User-Defined ROI Tracking for Estimation of the Myocardial Blush Grade

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Abstract

For a proper diagnosis and post treatment evaluation of acute myocardial infarction, angiographic measures of the myocardial perfusion such as the myocardial blush grade are pivotal. The presence of blood with contrast agent in heart tissue can be observed as a darkening of the target region. Currently, the myocardial blush grade is established by a visual analysis of this darkening. We present methods which allow the automatization this important procedure thereby improving from a what in clinical routine is termed a "semi-quantitative" analysis to a "quantitative" analysis with less inter- and intra- observer variability.

1. Introduction

Myocardial infarction (MI) is the most common cause of morbidity and mortality in the industrialized world. In most cases, an abrupt occlusion of a coronary artery leads to MI. Diagnosis and treatment usually takes place under X-ray supervision. To make the arteries visible under X-ray a contrast dye is injected through a catheter placed at the ostium (entrance) of the coronary arteries. Treatment is usually performed by Percutaneous Transluminal Coronary Angioplasty (PTCA) and aims at reopening the artery to reestablish both coronary blood flow and myocardial micro-circulation. However, reopening of the artery does not necessarily imply integrity of myocardial micro-circulation. The presence of blood with contrast agent in heart tissue can be observed as a darkening of the target region – i.e. myocardial blush (MB). Both for precise diagnostics and to assess the success of such intervention it has been proposed to investigate the MB by means of a dedicated measure: the myocardial blush grade (MBG) [6].

Presently the MBG is assessed "semi-quantitatively" (grades 0-3) by the angiographer and thus the procedure is afflicted by inter- and intra- observer variability [12]. In this contribution we therefore describe methods which permit a "quantitative" assessment of the MBG mainly by tracking a predefined region of interest (ROI) of the moving heart over a sequence of X-ray projections. The MBG is then obtained by analyzing the gray-level variations within this ROI during the investigated sequence. Tracking is needed to allow the observation of the same region during the entire analyzed sequence despite the heart motion. A subsequent robust analysis of the gray-level variations within the tracked region shall then yield the sought "quantitative" grades.

2. Methods

We analyze sequences of X-ray projection images recorded over several heart cycles from the moment the contrast agent is injected into the coronary vessel tree. Such a sequence shows three phases: inflow, when the contrast agent enters the coronary vessel tree, complete state, when the entire vessel tree is visible, and washout, when the contrast agent leaves the coronary arteries.

Typically the ROI has no dominant cues to support the tracking. As the vessels exhibit bendings and bifurcations (i.e. corners) while other structures do not, and the vessel motion is directly linked to the heart motion, we estimate the latter by tracking corners between consecutive images. Thus the ROI can only be tracked in images acquired during the complete state (Figure 1a), which are selected as described in [1]. The myocardial blush appears when the blood reaches the myocardium. This moment varies from sequence to sequence, depending on the way the contrast agent is injected. In some sequences it may appear as early as in the middle of the complete state, and continue until close to the end of the washout. For images acquired during the washout, the vessels are poorly or not at all visible, thus the ROI can not be tracked there. To analyze the myocardial blush during its entire duration, the images showing insufficient contrast are matched with respect to heart phase and breathing status of the patient as described in Refs. [4], [5]

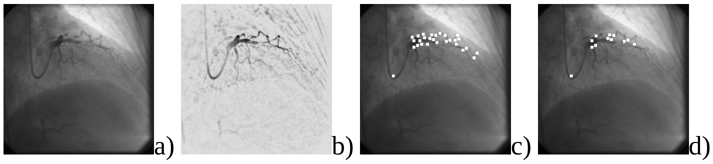


Figure 1. Detection and tracking of corners.

and [8] to the contrasted images which are acquired during the complete state. The ROI is then projected from the contrasted to the non-contrasted images.

