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MASTER THESIS DIPLOMA

Identification of capillary vessels and estimation of their density at microphotographic pictures

Identyfikacja i ocena gęstości naczyń włosowatych na podstawie obrazów mikroskopowych

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AUTHOR’S DECLARATION

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Abstract

Capillaroscopy is a young branch of medicine science. It's non-invasive in-vivo technique for diagnosing and monitoring connective tissue disease in adults. Nailfold capillary images can provide the valuable information about presence of such disorders as Raynaud's phenomena or rheumatoid arthritis. The aim of present work is design and development of semi-automatic image analysis software. The program collects some basic information to characterize the network of capillaries. Such parameters as length, thickness and regularity are computed. A new step in this field is imposing some structure over detected capillaries. Afterwards on the basis of this data medicine doctors may do certain conclusions.

Keywords

Nailfold capillaroscopy, image analysis, hessian filtering

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1 Introduction

Capillaroscopy is a young branch of medicine science. It's non-invasive in-vivo technique for diagnosing and monitoring connective tissue disease in adults. Nailfold capillary images can provide a valuable information about presence of such disorders as Raynaud's phenomena or rheumatoid arthritis. Capillary distribution for healthy patients is uniform. And the thickness of a single healthy capillary should be rather constant. Any deviation among vessel's parameters can be a sign of disease [1]. Thus it's very important to have accurate description of the tissue state.

The aim of work is design and development of semi-automatic image analysis software to help the medicine experts. The functionality of such program may be described in three following steps. First: user properly aligns the image and selects the area of interest. Second: extraction, analysis and characterization procedures are performed. And finally third: such parameters as length, thickness, area, etc. are computed. Usually one set of values is not enough for diagnosis. Thus for better accuracy few more observations should be held over some period of time.

Since good capillary identification is necessary for making any conclusions – variety of different image analysis techniques were used in this work. Different kinds of edge detection filters, noise cleaners, thinning approaches and segmentation algorithms were studied to achieve the goal.

A new step in this field is imposing some structure over detected capillaries. Organizing them into rows makes data more reliable. It's obvious that some capillaries are more clearly seen then others because of their location. Thus the first row capillaries, the sharpest one, provide the most truthful information, the following row is less useful but still worth consideration, and so on.

.NET platform was chosen for implementation of all the ideas described above. It resulted in creation of application with neat interface and efficient algorithm realization. That with a little help of human interaction performs the analysis of nailfold images.

The paper is organized as described below. Subsequent section covers the medical background. Afterward a short review of existing approaches and techniques for stated problem follows. Section four is dedicated to the model and methods that were chosen. Section five describes the practical implementation of the ideas from the fourth section. Then discussion and future suggestions are coming. The paper ends with summing up of the project.

2 Medical background

Nailfold image analysis appeared back in 1950s, it's helpful for detection of certain diseases on early stages, and tracing them. But the interpretation of clinical significances of these images needs certain training and delicate skills. The time spent on the analysis became a barrier to apply the quick, non-invasive and in-vivo method to help more patients in need. Computer-aided diagnosis system might bring the excellent solution for this gap [2].

The normal capillary landscape is a uniform palisade of loops which are uniform in size and morphology. Several researchers have observed that this pattern was completely disorganized in the nailfold in the presence of certain diseases.

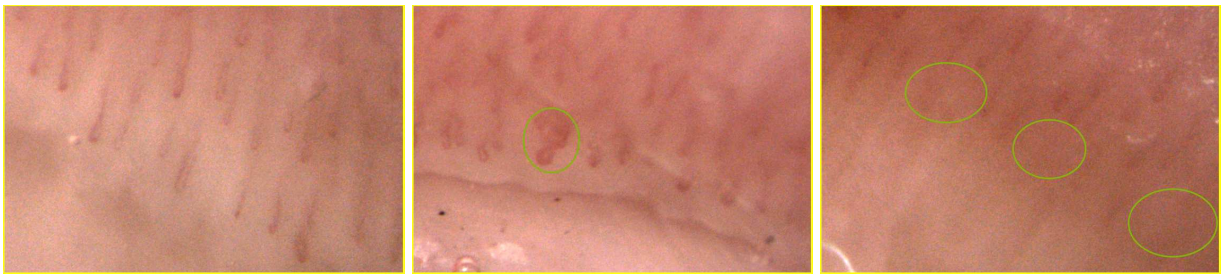

Fig. 1. Left: uniform distribution of normal capillaries; Middle: enlarged capillary is marked; Right: few avascular areas are marked;

One of the most important pathological findings in connective tissue diseases is a change in microcirculation, so called microangiopathia. We have no good clinical, immunological or biochemistry parameters dealing with this problem, so far. Capillaroscopy is a fundamental imaging technique used in the study of microcirculation and seems to be one of the best diagnostic tools for the early detection of microcirculation morphofunctional abnormalities. Microangiopathia is the term strictly connected with enlargement of capillary diameters, forming enlargement loops or megacapillaries.

Enlargement of nail-fold capillaries is the first striking sign of microangiopathy. However, this observation is not true for each case. Microvessels with normal diameter coexist in most instances with definitely enlarged (> 20μm) or giant loops or megacapillaries (> 50μm). An increase in capillary diameter can be found in a wide range of conditions, such as systemic sclerosis, dermatomyositis, undifferentiated connective tissue disease, Raynaud‘s phenomena, diabetes mellitus, acrocyanosis. Isolated morphological abnormalities are not unduly rare in the healthy subject. Such changes are homogeneous enlarged loops [3]. Megacapillaries and irregularly enlarged loops are amongst the first morphological abnormalities to be documented in

patients with systemic sclerosis. In Raynaud‘s phenomenon patients, single irregularly enlarged loops, even if surrounded by completely normal capillaries, can strongly support the hypothesis of subclinical scleroderma spectrum disorders [4].

If microangiopathy is present, the most likely diagnosis is systemic sclerosis, mixed connective tissue disease, systemic lupus erythematosus and dermatomyositis [3, 5]. Capillaroscopy is valuable tool for a correct diagnosis, provided with clinical, serological and immunological findings. It has also prognostic significance in Raynaud‘s phenomenon and scleroderma-pattern disorders [6].

Vascular injury is critical to the pathogenesis of some diseases and may be the primary event. Microvascular abnormalities with structural changes characterized by proliferative intimal arterial lesions and obliteration of the vessels can be visualized in the nailfold capillaries but it is also present in the small blood vessels of other viscera, muscle, subcutaneous tissues and skin. This process can lead to vascular loss and to chronic ischemia [7]. Capillary loss is one of the most characteristic features of systemic sclerosis. Vascular abnormalities observed in nailfold capillaries appear earlier in the course of the disease than at other sites. If capillary disappearance is not counterbalanced by an active process of angiogenesis, extended avascular areas (absence of capillaries in an area longer than 500μm) can appear. Avascular areas may have prognostic value, because they have been associated with a more aggressive disease. However, capillary loss has also been found to correlate significantly with the duration of systemic sclerosis as well as with patient age [1]. The patients with avascular areas associated with every other feature of microangiopathy show a greater degree of skin and visceral involvement and a more aggressive form of the disease.

