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Model-driven segmentation of X-ray left ventricular angiograms

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Chapter 7

Summary and Conclusions

7.1 Summary

The high prevalence of cardiovascular diseases worldwide underlines the importance of cardiac imaging based diagnostics. In assessing cardiac function, X-ray left ventricular angiography has been an important clinical standard for years and, despite the rapid development of both MRI- and MSCT-based techniques, it is expected to retain high value in daily clinical practice. As long as X-ray coronary angiography is employed during cardiac catheterization procedures, X-ray LV angiograms will be acquired most often in the same session as well. However, the manner in which LV angiograms are currently analyzed leaves room for improvement. The expert cardiologist either visually inspects the patient image data, estimates the cardiac ejection fraction and observes possible wall motion defects. Alternatively, patient analysis requires the manual delineation of the endocardial boundary in both the end diastolic and end systolic image frames. The latter method obviously is preferable, because it introduces a certain diagnostic standard and it enables patient follow-up studies. However, manual contouring is characterized by a high workload for the cardiologist or technician, it is time consuming and prone to inter- and intra-observer variabilities. The need for an automated technique for the analysis of X-ray LV angiograms therefore has been apparent for a long time.

The main goal of the work presented in this thesis was to develop an automated algorithm for the delineation of the cardiac left ventricle in the ED and ES phase in X-ray LV angiography, that would be robust enough so that it can be used in routine clinical practice. The general approach to achieve a higher degree of automation in the interpretation of X-ray LV angiographic images is based on the application of Active Appearance Models. With these statistical models of shape and appearance, an automatic delineation of the left ventricle can be realized. This thesis has identified both the challenges of automatic interpretation of X-ray LV angiograms, and the limitations of Active Appearance Models in general and in their application to segment the left ventricle in angiographic images. In exploring possible ways of solving this medical image processing problem, the following sub-goals were formulated in Chapter 1:

- The observed redundancies and similarities between the ED and ES frames should be exploited by a combined modeling of the shape and image intensity characteristics of both frames in the AAM framework.
- The sensitivity of AAM segmentation with respect to the unstable behavior of the error criterion should be decreased.
- Optimal settings regarding the size and composition of the model training data set must be investigated to increase AAM segmentation performance.
- The effect of model over-constraining towards the training data should be neutralized to improve local LV border delineation.

- The clinical relevance of the developed methodology should be demonstrated.

Chapters 2 through 6 provide a detailed description of the construction, benefits and clinical relevance of an automated methodology for the delineation of the left ventricle in X-ray angiograms.

In Chapter 2 the Multi-View Active Appearance Model was introduced, in which the desired combined modeling of the ED and ES image frame of an X-ray LV angiographic image sequence was realized. In this new extension on the general AAM framework, the shape statistics of both frames were correlated by concatenating the ED and ES shape vectors for every training sample and applying a Principal Component Analysis on the concatenated vectors. An identical method was applied to the image intensity vectors of the ED and ES training data. By further concatenation of the resulting shape model and intensity model, and applying PCA on the data, the Multi-View Active Appearance Model was constructed. The ED and ES scale, orientation and position were modeled separately, to accommodate for trivial pose differences. Another novelty introduced in Chapter 2 was the sequential application of two Multi-View AAMs in the segmentation of the left ventricle in the target ED and ES images. The first model was the proposed ‘general’ Multi-View AAM, the second was a dedicated model that was employed to improve local LV boundary delineation. In this latter model, only the image intensity characteristics in the direct vicinity of the LV border were modeled, discarding the majority of image information of the LV blood pool.

The benefit of these methodological innovations of the AAM framework were tested by applying the models on a patient data set of 70 subjects, describing a variety of pathologies and image acquisition artifacts. Without manual initialization a performance of 81% was achieved. The remaining 13 failure cases were subsequently initialized manually, by which the robustness of the algorithm was improved to 87%. Good correlation was observed between the projected areas and derived volumes of the manually drawn reference contours and the automatically generated contours. However, the automated algorithm showed a minor underestimation of the projected areas and derived volumes. Also the border positioning differences between the manual and automated approach were generally small and the calculated ejection fractions did not show a systematic error.