The border of the ROI is modeled as a closed elastic string, which is deformed under the action of certain external forces, defined in relation to the tracked corners by attaching virtual springs between each corner and each border point. The corners are detected by a tensor approach [2]. The behavior of the strings is regularized by internal forces [7].

2.1. Detection and tracking of corners

Corner detection. Corners are points in whose vicinity at least two prominent local orientations can be found, where by local orientation we understand the direction along which the gray-level profile shows the least variations in a certain neighborhood. Corners are characterized by relatively large values of the smallest eigenvalue (λ_2) of a 2×2 tensor used to fully describe a single orientation [2].

To detect corners, we set a threshold over the λ_2-image [9]. Thresholding returns corner surfaces and background. The corner surfaces consist of several points likely to be corners. We consider as true corners that points exhibiting the largest λ_2 value in a neighborhood (Figure 1c).

The assumption on which the ROI tracking is based is that in a coronary angiogram vessels and only vessels do show corners. With the purpose of eliminating potentially spurious corners, the background of the coronary angiogram is equalized – while preserving the grey level difference between background and vessels – by applying a tophat-operator [1] (Figure 1b). On the result obtained after applying the tophat-operator we compute then the second eigenvalue of the structure tensor.

Corner tracking. Once the corners have been detected in two consecutive angiograms, they are tracked with the help of a similarity function consisting of three terms: the first term is based on the Euclidian distance between corners, the second term uses the correlation coefficient, and the third term is based on a mixed orientation vector [2].

A corner travels from a past frame to a current frame over a certain distance which – considering the speed at which a heart moves during a beat, together with the frame rate at which the images are acquired (12 fps) – is usually far smaller than the distance between two neighboring corners in the angiogram. Thus, to find the same corner again in the current frame one should take the closest one. The similarity between two corners can be expressed using the Euclidian distance between their position vectors as:

$$s_p = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{d^2}{2\sigma^2}} \tag{1}$$

where σ weights the relevance of the distance d. In our experiments $\sigma = 1$. Clearly, the smaller the distance, the larger the position-similarity term and $s_p \in \left(0, \frac{1}{\sqrt{2\pi}}\right]$

However, there are cases when distance alone is not enough e.g. for images acquired during a ventricular systole, when the distance the vessels travel between consecutive frames is large. For a successful tracking we need also corner-specific information which we extract in two ways: by investigating the correlation between corner neighborhoods and by the mixed orientation vector. The correlation between corner neighborhoods is given by the correlation coefficient:

$$r = \frac{K(\overline{X_p}, \overline{X_c})}{\sigma(\overline{X_p})\sigma(\overline{X_c})} \tag{2}$$

with K the covariance and σ the standard deviation for the neighborhoods $\overline{X_p}$ and $\overline{X_c}$ for the past and current frames respectively. Theoretically $r \in [-1, 1]$, but in our case $r \in [0, 1]$. To fully describe two orientations, an extended 3×3 tensor is needed which involves second order derivatives. This tensor's eigenvector corresponding to the smallest eigenvalue is called *the mixed orientation vector* and can be used as a corner descriptor, as it contains a full but implicit description of the sought orientations [2]. We propose to use the Euclidian distance between the corresponding mixed orientation vectors d_o to build the orientation-similarity term:

$$s_o = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{d_o^2}{2\sigma^2}} \tag{3}$$

again with $\sigma = 1$.

The similarity function used to track corners between consecutive frames will then be:

$$s = w_1 s_p + w_2 r + w_3 s_o \tag{4}$$

The weights $w_i, i = 1, 2, 3$ can be used to force the tracking to rely more heavily on a certain term. In our experiments however, they were all set to one.

