Model-driven segmentation of X-ray left ventricular angiograms

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Chapter 6

Automated Left Ventricular Delineation in X-Ray Angiograms: A Validation Study

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Automated Left Ventricular Delineation in X-ray Angiograms: A Validation Study
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Abstract

Recently an automated analysis approach for X-ray left ventricular (LV) angiographic studies was proposed. This particular study aims to assess the clinical potential of this approach. Over the past 30 years much research has been carried out to develop a technique with automated contour detection of the left ventricular outline in the end-diastolic (ED) and end-systolic (ES) phases. Very few have made it into clinical practice. Our latest approach is based on innovative model-based image processing techniques. Two expert cardiologists analyzed 30 patient studies both by contouring the LV manually and by using the proposed automated methodology. In the latter procedure the experts were allowed to edit the automatically generated contours manually. The manual, automatic and edited automatic contours were compared, focusing on accuracy, workflow efficiency and inter- and intra-observer variabilities. No significant differences between the automatically derived and manual LV volumes were observed. The average patient study analysis time was reduced by 26%, from 4.2 to 3.1 minutes. When editing was required, 19% of the ED and 25% of the ES contour length needed manual correction. Furthermore, a reduction in inter-observer variability of 12.4% was observed. Employing the proposed automated methodology for X-ray LV angiographic study analysis, a considerable reduction in required analysis time and manual effort is achieved. Since the acquired results are of clinically acceptable quality and the inter- and intra-observer variabilities are reduced, this automated approach has the potential to optimize the analysis workflow for X-ray LV angiography in clinical practice.

6.1 Introduction

A quick and reliable assessment of cardiac function is essential in the diagnosis of patients with ischemic heart disease and possible heart failure. Various imaging modalities are available in clinical routine. Echocardiography is used for quick assessment of global cardiac function and valvular dysfunction. Both MRI and CT are evolving towards reliable standards for cardiac imaging based on the fact that the heart anatomy is available in three dimensions. Nonetheless, X-ray left ventricular (LV) angiography still is a widely used technique, due to it's high spatial resolution and widespread clinical availability. The left ventricular angiogram is acquired during each cardiac catheterization procedure and provides essential information for the (interventional) cardiologist and cardiac surgeon.
An objective and reproducible assessment of the cardiac ejection fraction requires the delineation of the left ventricular outline in the end-diastolic and end-systolic frames, and the subsequent calculation of the corresponding volumes, from which the ejection fraction can be derived [1]. Once the outlines are available other regional parameters can be derived as well.
Despite a higher resolution in comparison with MR or CT images, the general image quality in LV angiography is relatively low. Since it is a projection image, other anatomical structures, such as ribs or the diaphragm (when a patient cannot

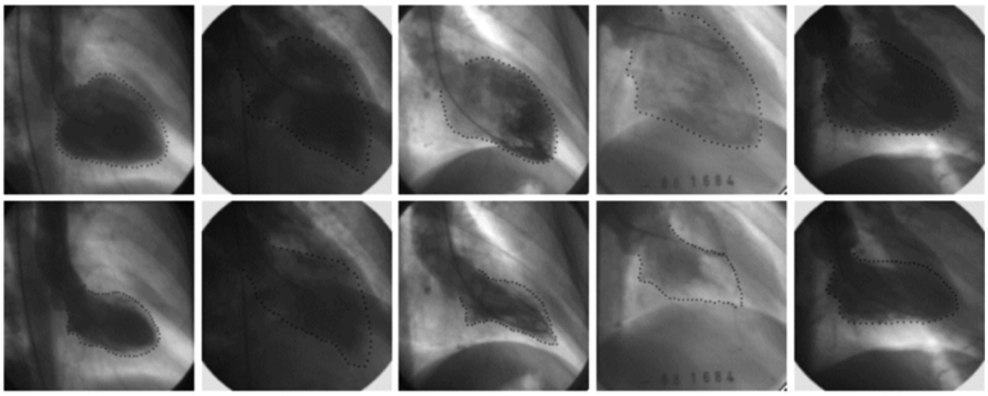

Figure 6.1: Typical examples of LV angiograms (upper row = ED; bottom row = ES): good contrast (a), poor contrast (b), uneven contrast agent distribution (c), partial overlap with the diaphragm (d) and substantial shadows caused by the shutter (e), expressed in this example as a diagonal dark band. The black dotted lines represent the LV boundaries as determined manually by an expert.

comply with the requirement of breath holding), can occlude the left ventricle in an X-ray projection. Additionally, shadows induced by the shutter of the imaging device may overlap with the LV, making the LV border harder to delineate. The biggest problem with LV angiography border detection however, is the presence of the trabeculations and the papillary muscles. Depending on the amount of contrast still visible between these trabeculations, it is difficult to decide where the actual boundary lies. All these challenging aspects make the analysis of LV angiograms difficult, time consuming and prone to inter- and intra-observer variability (Figure 6.1).