The negligible differences in robustness between ED and ES convergence and the similarity in the linear regression trends and correlation coefficients, demonstrated the advantageous effect of the Multi-View AAM. However, the benefit of the boundary AAM seemed arguable. Although a possible positive effect could be observed occasionally, systematic improvement could not be proven.

Chapter 3 described the application of the Multi-View AAM approach in two different modalities. First in X-ray LV angiograms, similar to the work presented in Chapter 2, and second in cardiac MRI images. With respect to Chapter 2, an optimization was made of the percentages of shape and image intensity information that were incorporated in the model, during the training of the AAM.

Applying the Multi-View AAM in cardiac MRI resulted in a model that was capable of combining shape and image intensity information of three views of one anatomical object, showing three substantially different geometrical shapes.

For X-ray LV angiography the same data set as in Chapter 2 was used. Without manual interaction, convergence was achieved in 87% of the cases. A small but statistically significant underestimation of the automatically defined projected LV areas was observed, while the automatically derived area ejection fraction showed a slight statistically significant overestimation.

For cardiac MRI the methodology was tested on a data set of 29 patients, providing short-axis views, two chamber views and four chamber views. The Multi-View AAM successfully segmented all three views in 27 cases. In the other two data sets only one contour did not converge properly, resulting in an overall success rate of 98%. Good correlation was observed between manually and automatically derived surface areas for all three views. Differences between manual and automatic area calculations proved to be statistically insignificant. No volumetric reconstruction was intended in this experiment. Hence, no registration between the three different views was performed. In future experiments more views (a stack of short-axis views, combined with the two chamber and four chamber views) could be modeled simultaneously, from which a 3D reconstruction could be made by registering all views.

The results presented in Chapter 3 proved that poor left ventricle definition in one view could be overcome by utilizing image information from a corresponding view. Furthermore, the generic potential of the Multi-View was underlined by the excellent performance in the cardiac MRI study, segmenting substantially different geometrical shapes simultaneously.

Chapter 4 presented a study into the optimal characteristics of a data set in training Active Appearance Models for medical image segmentation purposes. Three issues in construction a training data set were addressed, focusing on the application of AAMs in segmenting the left ventricle endo- and epicardial ED and ES contours in short-axis cardiac MRI images. First the optimal size of the data set was assessed. Second, the influence of the data composition in terms of healthy subjects versus patients was investigated and third, the effect of the data composition in terms of image material from different MRI scanners was explored.

When the training of the AAM and the model fitting were performed on short-axis cardiac MRI image data from healthy subjects, an optimal data set size was found to be approximately 200 to 250 images. No experiments on pathological data were executed, but numbers for such data sets were expected to be higher. In general, when increasing the number of training samples, the AAM segmentation performance trend showed asymptotic behavior, rather than a deterioration of accuracy when a surplus of training data was used.

Three different compositions of training data were constructed to assess the influence of healthy subject examples and patient data examples. For one model the data consisted of 80% healthy subjects and 20% patients, for another model healthy subjects and patients were equally represented and a third model was constructed for 20% on healthy subjects data and for 80% on patient data. In a cross validation study the Active Appearance Model that was composed of 80%

healthy subjects data and 20% patient data, showed the best overall performance. In the studies performed and discussed in Chapter 4, data material of three different MRI vendors was available. This data was used to assess whether an AAM constructed from images from multiple scanner brands would outperform a model that was trained on vendor specific image data. The obtained results proved the contrary; vendor specific Active Appearance Models showed a higher accuracy in automatic left ventricular contour delineation and ejection fraction calculation.