Outlier detection. The tracking may fail e.g. when false corner correspondences are used. Such outliers are detected end eliminated by comparing their similarity against a certain threshold. This threshold is set using a significance test. For the first two frames at the beginning of the analyzed sequence, the similarities of all possible corner pairs are computed. For each past corner, the pair made with a current corner for which the similarity is maximal, is considered as a true pair only if it is also the pair with the largest similarity from among all pairs formed between the corresponding current corner and past corners. The similarities of such pairs are eliminated from the set. What remains are only similarities between outliers which are used to estimate the corner pairs' similarity distribution under the outlier assumption – i.e. H_0. The outlier-detection threshold is then computed such that it corresponds to a significance level $\alpha = 10^{-4}$. Corner pairs with a similarity below the threshold are eliminated (Figure 1d).

2.2. Modeling the ROI

The tracked corners can be used as landmarks to compute the parameters of an elastic transform [3] which models the heart motion. The ROI image – as observed in the past frame – should then be modified according to this model and applied to the current frame to achieve the heart-motion-compensated ROI-tracking. Such a strategy is highly sensitive to the number of landmarks and the presence of outliers and thus an outlier robust implementation of the elastic transform [11] is needed. The results obtained with an elastic transform are usually negatively influenced by the fact that the landmarks are not dense around the ROI due to its typical positioning (Figure 3). Such difficulties can be partially solved if the solution is further constrained e.g. by introducing artificial landmarks.

In a more robust approach to tracking, one could use a physically motivated ROI model which is deformed under the action of forces generated by the corners' displacements between consecutive frames. Such a model can be constructed by sampling the ROI's surface – or only its border – by control points whose displacements are internally constrained by mass, damping, elastic and stiffness terms defined in agreement with the ROI's physical properties – i.e. the corresponding properties of the heart-tissue. Such models can be generated e.g. based on the finite element method (FEM) [10], or on energy minimization methods [7].

We propose here a physically based ROI model whose border is properly sampled by control points. The displacement of these control points is constrained by imposing an energy minimization condition. As there are typically less tracked corners than control points, the corners are used to build an external attraction energy field where the model evolves to a minimum energy position, under the additional influence of internal energy terms, much in the way active contours are defined. The total energy to be minimized for a model m is:

$$E(m) = E_{ext} + E_{int} = E_{ext} + E_{el} + E_s \tag{5}$$

where E_{ext} is the external attraction energy, and E_{int} is the internal energy consisting of two terms which control the elasticity E_{el} and the stiffness E_s of the model.

External attraction energy. Provided the number of tracked corners equals the number of control points and the same set of corners is tracked over the entire analzed sequence, to find the position of the ROI in a current frame one could establish corner-control point pairs and link them by a virtual string so that the motion of the corners is transmitted to the control points. The potential elastic energy which appears when a string anchored at a certain point is stretched over a distance x is: $E_p = \frac{1}{2}kx^2$ where k is a constant describing the elastic properties of the string. The internal energy defined between control points would then condition the behavior of the ROI as it travels to a new position seeking to reach a minimum energy state.

However, the number of corners is typically less than the number of control points and the set of tracked corners can vary from frame to frame. This is because it is practically impossible to track the same corners over an entire heart beat as their appearance varies significantly. Thus, to track the ROI between two consecutive frames, we attach a string between each control point and each tracked corner. The energy of this entire system – which is zero in the past frame – increases in the current frame due to the tensing of the strings as one of their anchor points (i.e. the corners) move over a certain distance. For all possible positions in a certain vicinity of a control point – as it is positioned in the past frame – the elastic energy obtained by spanning the strings between each corner in the current frame and each position are computed. The external energy which would influence that particular control point is then determined by considering at each position the mean contribution over all corners. The external attraction energy will then be:

$$E_{ext}(m, n) = \gamma \frac{1}{N} \sum_{i=1}^{N} E_p^i(m, n) \tag{6}$$

where γ is a weight factor, N is the total number of tracked corners and (m, n) are the Cartesian coordinates of a point in the vicinity. An example is shown in Figure 2. Clearly the vicinity should be large enough to include all possible end-positions of the control point.