As we may see in all cases the uniform pattern of healthy capillary network is broken either by enlarged capillaries or by avascular areas. Fig. 1 illustrates different cases of the nailfold image. Fast and accurate detection of this kind of deviations is a challenging task.

3 Previous achievements

As it was said above, the capillaroscopy is rather young field in medicine science. And only decade ago one started to use computers to improve the diagnosis procedure. Nevertheless there were achieved good results by few research groups allover the world.

This project is inspirited by works of Paradowski's group [8-12]. One of them is image annotation problem i.e. characterization of a given image with a set of predefined words. The characterization is done on the basis of features extracted from image. The similar task was challenged by Wen et al [13]. Both groups used the same approach: image enhancement, feature extraction and image characterization. And one must say that both groups obtained quite good results in their projects. That's why it was decided to work further in paradigm of image auto annotation.

The innovation of this work is to impose certain structure over the capillaries network. From medicine point of view it is known that capillaries are organized in rows, which come one after another. Capillaries in the same row tend to look alike and to be distributed homogenously. This gives one extra characteristic of capillary – the row it belongs to. Such structure allows to compute features for each row separately, thus to be more precise with results.

Nevertheless there are some other works, which are worth to mention. Some of them [10, 11] are dedicated to analysis of a singe capillary. The advantage of these methods: one can get really precise characteristic of a capillary. Its shape, radius, length all of this can be computed with high level of accuracy. But the disadvantages are following: initial image should have decent quality; user should select a single capillary from the image. This way is good for spotting enlarged or damaged capillaries.

On other hand there are approaches [12] that do not perform image segmentation. In other words those methods do not extract capillaries, but perform the overall analysis of the image. That's suitable for cases of avascular areas detection and non homogeneous distribution in general. This method tolerates a poor quality of the initial data, but doesn't give as much information as those mentioned earlier.

4 Proposed approach

Capillaries are the thinnest blood vessel. They are connecting arterioles and venules, enclosing the blood circulation cycle. These vessels are 5-10μm in diameter; it is equal to size of one cell. Close to the surface, capillaries are oriented outward, then at some point they turn back, creating so called capillary loop. Exactly these capillary loops are presented on the photo of nailfold.

To perform efficient analysis we need to have good model. The chosen model is rather simple but it is very robust and flexible. Two branches of the loop are located very close, and often can be twisted around each other in helix. Thus in our model capillaries are simplified and approximated with a single tubular structure which contains both branches. From now on under the word “capillary”, this approximation is meant if other is not specified. In such model the main characteristics of capillary are position and shape. In case of healthy patient, we don’t expect any variations within those characteristics. Healthy capillaries have similar shape and are distributed homogenously.

The single capillary can be stored as its topological skeleton. More will be explained in the corresponding section of this work. In few words - it is thinned version of the original that preserves the geometry and is sufficient for computing all required data. There is associated local radius with each point of the skeleton. Thus we can compute length, thickness, curvature, area of capillary.

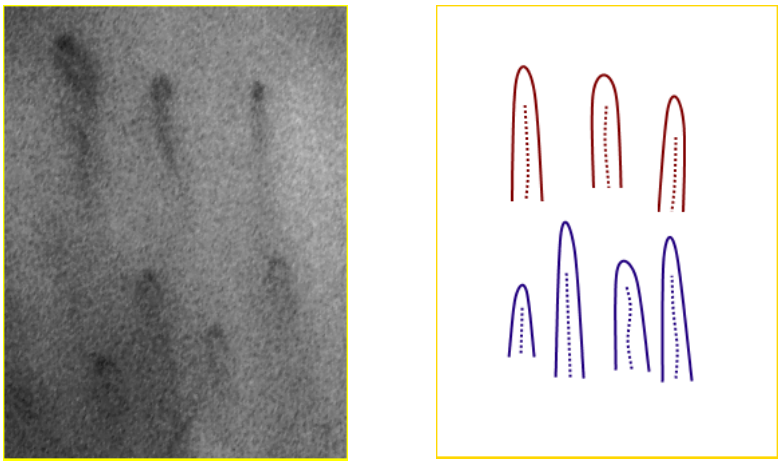

Fig. 2. Left: part of real input image;
Right: illustration of model corresponding to the left image;

Several filtering techniques should be applied to the image in order to increase the visibility of capillaries. Strengthen capillaries are easier to identify and extract.

Thus final representation of the capillary is list of points of its skeleton, together with the local radii. Having the collection of such capillaries we're able to compute some distributional parameters, like mean distance or area coverage. To obtain more precise data we embedded row structure is into a model. It means that every capillary belongs to certain row. Capillaries within the same row tend to be more alike then between different rows. Fig. 2 shows the idea of the model. Different colors correspond to different rows; dotted line represents the skeleton of the capillary.

The final task is to obtain medical characterization from the original input image. To achieve this goal following steps should be performed:

- Enhancement of image in order to increase the visibility of capillaries.
- Extraction of model data from the image.
- Analysis of model data and collection of statistic.

These steps are going to be discussed in the upcoming sections.

4.1 Image enhancement

An original image is color RGB photography made in a medical laboratory. Such kind of image is very inconvenient for analysis. That's why it should be treated appropriately before the actual analysis. This section contains several digital image transformation techniques. The aim of these transformations is to increase the visibility of capillaries as much as possible. The resulting image, in ideal case, is expected to contain capillaries only, without any noise and artifacts. Next transformations will be applied one by one to the image:

- Green channel extraction
- Contrast adjustment
- Hessian filtering
- Binarization and noise removal

Following subsections will discuss each of them.

4.1.1 Green channel extraction

A common RGB color image is rather uncomfortable for image analysis. In this color model each pixel is represented by 3 bytes, one for each of basic colors: red, green and blue. Such scheme actually contains excess of the information. That's why grayscale images are more suitable to use.

Due to the nature of blood vessels – blue and red channels of the image don't provide any relevant information [9]. But the green one significantly increases the visibility of capillaries. Fig. 3 demonstrates the significant difference between color channels.

