Image Sequence Analysis for on line Observation of Thrombus Formation in Blood Vessels

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Abstract. An image analysis system for in vivo observation of thrombus formation in skin blood vessels of small marmals is presented. A model based approach is applied, allowing automatic segmentation of thrombus, blood vessel, and tissue in low contrast images. Image sequence analysis takes advantage of preceeding results in three ways: data reduction, improvement of algorithm efficiency, and robustness. This is achieved by a fast motion compensation that takes the image movements in the in vivo observation into consideration. For clinical use in a biomedical laboratory a graphical user interface was developed.

Key words: biomedical image processing, image sequence analysis, model based image analysis, motion compensation, real time analysis

1. Introduction

In thrombus research the in vivo observation of blood vessels in the skin of small marmals is used to study thrombus formation. After triggering thrombus formation by a controlled local injury at the inner blood vessel wall the generation and temporal development of the thrombus can be observed under the microscope and recorded via camera. The subsequent evaluation requires the segmentation into the three regions vessel, thrombus, and surrounding tissue. Till now evaluation was done manually, since automatic segmentation of the images suffered from low contrast.

Automation is achieved in three steps:

1. Vessel and thrombus are emphasized by a special mixed illumination with halogen and laser light [1][2].
2. A priori knowledge is integrated in the image analysis by using a geometric vessel and thrombus model.
3. Image sequence analysis is applied to deal with the uncertainties caused by the analysis of single low contrast images.

2. The Model

Two types of a priori knowledge can be distinguished, describing static and dynamic features concerning thrombus formation.

For segmentation (chapter 3) the static features F1 to F3 are relevant:

(F1) Blood vessel and thrombus are threedimensional. However for the observation of the thrombus formation the 2D projection is sufficient. Figure 1 shows a schematic view of (a) the real vessel and (b) the 2D projection model.

(F2) Due to the short length of the considered vessel segment, the outer vessel boundaries can be approximated by two almost parallel straight lines, named vessel walls in the following. It is assumed, that both vessel walls lie within the image at the beginning of the sequence.

(F3) The thrombus is situated within the vessel at the injured vessel wall and forms a compact region.

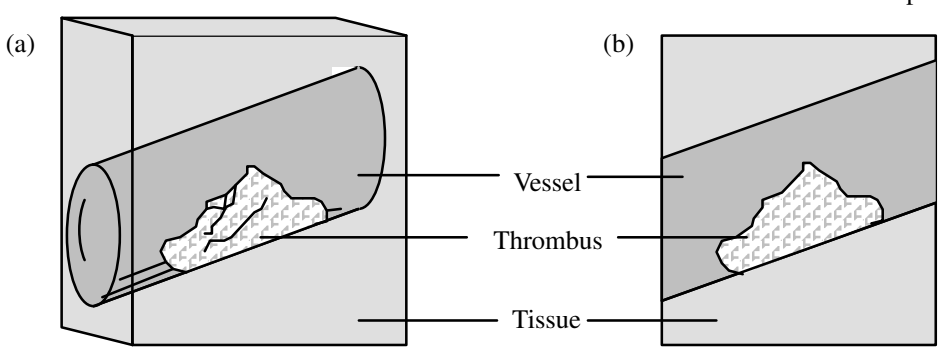

Figure 1. (a) Vessel with thrombus and (b) 2D Model

For image sequence analysis (chapter 4) the dynamic features F4 to F6 are applied:

(F4) The illumination conditions vary slowly.

(F5) The temporal change of thrombus geometry is limited by the physiology of thrombus formation and the thrombus position is fixed till it is torn off by the blood stream.

(F6) The geometry of the vessel is constant, but the observed scene exhibits a common translatory movement which is caused by breathing and jerking of the marmal.

3. Segmentation

Goal of the segmentation is to devide the single image into the regions vessel, thrombus, and surrounding tissue. Characteristic features for segmentation of the original image (figure 2a) are:

– brightness differences between vessel and surrounding tissue

– spatial inhomogeneities of intensity in the tissue due to cell contours and speckle pattern caused by coherent illumination.

3.1 Vessel Segmentation

Vessel segmentation exploits the speckle pattern, which is caused by the choosen illumination [2]. The coherent light shows an interference i.e. speckle pattern. However, while taking a picture the blood flow averages the speckle pattern. This texture is tested by a local difference operator and the vessel label is assigned to the largest non speckle region.

