanged.

Optimal Weights: This classification method is inspired by neural networks. In fact, you can look at it as single neuron with sigmoidal transfer function. The input weights are set using optimization for current set of patients the knowledge of real diagnosis is necessary to optimize weights, but once finished, we can classify any new patients simply by using the same weights.

There are many methods for learning (e.g. finding the values the weights) the neural network (the most common is back propagation), however for such easy task as learning one neuron it is possible to use standard MATLAB® function *fminsearch*, which uses Nelder-Mead simplex (direct search) method [4][10].

Optimal Weight Reduced: This method is a modification of the previous one. The key idea is that if the methods have different weights, we can use just the methods with high influences (high weights) and reduce

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the number of features. This is beneficial because we must not even calculate them and this will speed up the detection.

Data: Properly calibrated digital infrared camera FLIR PM575 is used for thermogram acquisition. Each examination consists of three images. Patient sits on a chair and after twenty minutes long equilibration within air-conditioned room one frontal and two slightly lateral pictures are taken. The analysis is performed in the frontal picture.

The thermogram set consists of 200 patients; 50 with a malignant finding and 150 with a benign one or without any finding. All the patients underwent the X-ray mammography examination and all malignant findings were confirmed by histological analysis of a bioptic sample.

Results and Discussion

Presented methods of feature extraction and thermogram classification were implemented in easy-to-use MATLAB® environment and tested on our thermogram set. We used 100 thermograms as a training set for classifier design and the other 100 samples as a control set. Results of each step are presented in tables 1 and 2.

Table 1: Results of feature selection

Method	Intersection	Spec90	Senz90
Cross co–occurrence matrix - Homogeneity	67%	32%	0%
Moment analysis - Larger of moments m00 for the left and the right side	65%	12%	26%
Difference of averages	64%	16%	22%
Cross co–occurrence matrix - Symmetry	61%	44%	22%
Cross co–occurrence matrix - Contrast 1	60%	32%	13%
Fourier analysis - The distance of maximum of modulus difference	60%	32%	13%
Cross co–occurrence matrix - 2nd order axis moment	60%	32%	13%
Difference of index 90	60%	24%	26%
Laplace - Difference of averages	60%	16%	22%

The best feature found is homogeneity of cross co-occurrence matrix with intersection of specificity and sensitivity at 67%. Combining features together further enhanced the results obtained by individual features - the best of them, optimal weights, reached intersection of specificity and sensitivity 79%, and has 53% specificity for 90% sensitivity.

The thermogram classification results are comparable with commonly used diagnostic techniques (Tab. 3). X-Ray mammography, on which is based screening programme in Czech Republic, have a bit better results, but the results are strongly dependent on the radiologist and further, it employs dangerous radiation, which may caused new cancer genesis.

Ultrasonography has low spatial resolution, which may be problem in early stage cancer detection. Examination on MRI system is very expansive. For thermography speaks, except the comparable results, its non-invasiveness, low expenses and applicability to young women where the mammography fails because of high density of breast tissue.

Table 2: Results of classification

Method	Intersection	Spec*90*	Senz*90*
Optimal weights	79%	53%	79%
Optimal weights reduced (five features)	64%	28%	30%
Weighted relative rank	60%	36%	35%
Average relative rank	60%	36%	35%

On the other hand, we are aware that reliability of presented results is strongly limited by size of the thermogram set. We cooperate in new thermogram acquisition with mammography clinic of Faculty Hospital of Brno and Masaryk Memorial Cancer Institute.

Table 3: Statistical parameters of commonly used diagnostic techniques

Modality	Sensitivity	Specificity
X-Ray Mammography	80-90%	65-85%
Ultrasonography	70-80%	60%
MRI systems	80%	70%
DOBI (optical system)	90%	70%
Thermography)*	79%	79%
*the intersection of sensitivity and specificity of our best combined feature		

Conclusions

Thermography proved the ability to correctly classify significant number of patients in our dataset. Results are comparable with commonly used diagnostic techniques.

It will be necessary to enlarge the dataset to reach more reliable results. Currently we work on development of interactive internet thermograms database, which would be suitable for thermogram exchange. We would like to call on all organisations or departments concerning with the similar topic to join our effort. For more information we encourage you to visit our web page www.irmammodbase.tk .

Our current research is focused on design of classifier with unsupervised learning which would be helpful in discovering of naturally existing clusters in patients set. We also seek new features and new methods of feature selection to employ it in the classifier design.

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