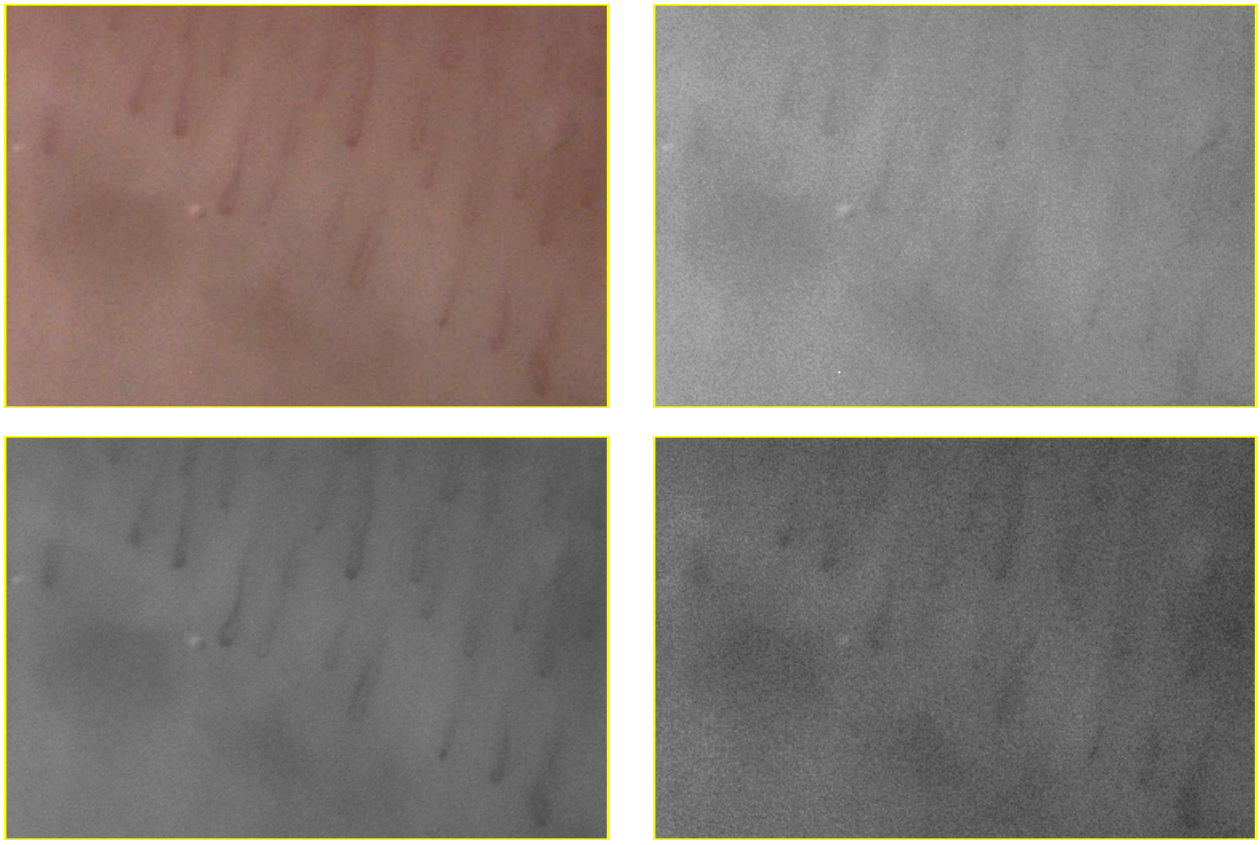

Fig. 3. Top left: original RGB image; Top right: red channel;
Bottom left: green channel; Bottom right: blue channel;

There are no parameters to control during the extraction of the green channel. But one may try to use a certain combination of channels, or to work with another color models (HSV, CMYK) to achieve better result.

4.1.2 Contrast adjustment

Each pixel of grayscale image has a byte value in [0, 255] range. In the images that we work with, this range is not covered completely. From statistic: usually only [70, 185] range is included. It means that we use 115 shades of gray instead of 255. The consequence is: that it's harder to distinguish one feature from another. The adjustment transformation [14] (also known as histogram equalization) simply "stretches" the byte values to the full range. More contrasted image gives better chances for capillary identification.

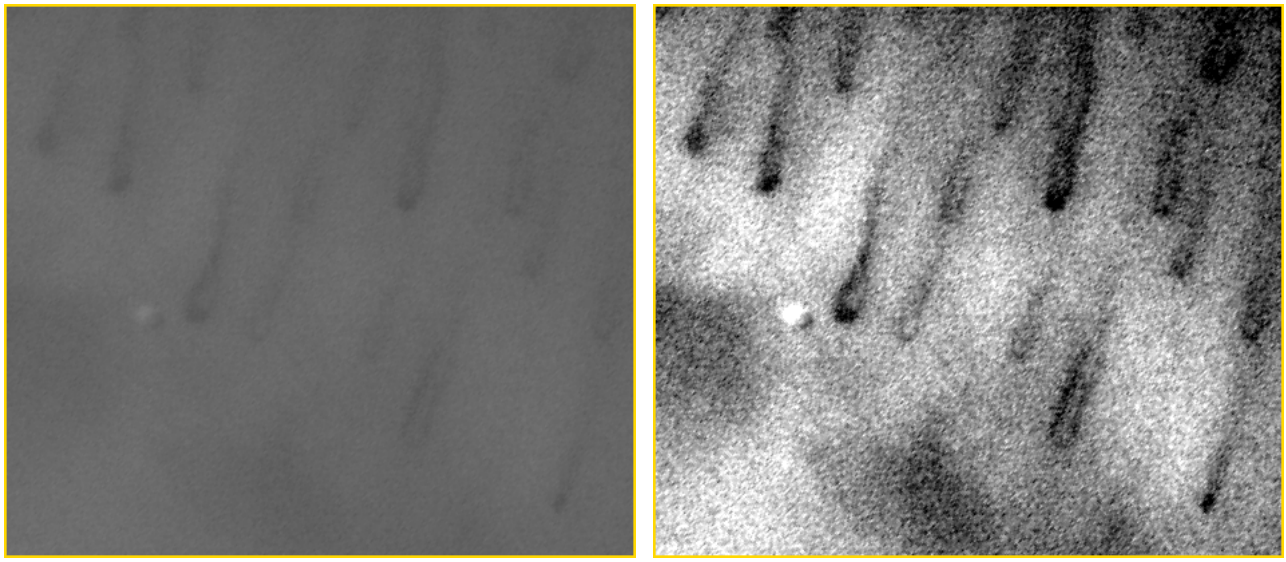

Fig. 4. Left: grayscale image; Right: contrast adjusted

In order to perform adjustment procedure one needs to find lower (L) and upper (H) bounds of the image.

$$L = \max_{low}[\sum_{p \in \mathrm{Im}} (\mathrm{Im}(p) < low) < \alpha \,|\, \mathrm{Im}\,|]$$
$$H = \min_{high}[\sum_{p \in \mathrm{Im}} (\mathrm{Im}(p) > high) < \alpha \,|\, \mathrm{Im}\,|] \qquad (1)$$

where: $\mathrm{Im}(p)$ represents the byte value of image Im at pixel p.

$|\,\mathrm{Im}\,|$ is the total number of pixels in the image Im.

α is the controlling parameter.

Afterwards the fitting is performed:

$$\mathrm{Im}(p) = \begin{cases} 0 & \mathrm{Im}(p) < L \\ (\mathrm{Im}(p) - L)/(H - L) & L \le \mathrm{Im}(p) \le H \\ 255 & \mathrm{Im}(p) > H \end{cases} \qquad (2)$$

Typically, the value of α is 0.01, it means that 1% of the brightest pixels are replaced with the maximum range value (255), and 1% of the darkest pixels are replaced with the minimum of the range value (0). Those 2% (clip interval) of data are actually lost, but they rarely hold any

relevant information. Varying the size of clip interval one may specify the “stretching” level, compromising between increased contrast and data lost.

4.1.3. Hessian filtering

The idea of Hessian filters is based on analysis of the second order local structure of an image (Hessian). The eigenvalues of Hessian provide the information about likelihood of point to belong to a tubular structure (capillary). Several researches were done in this field. Among the others the work of Frangi at al [15] was used in this project. But one may find works of Lorenz and Sato worth consideration as well [16].