In Chapter 5 the Multi-View Active Appearance Model, first explored in Chapters 2 and 3, was further optimized for automated segmentation of the ED and ES frames in X-ray LV angiography. A novel model matching scheme, the Controlled Gradient Descent, was developed, in which the updates of the model parameters were evaluated and only the most significant updates were processed. Furthermore, a dedicated Dynamic Programming algorithm was employed to improve local border delineation. The search area of the Dynamic Programming scheme was restricted to the direct vicinity of the final AAM segmentation result. Another novelty was the incorporation of information on the contraction dynamics of the left ventricle by constructing the cost function from both image features and from features of a subtraction image (ES minus ED). The described approach was validated both as a semi-automatic method, in which the upper and lower valve points and the apex position were specified, and as a fully automatic method.

The semi-automatic algorithm attained a performance of 100% for ED segmentation and 99% for ES segmentation, in which only one failure was observed. Border positioning errors were generally low, also in examples with a poor LV definition. Although a slight underestimation was perceived, excellent correlation was observed between the manually and semi-automatically derived volumes and the resulting ejection fractions ($R^2 = \{0.99; 0.95; 0.84\}$ for ED, ES and EF respectively). Differences between manual and semi-automatic results were found statistically insignificant.

The accuracy of the fully automatic algorithm was comparable to the accuracy of the semi-automatic method. The correlation with the manual reference was similarly good ($R^2 = \{0.99; 0.96; 0.82\}$) and besides the ED calculation, all differences were found statistically insignificant. However, the robustness of the fully automatic approach proved to be inferior, converging in 91% of the ED and 83% of the ES cases.

The efficacy of the four novel elements of our approach (Multi-View AAM, Controlled Gradient Descent, dedicated Dynamic Programming as post-processing step and the incorporation of cardiac contraction dynamics in Dynamic Programming) was validated by comparison with baseline AAM and Dynamic Programming techniques. The Multi-View AAM resulted in a tremendous improvement of the segmentation results for ES, while the initial high quality results for ED remained unaffected. Both the ED and ES segmentation results were significantly improved by the Controlled Gradient Descent algorithm. This effect was mainly observed in the fully automatic approach. The hybrid application of the Multi-View Active Appearance Model and Dynamic Programming outperformed the separate utilization of both methods. Furthermore, the benefit of the incorporation of cardiac contraction dynamics in Dynamic Programming was

clearly shown.

The semi-automatic algorithm showed better results than previously reported approaches. It was clearly proven that, due to the wide range of information that was incorporated in the algorithm, it had the capacity to mimic the drawing characteristics of a clinical expert. The resulting algorithm satisfied the first, second and fourth requirements as formulated in Chapter 1. Because the errors in the volume calculations were within the limits of inter-observer variability, the fifth goal, clinical relevance, was also suggested.

Chapter 6 investigated whether the proposed algorithm could be viable in daily clinical practice. For this clinical validation study, two expert cardiologists were asked to analyze a set of 30 patient studies. This was done in two ways; first by drawing the left ventricular contours manually, and second by using the proposed automated method. In the latter situation, the two experts had to manually localize the upper and lower aortic valve point and the apex for initialization. Furthermore, the cardiologists were allowed to correct the automatically generated contours by hand. The focus of the experiments was to gain insight in the accuracy, workflow efficiency and inter- and intra-observer variabilities when using the automated methodology.

In comparing the automated and manual LV outlines, no statistically significant differences were observed. For both the ED and ES image frames an excellent correlation was found between the volumes, calculated by the two approaches: $R^2 = \{0.96; 0.99\}$ for ED (for the two cardiologists) and $R^2 = \{0.96; 0.98\}$ for ES. Also the derived ejection fraction showed good correlation: $R^2 = \{0.92; 0.94\}$. Only a small systematic difference of 2% ejection fraction was observed when comparing the automated results with the manual results.

The overall reduction in the analysis time required for a patient study was 26%, from 4.2 minutes to 3.1 minutes. In addition, according to the expert cardiologists, 60% of the automatically generated ED contours did not need any manual modification. Obviously for ES this number was lower: 11%. However, when editing was required, only 19% of the ED contour length and 25% of the ES contour length was manually corrected.

The inter-observer variability was reduced when the automated methodology was used. The point-to-curve difference between both experts dropped from 0.75 mm to 0.64 mm for ED and from 1.48 mm to 1.33 mm for ES. Also the obtained intra-observer variability was low: 0.82 mm for ED and 1.08 mm for ES.