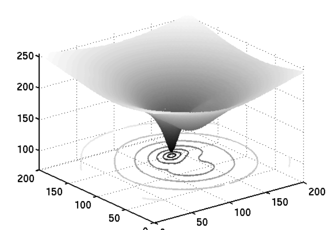


Figure 2. External energy field.

Internal energy. To define the internal energy we place rods between each pair of control points. The elasticity

	c	std	Av	Pv
Results	94.19	3.02	7.87	4.06
Reference	0	5.56	7.23	3.28

Table 1. The results obtained on the test data.

and stiffness of these rods are controlled by special energy terms. The elasticity is modelled by:

$$E_{el} = \alpha \left[\sum_{i=1}^{M} \|\vec{p}_i - \vec{p}_{i-1}\| - L_0 \right]^2 \tag{7}$$

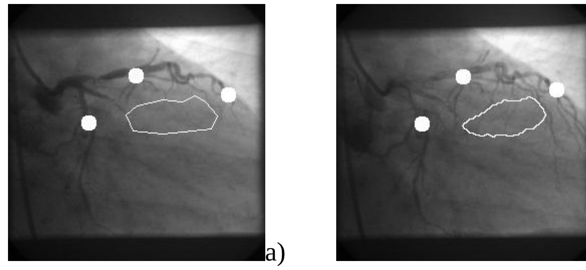
with α a weight factor, $\vec{p}_i = [x_i, y_i]$ the vector containing the Cartesian coordinates for each of the $M+1$ control points and L_0 the average distance betwee them. This energy term increases if the model is stretched or compressed. The stiffness is modelled as:

$$E_s = \beta \sum_{i=1}^{M-1} \|\vec{p}_{i-1} - 2\vec{p}_i + \vec{p}_{i+1}\|^2 \tag{8}$$

with β a weight factor. This energy term increases if the model is bended. As we model a closed curve, $\vec{p}_{-1} = \vec{p}_M$ and $\vec{p}_{M+1} = \vec{p}_0$, thus the sum in equations (7) and (8) runs from 0 to M. Adjusting the parameters α, β and γ controls the relative importance of the respective energy terms inducing thus a specific model behavior.

3. Results

We have tested our algorithms on a number of seven sequences of 15 to 28 images each, showing only the complete state. The angiograms had a resolution of 512×512 pixels and were acquired at a framerate of 15 fps. To increase the processing speed during experiments, the resolution was reduced to 256×256. The size of the tophat-window was chosen to be nine pixels. The size of the derivative kernels used to compute the orientation tensor was chosen to be seven pixels and that of the pixel-neighborhood where the orientation tensor is computed was again nine pixels. The energy weights were chosen: $\alpha = 15$, $\beta = 3$, $\gamma = 5$. The sequences had neither table nor patient movement and were acquired in clinical routine with different projection angles. We have computed several measures to show that the result is conform with an expert's opinion, and that it follows the variation of the heart surface. As reference we have artificially built a failed tracking result for each sequence by defining a static rectangular ROI in the lower left corner of each image. We have then computed all measures again for this tracking result. The results are given in Table 1 and an example is shown in Figure 3. To verify if a tracking result is in agreement with an expert's opinion, we have defined



a) b)

Figure 3. First (a) and last (b) image of an analyzed sequence with markers and ROI.

by hand the ROI in each frame of the analyzed sequences and defined correct and incorrect tracking results in relation to this ground truth. A result was considered correct if the overlap between the tracked ROI and the manual groundtruth was larger than 50%. We have computed the mean percentage of correct classifications over all sequences (c).

To verify whether the tracked ROI keeps its position relative to the projected heart surface, we have marked three vessel-points distributed over the entire vessel tree such that they are situated around the tracked ROI. We have typically chosen bifurcations and bendings of the main vessels (Figure 3). Then we have determined the center of mass of these three points and the center of mass of the ROI and computed the Euclidian distance between them in each frame of the sequence. We have then computed the standard deviation in each sequence and the mean over all sequences (std).