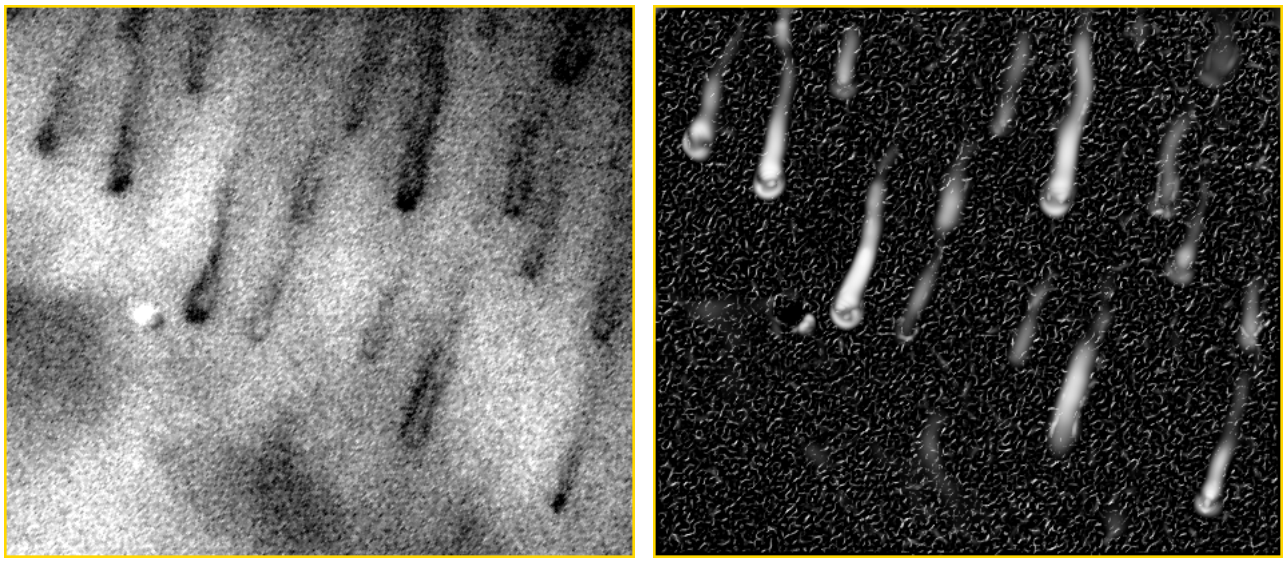

Fig. 5. Left: grayscale image; Right: result of Frangi filter;

The Hessian of digital image [17] can be introduced in similar way as for continuous functions. Assuming that image represents the function of two variables, one may see that:

$$\begin{aligned}
\frac{\partial \,\mathrm{Im}(i,j)}{\partial x} &= \mathrm{Im}(i+1,j) - \mathrm{Im}(i,j) \\
\frac{\partial \,\mathrm{Im}(i,j)}{\partial y} &= \mathrm{Im}(i,j+1) - \mathrm{Im}(i,j) \\
\frac{\partial^2 \,\mathrm{Im}(i,j)}{\partial x^2} &= \mathrm{Im}(i+1,j) - 2\,\mathrm{Im}(i,j) + \mathrm{Im}(i-1,j) \\
\frac{\partial^2 \,\mathrm{Im}(i,j)}{\partial y^2} &= \mathrm{Im}(i,j+1) - 2\,\mathrm{Im}(i,j) + \mathrm{Im}(i,j-1) \\
\frac{\partial^2 \,\mathrm{Im}(i,j)}{\partial x \partial y} &= \mathrm{Im}(i,j+1) - 2\,\mathrm{Im}(i,j) + \mathrm{Im}(i+1,j)
\end{aligned} \qquad (3)$$

where: $\mathrm{Im}(i,j)$ represents the byte value of image Im at pixel $p(i,j)$.

The expression for Hessian is:

$$Hes(\mathrm{Im}) = \begin{pmatrix} \frac{\partial^2 \mathrm{Im}}{\partial x^2} & \frac{\partial^2 \mathrm{Im}}{\partial x \partial y} \\ \frac{\partial^2 \mathrm{Im}}{\partial y \partial x} & \frac{\partial^2 \mathrm{Im}}{\partial x^2} \end{pmatrix} \tag{4}$$

In order to proceed with computing of Hessian the notion of digital convolution should be introduced. Assume having an input image Im and convolution mask Ker. The result of convolution may be computed as follows:

$$\mathrm{Conv}(i, j) = \sum_{x,y} \mathrm{Im}(i - x, j - y)\mathrm{Ker}(x, y) \tag{5}$$

Thus all differentiation operators may be represented as corresponding convolution patterns.

$$\begin{aligned} \frac{\partial^2 \mathrm{Im}(i, j)}{\partial x^2} &= \mathrm{Im} * \begin{pmatrix} 0 & 0 & 0 \\ 1 & -2 & 1 \\ 0 & 0 & 0 \end{pmatrix} \\ \frac{\partial^2 \mathrm{Im}(i, j)}{\partial y^2} &= \mathrm{Im} * \begin{pmatrix} 0 & 1 & 0 \\ 0 & -2 & 0 \\ 0 & 1 & 0 \end{pmatrix} \\ \frac{\partial^2 \mathrm{Im}(i, j)}{\partial x \partial y} &= \mathrm{Im} * \begin{pmatrix} 0 & 1 & 0 \\ 1 & -2 & 0 \\ 0 & 0 & 0 \end{pmatrix} \end{aligned} \tag{6}$$

The disadvantage of second order methods is that while enhancing the visibility of the edges they will enhance the noise as well. That's why prior noise reduction is very important. The most reliable approach is Gaussian smoothing [18]. Gauss distribution function is defined as:

$$g(x, y) = \frac{1}{2\pi\sigma^2} e^{-(x^2+y^2)/2\sigma^2} \tag{7}$$

where: σ is standard deviation of such distribution.

To obtain smoothed image we simply have to convolve original image with the Gaussian kernel.

$$\mathrm{Smoothed} = g(x, y) * \mathrm{Im}(i, j) \tag{8}$$

Combining both facts one may think that we need to perform two convolutions, if we wish to get the Hessian. But there is much faster way around – using the differential property of the convolution. It states:

$$\frac{d}{dx}(g * f) = \frac{dg}{dx} * f \tag{9}$$

Thus second derivative distributions will be following:

$$g_{xx}(x,y)=\frac{1}{2\pi\sigma^4}e^{-(x^2+y^2)/2\sigma^2}(\frac{x^2}{\sigma^2}-1)$$
$$g_{yy}(x,y)=\frac{1}{2\pi\sigma^4}e^{-(x^2+y^2)/2\sigma^2}(\frac{y^2}{\sigma^2}-1) \quad (10)$$
$$g_{xy}(x,y)=\frac{1}{2\pi\sigma^6}e^{-(x^2+y^2)/2\sigma^2}xy$$

The straight forward implementation of the digital convolution has $O(size[\text{Im}]\bullet size[\text{Ker}])$ time complexity. And for typical nailfold image it may take several minutes to compute. Since our kernel is separable we can split 2D convolution into two 1D convolutions. This optimization raises a significant boost in performance. For example g_{xx} kernel may be split into:

$$g'_{xx}(x)=\frac{1}{\sqrt{2\pi\sigma^4}}e^{-x^2/2\sigma^2}(\frac{x^2}{\sigma^2}-1)$$
$$g''_{xx}(y)=\frac{1}{\sqrt{2\pi\sigma^4}}e^{-y^2/2\sigma^2} \quad (11)$$

After performing the convolution and computing the Hessian. Its eigenvalues are calculated. Let λ_1,λ_2 be eigenvalues, sorted by absolute values. Thus research of Frangi states that likeliness of point to belong to tubular structure is computed as follows:

$$F(\lambda_1,\lambda_2)=e^{-B/\beta}(1-e^{-C/\gamma}) \quad (12)$$

where: $B=\frac{\lambda_2^2}{\lambda_1^2}$, $C=\lambda_2^2+\lambda_1^2$ and β, γ are controlling parameters.