The local difference of the grey values $g_{x,y}$ for the image coordinate (x,y) is measured by a modified roberts gradient $r_{x,y}$ as definied in eq. (1).

$$r_{x,y} = \max(\mid g_{x,y-1} - g_{x,y+2} \mid, \mid g_{x-1,y} - g_{x+2,y} \mid) \quad (1)$$

This operator enhances the speckle features better than averaging gradient operators. Further in opposition to difference operators of higher order it avoids suppression of low contrast speckle regions due to overproportional amplification of high differences.

The local difference image is smoothed by low pass filtering. The histogram based thresholding and subsequent shrinking and blowing for smoothing and small blob closing yields a binary image where the largest non background region represents the vessel.

The detection of the vessel walls is made insensitive to false segmentation by applying the tube model (F2). The vessel walls, i.e. contours between the vessel and tissue regions, are approximated by straight lines using linear regression [2].

3.2 Thrombus Segmentation

Thrombus segmentation is primarily model based, because thrombus and surrounding tissue exhibit no significant texture differences. Assuming a tubular vessel (F2) the thrombus is defined by the part of the thrombus–tissue region that projects into the vessel at the injury (F3).

Initially vessel geometry is unknown and thrombus and vessel must be determined together. Segmentation is achieved in two steps. First the free blood vessel, i.e. the non speckle region, is approximated by a tube. Due to the thrombus the tube is estimated too small with a low regression coefficient for the wall at thrombus side. Hence in a second step the linear regression is repeated neglecting the thrombus part of the contour, i.e. the contour projecting into the current tube. The regression is iterated until convergence of the contour approximation is obtained.

Thrombus segmentation suffers from low contrast within the vessel and a solely texture based segmentation approach fails. Hence a weighted sum of the brightness and speckle features is used. The weights are automatically adapted to varying illumination conditions.

The results of vessel and thrombus segmentation are shown in figure 2b with the straight lines approximating the vessel walls and the thrombus being the area beneath the white curve.

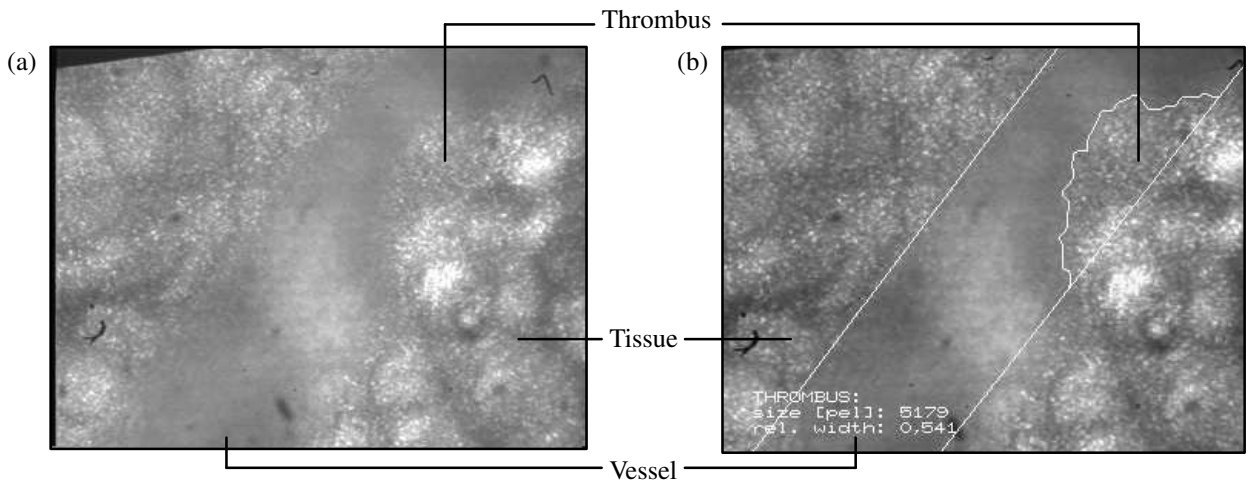

Figure 2. (a) Original image and (b) results of vessel and thrombus segmentation

4. Image sequence analysis

Image sequence analysis is used to profit from preceeding results in three ways: data reduction, improvement of algorithm efficiency, and robustness (table 1).

a priori knowledge	**profit**	**required control**
intermediate results of previous image analysis	robust computation	verification
location and contour of thrombus	data reduction	thrombus window
location and contour of vessel	algorithm efficiency	motion compensation

Table 1. Profit of a priori knowledge for image sequence analysis

Illumination and contrast vary slowly (F4). Thus previous results are used for parameter prediction. The image analysis parameter, which are automatically adapted to varying illumination and contrast conditions, are verified and, when not satisfying the predictions, modified.