Over the past 30 years various approaches have been developed for the automated delineation of the left ventricular contours [2-16]. The fact that so many researchers have attempted to solve this problem over such a long period underlines that it is a difficult image recognition problem. One of the main recurrent conclusions in recent literature is that this challenge of achieving a sufficiently high degree of robustness, that is acceptable in clinical practice, cannot be solved without a priori knowledge about the ventricular shape. One such method with a limited amount of a priori information was developed towards a commercial application [8]. However, our approach represents a next generation in automated LV analysis [16]. The method, based on Active Appearance Models [17,18], has been described and technically validated in [16]. This paper illustrated excellent results and, as the main conclusion, showed the algorithm's capacity of mimicking the drawing behavior of expert cardiologists. However, it did not investigate any improvements in analysis speed and workflow in a clinical setting.

The goal of this chapter is to investigate the clinical efficacy of this novel methodology. To this end the algorithm was incorporated in a clinical software package to evaluate three performance aspects:

- Speed and efficiency of the workflow.
- Accuracy with respect to manual analysis.
- Inter- and intra-observer variability.

On all these points a quantitative comparison between the automated system and the manual analyses has been carried out. The software package that has been used in these experiments is the QAngio® XA package by Medis medical imaging systems B.V., which until recently only provided manual contour drawing facilities.

6.2 Materials and Methods

6.2.1 Image Data Acquisition and Processing

Thirty randomly selected patient studies, all acquired at the department of cardiology at the Leiden University Medical Center (LUMC) for diagnostic purposes, were evaluated. These cases were selected from the data base of the department, and served only for validation purposes in this study; as a result, informed patient consent was not necessary. All studies were single-plane 30° right anterior oblique view acquisitions. Each study was a full image run consisting of approximately seven to nine cardiac cycles, covering the arrival and washout of the contrast fluid. Two eligibility criteria were pursued in the data selection and analysis procedure: within an angiographic image sequence there should be at least one pair of an ED frame and subsequent ES frame available in which, according to the cardiologist, the ventricle was acceptably filled with contrast medium. Furthermore the upper valve point, lower valve point and apical point should be visible in and around the two frames that were to be evaluated.
Two expert cardiologists examined the data set in two ways: first by drawing the ED and ES contours manually on a LV workstation, and second by using the automatic method presented in [16]. In the latter situation, the cardiologists were allowed to edit the contours when the delineation was not fully satisfactory. To prevent possible influence of the automatically generated contour on the drawing behavior of the expert, the experts were asked to perform the manual contouring first.

6.2.2 Automatic Contour Detection

Automating the process of delineating the left ventricle in X-ray angiograms cannot be achieved without the integration of a priori information. Knowledge about the expected shape and image intensity characteristics of the LV is essential. This knowledge can be captured and described by an Active Appearance Model (AAM), which is a statistical model trained on information from a large data set of manually delineated example images. When applying such a model to automatically detect, for example, an anatomical structure in a medical image, the model deforms its shape and image intensity representation to optimally fit the underlying image. By maintaining these deformations within the statistical boundaries of the training data set, only plausible shapes are found.

AAMs have been widely applied in segmenting medical images, as summarized in [19]. As mentioned previously, in X-ray angiography the left ventricle is notoriously difficult to segment in the ES image frame and in general AAMs will perform poorly in these images. To improve the automatic delineation results, Multi-View AAMs have been created, in which the shape and intensity of the LV in both the ED and the ES frame have been modeled in a combined fashion [14-16]. As Oost *et al.* described, this combined modeling improves the overall segmentation results significantly [16].
It is generally known that AAMs are a very strong tool for fitting the model globally to the object of interest. However, when no clear edges are available, or the overall contrast of the image is not optimal, the local border delineation results are not satisfactory. In the method described by Oost *et al.* and used in this study, local border detection is improved dramatically by using a dedicated Dynamic Programming algorithm as a post-processing step, in which both image information and LV motion characteristics are incorporated [16]. A general and elaborate description of AAM training and matching can be found in [18].