The results presented in Chapter 6 showed that by utilizing the proposed automated methodology a considerable reduction could be achieved in patient analysis time, manual contouring effort and inter- and intra-observer variabilities, while the calculated ED and ES volumes were equally accurate as manually derived volumes. Hence, these results proved the applicability of the method in daily clinical practice to optimize the analysis workflow for X-ray left ventricular angiography.

7.2 Conclusions and Future Work

Based on the results presented in Chapters 2 to 6 it can be concluded that all formulated goals have been achieved to a large extent. The coupling of different views of one single object significantly improved the AAM segmentation, the robustness of the model has been improved and the accuracy in local LV border delineation has been increased. When utilizing the created algorithm in clinical practice, it proved to decrease the analysis time, the manual effort and the inter-observer variability, while providing ED and ES volumes that did not show any statistical difference from manually derived volumes.

Given the satisfactory results of the presented methodology, the algorithm presented in Chapters 5 and 6 has been recently incorporated in a clinical software package (QAngio® XA, by Medis medical imaging systems bv, The Netherlands), which is sold worldwide.

Though the overall performance of the proposed methodology was satisfactory, some further improvements can still be made. In Chapter 4 insight was gained in the optimal composition of the model training set. However, this knowledge was not yet integrated in the proposed algorithm.

Furthermore, the resulting Multi-View AAM was trained only on manually drawn LV contours from one clinical expert. As a result, Chapter 5 proved the remarkable mimicking behavior of the algorithm, showing a clear bias towards the preferred contour drawing characteristics of the expert cardiologist. Although the clinical validation of the model, performed in Chapter 6, showed no statistical difference between manually and automatically derived ED and ES volumes, a model based on contours from a variety of different clinical experts is expected to improve the standardization of the analysis of X-ray LV angiograms even further.

Due to the availability of clinical data, all the experiments described in this thesis concerning X-ray LV angiography were based on single-plane angiograms. Hence, the applied Multi-View Active Appearance Model was constructed on only two images; the ED and ES projections in the 30° right anterior oblique view. A more comprehensive model description and possibly better segmentation results could be obtained when the Multi-View AAM is constructed from bi-plane acquisitions.

Zhang *et al.* [1] showed the additional value of statistical shape models of the heart, in distinguishing between normal subjects and pathological cases. The two strongest modes of variation of a 3D or 4D statistical model of the left and right cardiac ventricle proved to be good classifiers to separate normals from Tetralogy of Fallot patients. Similarly, Suinesiaputra *et al.* showed that the strongest principal component of a statistical model of short-axes MR images could discriminate between normal subjects and infarct patients [2]. Furthermore, when the statistical shape model was constructed using independent component analysis, the infarcted region could be localized more precisely [3]. Future work in employing the proposed methodology as described in this thesis could include a similar approach in recognizing various pathologies. However, because the proposed method is a hybrid algorithm combining the Multi-View Active Appearance Model and Dynamic Programming, the contours provided by the Multi-View AAM are not the final result. Hence, using Dynamic Programming as a

post-processing tool to refine the AAM contours, a discrepancy between the resulting model parameters and the final endocardial contours is created. This might reduce the efficacy in distinguishing between normal and pathological cases. In addition, improvements in model initialization could be considered. The results in Chapter 2 pointed out that the accuracy in local border detection was considerably lower in the vicinity of the upper and lower aortic valve points and the apex, when compared to overall border delineation accuracy. Because of the sensitivity of the area-length method to sub-optimal placement of these three points, the implemented clinical version of the algorithm required the manual localization of these landmarks. To establish a fully automatic delineation algorithm, dedicated Active Appearance Models describing only the valve plane or the apex could be considered. This could be either employed to provide image coordinates of the desired landmarks, or it could be implemented similarly to the method proposed by Roberts *et al.* [4].

A final modification to come to a fully automated methodology is the design of an algorithm to automatically extract the optimal ED and ES frame from a full X-ray left ventricular angiographic image sequence.

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