The vessel geometry is assumed to be constant (F6), but form, size and position of thrombus vary with time (F5). Thus only the image part including the thrombus must be analysed. The thrombus window is determined by the location of the thrombus in the previous image and a border for growth and movement.

Due to the motion of the animal during the in vivo experiment, a global shifting is superimposed on the image (F6). Thus thrombus and vessel are shifted during the image sequence. To take advantage of known thrombus location and vessel geometry a fast motion compensation is required.

For motion estimation a hierarchic blockmatching algorithm is applied [3]. Because the whole image is shifted uniformly it is sufficient to determine the displacement of a single image section in consecutive images. An image section with characteristic pattern [4] is selected and matched with neighbouring sections within the maximal displacement range of the consecutive image using mean absolute intensity difference as a quality measure. For matching a truncated calculation is applied, that terminates the test of a displacement, if it gets worse than the hitherto optimum. The search is accelerated by a coarse to fine strategy with logarithmic raster reducing computational cost. To increase efficiency further multiple pixels are matched at once by comparing binary images and collecting 16 pixels in a word.

Figure 3 shows the motion compensated updating of the vessel and thrombus window location. From the match windows the displacement of image(t) to image(t–1) is calculated and added to the location of the vessel and thrombus window in the previous image(t–1), thus reducing image analysis to segmentation of the thrombus within a window.