The greater value of $F(\lambda_1,\lambda_2)$ – more likely that current point belongs to a capillary.

In order to obtain better results the multi-scale approach is used. It means that filtering is performed on different scales i.e. filter sizes. Afterwards the singe frames are merged into the final image.

The part of Hessian filtering is one of the corner stones of the project. Since clear visibility of capillaries is crucial for their detection and further analysis. Thus summing it up – we have three parameters to control: β, γ and filter size. The controlling parameters β, γ are fixed, because their values have rather weak influence. The size of the filter corresponds to a size of the feature we wish to extract, so this value is correlated to the radius of capillaries.

4.1.4. Noise reduction

The last step of image enhancement process is noise removal. It consists of two parts: binarization and mean filtering.

Binarization is transformation of image from grayscale to binary (black & white). This process is controlled by threshold value. If shade of grade is less than this value – it becomes black, otherwise it becomes white. Bigger threshold value means that only very clear parts of image will be extracted.

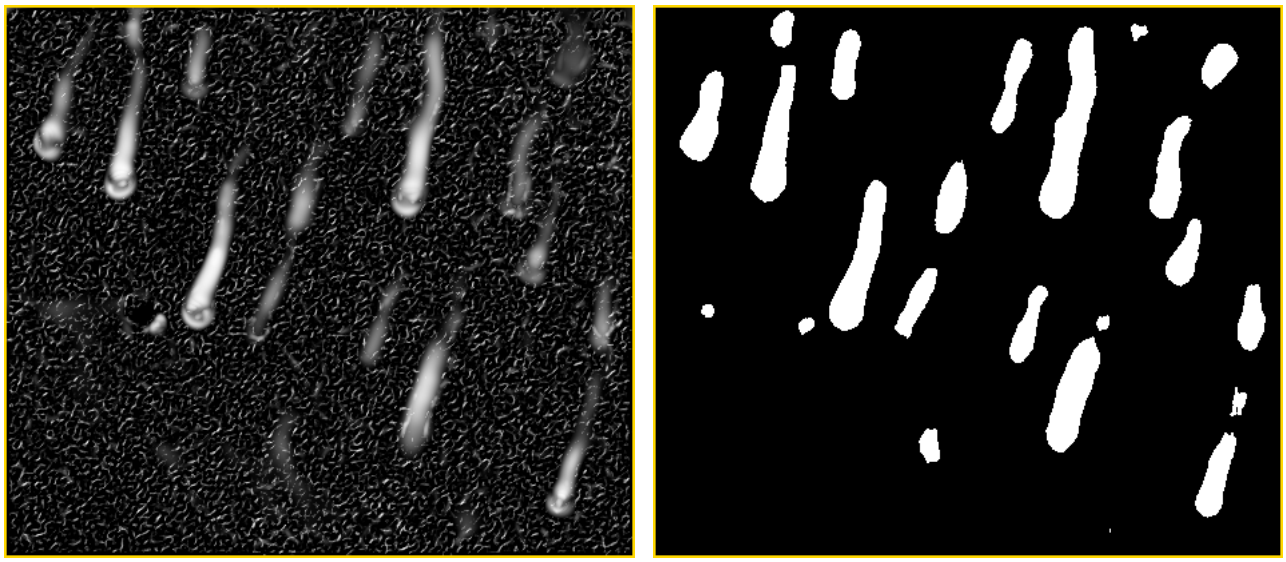

Fig. 6. Left: grayscale image; Right: result of noise removal;

Mean filter is linear filter that replaces the pixel with average value of its neighbors. In case of binary image the result is the same as for median filter. The procedure of mean filtering can be represented as result of convolution. The kernel of such convolution (for 3*3 filter) has following shape:

$$\mathrm{Ker} = \frac{1}{9}\begin{pmatrix} 1 & 1 & 1 \\ 1 & 1 & 1 \\ 1 & 1 & 1 \end{pmatrix} \tag{13}$$

The only parameter here – is size of the filter. The greater size of the filter means that larger noise particles will be removed. But one should remember that with removal of unwanted noise, capillaries are distorted as well.

This is the last section of image enhancement. If all parameters were set correctly, we should get good representation of original capillaries, in monochrome resolution.

4.2 Image analysis

This section of the report covers the data harvesting part. Having preprocessed black and white image one wishes to extract data, he's interested in. In other words we want to obtain some quantitative description of the image. We expect to get such characteristics as number of capillaries, length, thickness, location and row number of each of them. This procedure consists of four following steps:

- Thinning
- Extraction
- Characterization
- Row identification

Beyond subsections will cover each step.

4.2.1 Thinning

At this stage we have black and white image with capillaries on it. We can clearly distinguish one capillary from another. We can even store them as set of pixels. But we cannot tell anything about them. We can't measure their length or thickness, the only thing we can probably have is the area of capillary. As one may see such form is very inconvenient both for storage and characterization. That's why some more precise data structure is required. The topological skeleton is good solution of this problem.

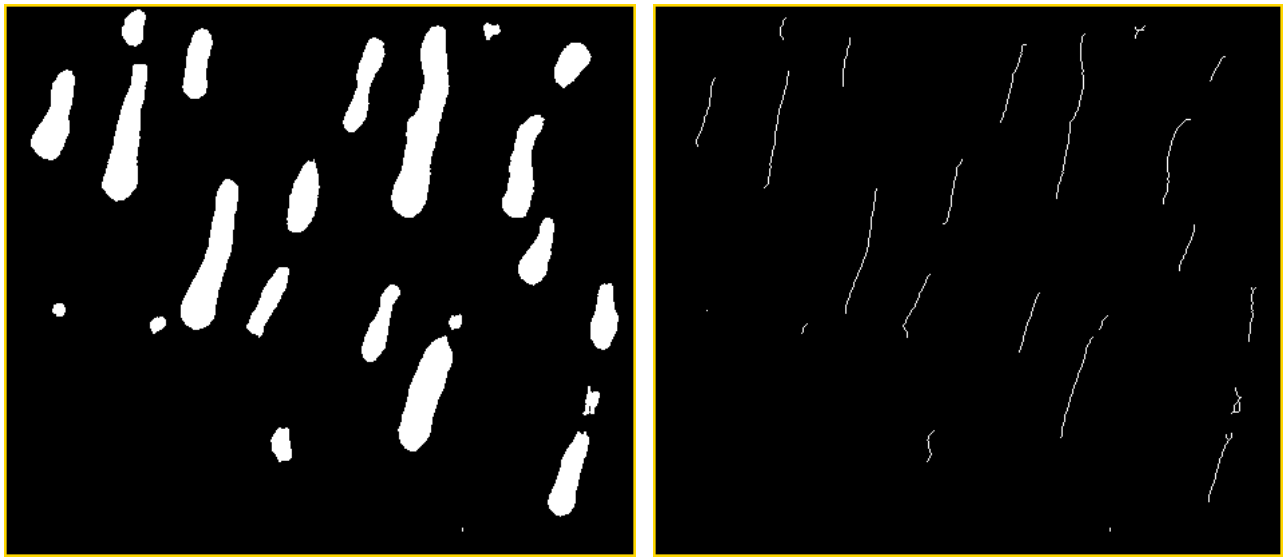

Fig. 7. Left: monochrome image; Right: its morphological skeleton;