To verify whether the tracked ROI changes its surface in agreement with the changes of surface of the heart, we have computed the area and perimeter of the triangle defined by the three marked points and then we have computed their variation in percents between consecutive frames. We have compared this with the same variation computed for the ROI's area and perimeter by taking the difference between the ROI and the triangle variation and then computing the mean of absolute differences over the entire sequence. We have then taken the mean over all sequences: Av and Pv for area and perimeter respectively.

4. Discussion, conclusions and outlook

The results show that the proposed ROI tracking method is able to follow the movement of the heart and that the tracking results are in agreement with human intuition. However, although the ROI as a whole follows the heart, it seems that its area and perimeter do not follow the local variations of the heart tissue but they remain approximatively constant. One possible reason is that a majority of the tracked corners are typically situated on the same vessel or on vessels that were very close and thus they are representative for the motion of the heart, but they are not representative for the local variations of the heart tissue in and around the ROI. We believe that a 50% overlap between the tracked ROI and the real MB region suffices for an automatic estimation of the MBG by a robust feature. Experience shows that it is practically impossible to define the ROI to include all and only the blush region. Thus the ROI will normally include also regions where no blush has been observed. To measure the blush in each frame, we propose to use a low-percentile of the histogram of the gray levels from within the ROI. At the same time, vessels entering the ROI should be detected and eliminated. The MBG can then be computed by comparing the curve of percentile-feature over frame index for an ill coronary artery with that obtained for a healthy coronary artery of the same patient. Special care has to be taken to handle the effects of the automatic gain control (AGC) – which keeps the overall-brightness in the analyzed images constant.

The surface of the heart which is observable in an angiogram varies as a consequence of the heart changing its volume. The coronary vessels follow this variation by bending and stretching, thus many of the corners change their appearance sometimes drastically over a heart beat. Instead of tracking a set of particular corners over an entire sequence, we track different sets of corners only between consecutive images, as only in such a case the change in appearance of most corners is small enough – considering the speed of the heart beat in relation with the frame rate – to permit tracking. It is very important for the tracking that the corners do not change their appearance drastically between consecutive frames. This may happen e.g. during the ventricular systole when the speed at which the heart moves reaches a maximum. Thus it is expected that the tracking improves with the frame rate.

By its energetic formulation and by its adaptive approach to corner tracking, the ROI-tracking is also marginally robust against slow, small-amplitude table and patient movement. However, to analyze the MB in those cases when it extents over the washout, and generally for a precise tracking, motion-compensation clearly is needed. Ideally the table should not be moved during image acquisition and the patient should remain still. Depending on the angle under which the the X-ray imaging system looks at the patient, the coronary vessels can be imaged under different projections. Only those projections where the vessels show a minimal overlap are suited for processing. Otherwise e.g as the heart has also a rotation motion this may result in some vessels traveling upwards and some downwards in the projection images, then in a worst case scenario, the algorithm will track alternatively corners on vessels traveling in opposite directions, resulting in a stationary ROI.

We have presented a new method for the tracking of a heart-motion-compensated ROI which is defined by hand in X-ray projection images of the heart. This should then allow an observer-independent measurement of the MBG. The behavior of the ROI model is controlled by the energy weights which gives our approach adaptability and robustness. Heart-motion-information is extracted from complete-state-images by tracking the vessel-corners between consecutive images. Corner tracking is done using a similarity function which takes into account: the distance between corners, correlation between their neighborhoods and similarities in their orientations. Falsely tracked corners are detected by comparing the corresponding values of the similarity function with a threshold and accepting only those above it. The tracked corners are then used to fit a physically-motivated ROI model which evolves under internal and external constrains – expressed as energy terms – to a position with minimal energy. Currently we model only the border of the ROI. In a similar manner it is possible to model the whole ROI surface by sampling it with control points and linking the them by elastic rods. Also an additional energy term can be introduced to model the mass of the ROI. A more adaptable model can be obtained like this.

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