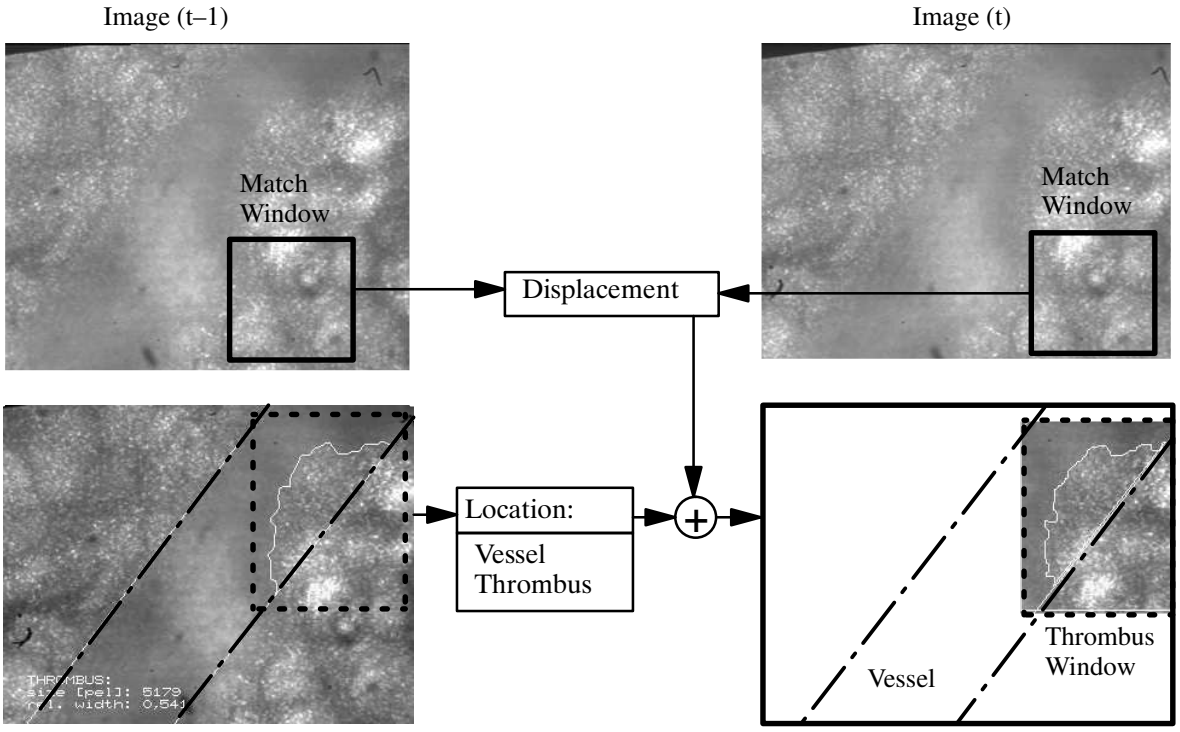

Figure 3. Motion compensation for localization of vessel and thrombus window

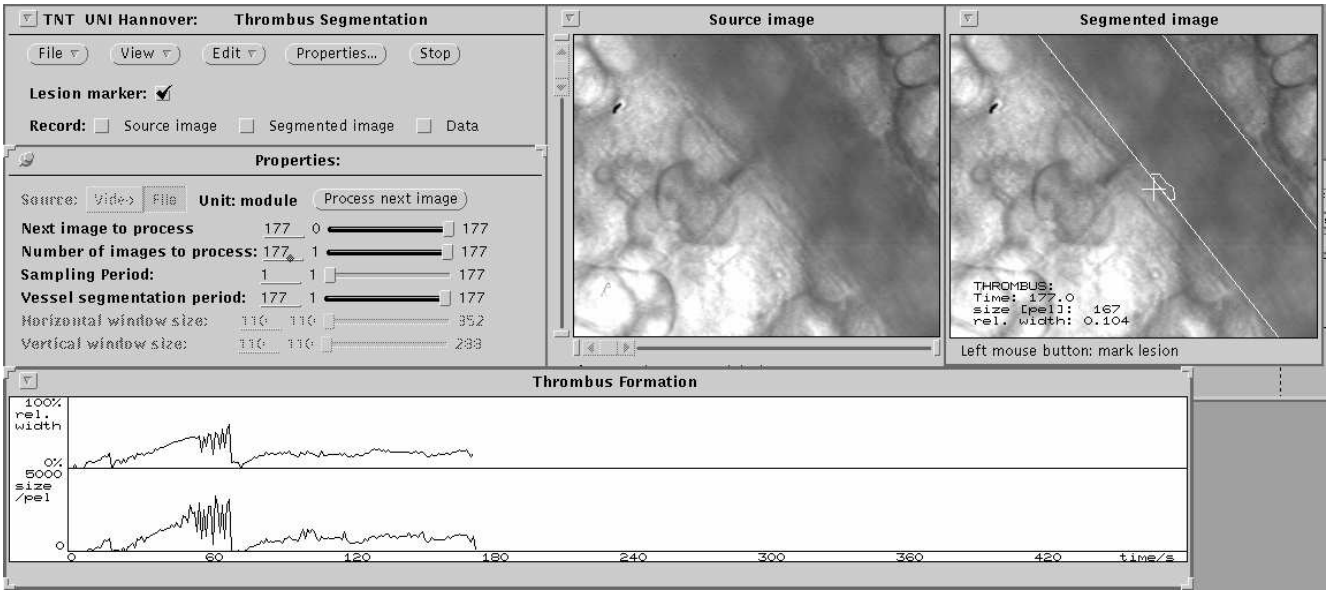

Figure 4. Graphical user interface in OPEN LOOK style

5. Implementation and results

The algorithm was implemented on a UNIX operated workstation with a frame grabber. For a SPARCstation 10 processing of 3 frames per second was achieved. Because the image sequence analysis must not be interrupted to wait for user inputs, the user interface is realized as independent process. Data transfer via shared memory is controlled by two communication mechanisms. For inter process communication the UNIX signal mechanism guarantees asynchronous process control and the X–Window selection model provides the update of the windows for image output of the process. The graphical user interface conforms to the OPEN LOOK standard [5]. Figure 4 shows the graphical user interface with windows for process control and visual feedback displaying segmentation results and temporal development of thrombus size and vessel blocking. The thrombus formation graph shows a thrombus growing for 70 s until it is torn off and a new thrombus formation starts.

6. Conclusion

An image analysis system was realized, that provides an on line evaluation of image sequences with in vivo microscopy images showing the formation of a thrombus after a vessel injury. Segmentation of low contrast images is achieved by exploiting a priori knowledge and results from analysis of preceeding images. The latter is based on a fast motion compensation.

Acknowledgement

This work has been supported by a grant of the THOMAE GmbH, which also provided the image data.

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