The thinning procedure is typical for feature extraction problems. After applying it, we obtain morphological skeleton of the image. Skeleton is a thin version of the original image that is equidistant to its boundaries. It preserves both geometry and topology of the shape. Due to the nature of our problem – capillaries don't suffer large distortion during the thinning.

The approach used in this project is described in the work of Lam et al [19]. It is iterative process. During the iteration, we peel one layer of pixels after another from the image until we converge. It consists of four steps. First: we mark all pixels that satisfying conditions 1-4. Second: after looking through the entire image we delete marked pixels. Third and fourth steps are same as first two, but instead of condition 4, condition 4' is used. These conditions are following:

0. Denote the neighborhood of pixel that is considered as: $\begin{pmatrix} x_4 & x_3 & x_2 \\ x_5 & p & x_1 \\ x_6 & x_7 & x_8 \end{pmatrix}$.

1. $p = 1$. (14)

2. $\sum_{1}^{4} b_i = 1$, where $b_i = \begin{cases} 1, \textit{if } x_{2i-1} = 0 \textit{ and } (x_{2i} = 1 \textit{ or } x_{2i+1} = 1) \\ 0, \qquad\qquad \textit{otherwise} \end{cases}$ (15)

3. $2 \le \min\{n_1(p), n_2(p)\} \le 3$, where (16)

$$n_1(p) = \sum_{k=1}^{4} x_{2k-1} \vee x_{2k} \text{ and } n_2(p) = \sum_{k=1}^{4} x_{2k} \vee x_{2k+1}$$

4. $(x_2 \vee x_3 \vee \overline{x}_8) \wedge x_1 = 0$ (17)

4'. $(x_6 \vee x_7 \vee \overline{x}_4) \wedge x_5 = 0$ (18)

Current approach is just one of many. One may consider distance transformation or Voronoi diagram methods. But as was said above, the geometry of capillary is rather simple. Thus even such robust method as Lam's is doing well. One may also notice that there are no parameters to control this process.

4.2.2 Extraction of skeleton

In case of good quality image the skeletons of capillaries should be straight lines. These lines should be one pixel wide. Thus extraction of a capillary becomes rather a trivial task. We look for a point with exactly one neighbor – this should be the edge of a capillary. We proceed extracting the skeleton pixel by pixel, till its end.

But there might be some troubles in this process. The problems arise when couple of capillaries overlap. Or due to some artifacts there are some junction points in the skeleton. In this case every singe branch (part from the edge to the junction point) should be extracted in the way described above. Afterwards it is very important to merge correctly these branches. Current approach is following: at the junction point with three of more branches a couple that is the most capillary-like is chosen. This couple is merged into a single capillary and remaining branches are considered as artifacts and are ignored. Fig.8 illustrates this. The criteria of capillary-likeness are: resulting structure should have vertical orientation and be as long as possible. This part of the project is probably the weakest one, and requires improvement at the first point. In case of low quality images it produces rather unnatural results.

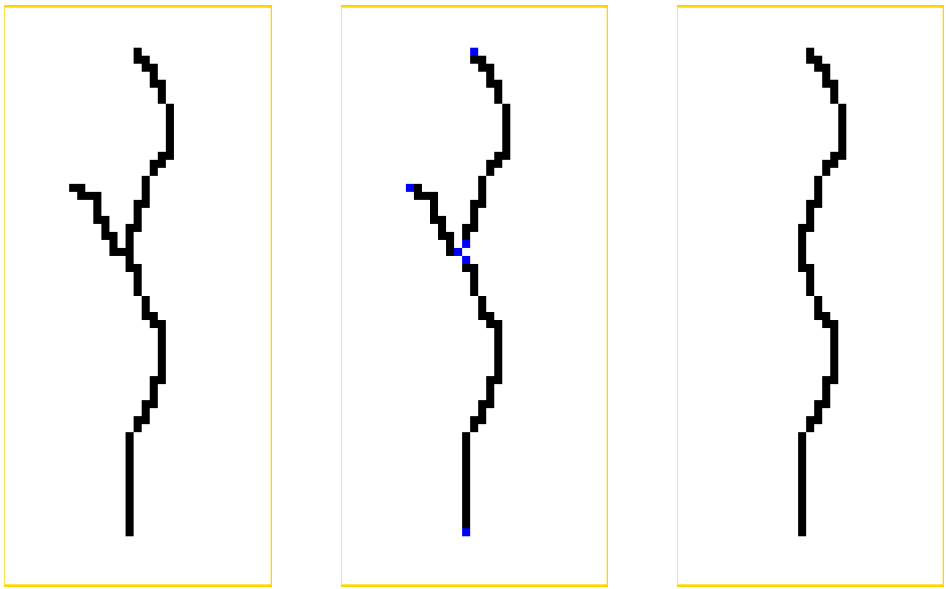

Fig. 8. Left: defected part of the skeleton; Middle: extracted branches: Right: reconstructed capillary

There is no way to control this process. One may just introduce another criterion for skeleton reconstruction.

4.2.3 Characterization

The skeleton can give us the information about the location and the length of the capillary. But it can tell nothing about one of the most important characteristic of a capillary is its thickness. Usually this parameter is changing due to the effect of different kind of drugs. Also it is required for computation of area of capillary.

In order to compute thickness of a capillary we have to combine the skeleton and the image it was obtained from. So the task is to get the minimal distance from certain point of skeleton to the edge of the capillary. The approach to solve it is rather straight forward. The binary search method is used to fulfill the task. Idea of the method is given below. Set two initial limits of the radius, the lower $R_l = 0$ and the upper $R_u = 100$. The current radius is mean value of the limits, $R = \frac{R_l + R_u}{2}$. Consider a circle of current radius with a center in the given point in the filtered image. If there is at least one black point it means that the current radius is too big, if all points are white – it's too small. Thus limits are changes appropriately. Iterating this process will converge to the value local radius at given point.

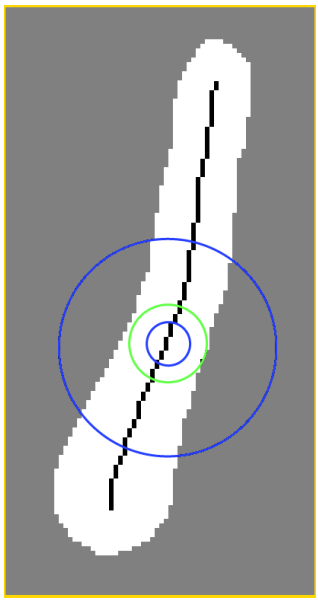

Fig. 9. Idea of capillary characterization

Having the values of local radii at each point of the skeleton, one can approximate the thickness of whole capillary as the mean.

4.2.4 Row identification

One of the characteristics of a capillary is the row it belongs to. The capillaries of the first row are the closest to the skin surface so they are the most visible. Thus information obtained from the fist row is the most reliable. The subsequentrows are not as informative as the first one but still they're worth of correct identification. The input image is oriented (with the help of human operator) in such way that top capillaries vertical and oriented upward. Thus first row is in top part of the image, the second one is beyond it, and so on.

But before the actual row identification extracted capillaries should be filtered. Because due to some artifacts, image quality or heavy noise there can be some non capillary structures that passed all the filters. The successful capillary should:

- have certain minimal length;
- have a thickness within certain range;
- be properly aligned;

If any of these criteria does not hold the structure is considered as artifact/noise and is ignored.

Now having capillaries only we can proceed. At this stage we can represent the capillary with a single point – top of its skeleton. In these terms the first row can be characterized as follows:

- points within row should be as high as possible;
- there should be as much point as possible;
- the row should be horizontal aligned;

These requirements should be formalized. In order to do so certain weight was associated with each point:

$$w(p) = (p(y) - \min y) / (\max y - \min y) \qquad (19)$$

where: $p(y)$ the height of point p

$\min y$ minimal value of height among all the points

$\max y$ maximal value of height among all the points

Thus first two requirements can be interpreted as maximization by weight problem. The third one should put some restrictions (otherwise all points would be picked). Such restriction is angle between any two points in a chosen row and straight horizontal line. If this angle is greater than a certain value – these two points cannot be in the same row simultaneously. Fig. 8 illustrates this explanation. Keep in mind that not all lines are drawn, in order to keep the image neat.

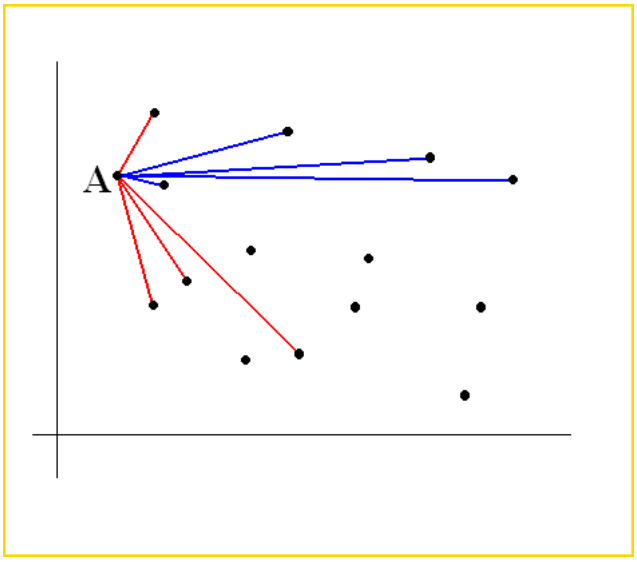

Fig. 10. Points that are connected to A with a blue line can be in the same row, but those that are connected with a red one no.

Summing up our assumptions we can rewrite the row identification problem in next form:

$$\text{Find } G \subseteq P \text{ such that } F(G) = \max_{S \subseteq P} F(S) \tag{20}$$

$$\text{where: } F(G) = \sum_{p \in G} w(p) \tag{21}$$

with following restriction:

$$\forall p, q \in G : \{ p \neq q, \angle pq < \alpha \} \tag{21}$$

here: P represents the set of all points.

$\angle pq$ denotes the acute angle between segment pq and horizontal line.

α is controlling parameter.

4.3 Statistics

After extraction of all capillaries is done the basic statistic is collected. The parameters of interest are following:

- number of capillaries; in total; in each row separately;
- length of single capillary; the distribution of length in a row;
- thickness of single capillary; the distribution of thickness in a row;
- the distance between successive capillaries;
- area of capillaries; ratio between area of capillary and total area of a row;

Collection of such kind of data is rather straightforward. Basic tools of statistic analysis are used. Due to its simple nature, details of this process will not be discussed here.

5 Implementation of the approach

This section covers an implementation of all the ideas and methods discussed above. Microsoft C# language and.NET platform were used in this project. Such choice resulted in developing fast and efficient software that fulfils all the given tasks. The only requirement to run the software is presence of Microsoft .NET 2.0 platform or higher, which nowadays is preinstalled on the majority of computers.

Next part of the report is step by step user guide, which explains main features of the software.

- File loading. At first user selects a file for an analysis. Any raster RBG image format is supported. Green channel will be automatically extracted and displayed.

- Alignment of the image. One of the requirements for successful row identification is that capillaries should be vertical and directed upward. To do so, user simply sets a new orientation by drawing a line on the image. Fig. 9 illustrates the process.

Fig. 11. Left: original image, new direction is selected; Right: rotated image;

- Cropping of the image. In most cases the original image is too large for analysis. Some parts of the image don't have any information about capillaries. Thus in order to get faster and more precise results only certain area should be processed. User should select rectangular area with few rows of capillaries that are clearly visible. This procedure can be seen on the Fig. 10.

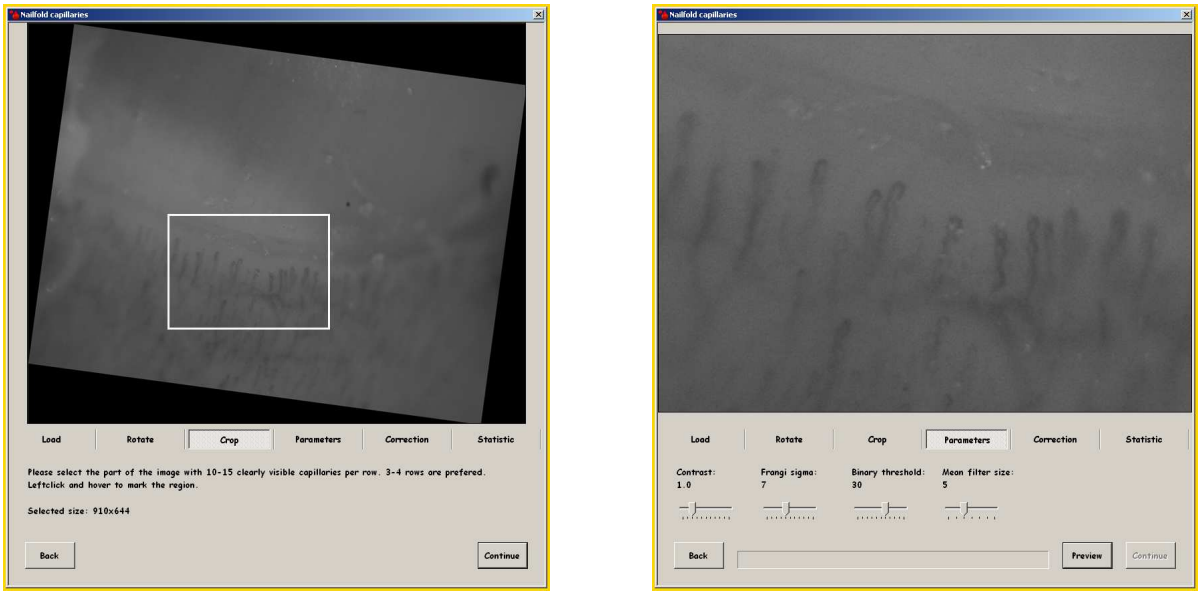

Fig. 12. Left: rotated image, new size is selected; Right: cropped image;

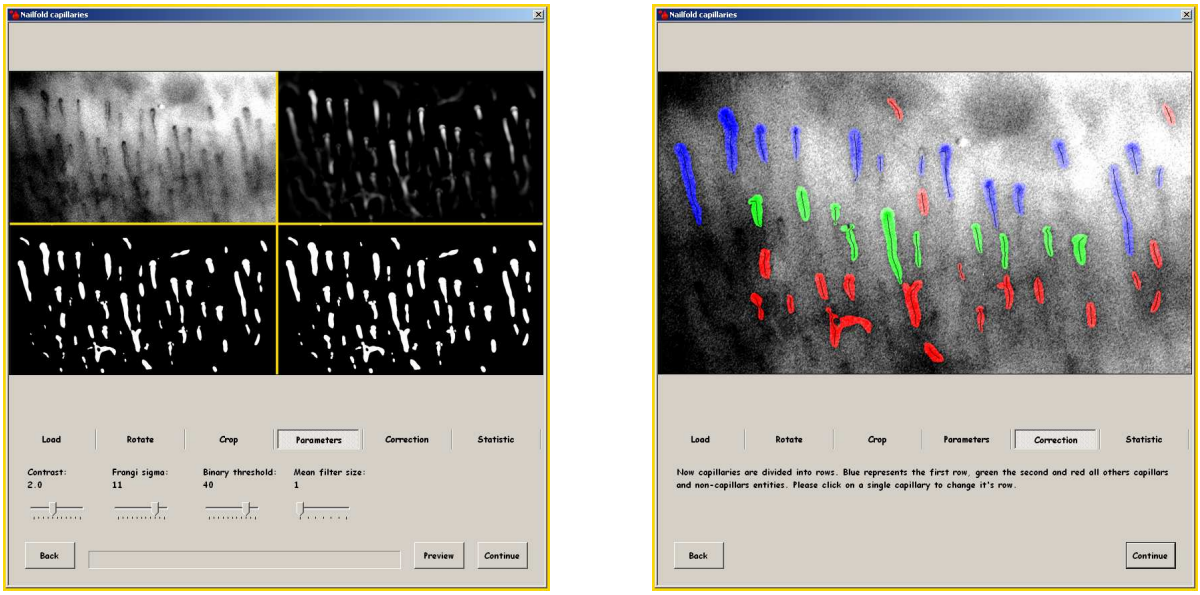

Fig. 13. Left: parameters tuning process; Right: correcting screen;

- Setting the parameters. Almost each step of the image treatment has certain controlling parameters that could be varied. The default values are chosen in such way that majority of images would be filtered optimally. But in some extra ordinary cases user may tune those parameters to achieve a better result. As Fig 11 shows, all the intermediate stages are shown, so user can easily track the changes.

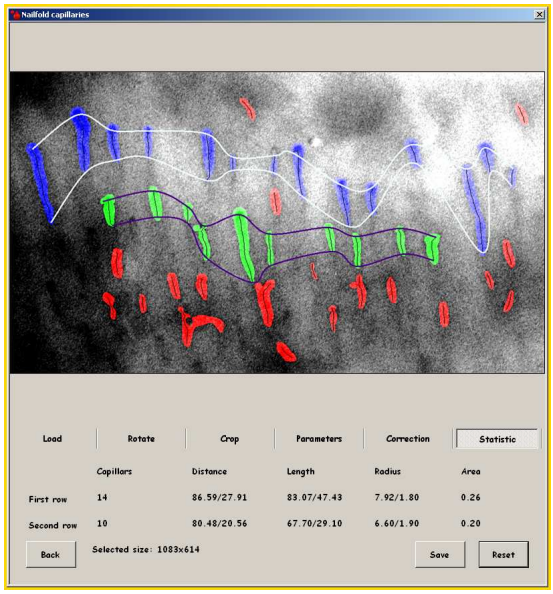

Fig. 14. Statistic screen

- Correcting the rows identification. After the capillary extraction and running the row identification procedure, user may correct its result. Even due to good solution of identification problem sometimes it may fail, because of huge variety of treated pictures. With a single click capillaries row can be changed. Different rows are marked with different colors. So user can easily see the changes.

- Statistic screen. All the collected data is displayed here. Rows of capillaries are highlighted. At this final stage user may save the obtained result.

6 Future works

The main required features were successfully implemented. But there is always a possibility for improvement. Some of them a listed below:

- Dual analysis. At this stage the developed program allows to analyze a single image. But the from medicine point of view a comparison of a pair of images is more interesting. Usually one image is marked as ‘pre’ and another is ‘post’. In such case one can track the evolution of the capillaries. For example one can see if certain drug is effective or not. At this moment user have to perform two separate analyses and to do the comparison by himself.

- Complete automation. The part of user in the overall process is aligning and cropping the piece image to analyze. Both functions may be automated completely. So the part of user would be controlling the process and interrupting in case of extraordinary situations. The result of complete automation may be a console application that gets the filename as parameter and after works on its own.

- Knowledge database. At this moment each analysis is separated from others. And the results are stored in the local file. Good idea is creation of general database that would contain whole extracted information from all the images. Having much larger amounts of data one can perform more precise statistic analysis. For example with help of machine learning techniques one can teach an application to distinguish healthy and ill capillaries. Also such data may be very useful to distinguish capillaries from image artifacts.

7 Summary

The goal of the project was design and development of semi automatic desktop application for nailfold image analysis. Such tool was created; it can perform fast and high quality processing of the provided image. Plenty of materials were studied in order to complete the task.

From the medical background and with a help of medicine expert we got the general knowledge about capillaries. Also studies of previous work gave us an idea of the ways to treat the problem. On this basis, current model was designed. It extended existing approaches, bringing new sight in this field.

To realize the task we required to have a decent level in image processing. A lot of combinations of different filters with different parameters were tried in order to achieve the best result. The final pick is histogram equalization and hessian edge detector. Together with few more filters we obtained high quality image enhancement.

The extraction of the data is rather tricky part. The difficulty is the lack of the material on this topic, thus everything should be developed from the scratch with try and error method. The chosen method is rather simple and robust but it fulfills the task.

In addition some basic knowledge of statistic methods is required for the final part. Good representation of the data has the same importance as data itself.

Finally, we've implemented all the methods and techniques with help of Microsoft C#. And the final product was obtained. We hope that it will serve for the sake of the science.

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