The AAM used in this validation study was constructed from 65 ED example images and 65 ES example images in which the LV contours were drawn manually by an expert cardiologist.

6.2.3 Analysis Workflow

Manual Workflow
In manual patient study analysis, the expert cardiologists were asked to first calibrate the image data by means of catheter calibration, then select a properly displayed ED frame, draw a contour curve delineating the LV using the workstation's mouse, select the subsequent ES frame, and once again delineate the LV. After these actions the mitral valve position could be adjusted along the drawn contour and a pane, containing the calculated ejection fraction and the results of a set of wall motion models (Slager model, centerline model and Stanford model), was presented to the user for evaluation purposes. After inspection of this pane the study was saved and closed.

Automated Workflow
When analyzing the image sequences automatically, the workflow was similar, apart from the drawing activities: after selecting the ED frame, the upper valve point, lower valve point and apical point had to be localized by mouse-clicks. This could be done in arbitrary order. Subsequently the ES frame was selected. After again identifying the upper valve point, lower valve point and apical point, the program automatically started the automatic delineation of both ED and ES

frames. Generated contours could be edited by redrawing unsatisfactory contour regions manually with the mouse. Further handling was identical to the fully manual investigation of a patient study.

Time Recording
During all analyses, the software package created a log file in which the timing of activities was recorded. This data was used to evaluate differences in time requirements between the manual and automatic segmentation of the LV. Hence, experts were asked to perform all examinations in a fluent fashion, without other activities intervening.

6.2.4 Comparison Metrics and Statistical Analysis

In terms of generated ED and ES contours, the output of this study is threefold: manually drawn contours, automatically generated contours and edited automatic contours. Differences in accuracy and required time are presented by comparing these contours interdependently, in terms of the following quantified metrics.

Time Requirement
Two measures were used to assess differences in time requirements between manual and automated analysis of patient studies. First, a comparison was performed of the time interval from the start of the drawing (manual analysis) or landmark identification (automated analysis) in the ED frame until acceptance of both ED and ES contours. Second, the entire time required from opening a study until closing the study was evaluated. Because a different approach in contour generation might lead to different evaluation of the quantified clinical data by the expert cardiologists, the total study duration can provide additional insight. From hereon these two time periods will be referred to as 'LV function analysis duration' and 'total study duration'.

Volumetric Comparison
Estimating LV volumes from drawn contours was done by means of Sandler and Dodge's area-length method [1], formulated as:

$$V = \frac{8A^2}{3\pi L_A} \tag{6.1}$$

in which A denotes the projected surface area and L_A is the distance from the upper aortic valve point to the apex. To correct for shape irregularities and the presence of papillary muscles and trabeculations, a regression equation was applied [20]. Linear regression and Bland-Altman analysis were used to determine volume and ejection fraction relationships between manually traced, computer determined and edited automatic LV outlines. A two-tailed paired samples t-test was applied to investigate systematic errors, where a p-value smaller than 0.05 was considered statistically significant.

Contour Comparison

All drawn or calculated contours are defined as a discrete set of points. When comparing two differently generated contours with each other, point-to-curve differences were measured mutually and averaged. A point-to-curve distance is herein defined as the geometrical distance from a single discrete point of contour A to the closest interpolated position on contour B.

An additional measure is the percentage of the contour length that was edited manually. This percentage represents the amount of effort required to achieve clinical quality contours in cases where the automatic contours are sub-optimal. When comparing an edited automatic contour with an automatically generated contour, the percentage of required editing can be simply derived. However, when comparing the manually drawn contours with the edited automatic contours, both could be regarded as gold standard, because both contours have been approved by the expert. The same holds when comparing a contour approved by expert cardiologist #1 with a contour ratified by expert cardiologist #2. To evaluate this, a comparison was made of the amount of editing when for example expert cardiologist #1 would evaluate a contour generated by expert cardiologist #2. A point-to-curve distance exceeding 8 pixels (i.e. approximately 2 mm.), persisting over at least 3 percent of the total contour length, was defined as the threshold for editing requirement. This definition is designed to include significant local detail differences, while longer contour parts with insignificantly low point-to-curve differences are excluded.

6.3 Results

Evaluation of the results was carried out on 29 of the 30 initial data sets. After inspection one outlier was detected in which the apical area of the LV moved out of the image frame. All experiments related to automatic or edited automatic contours of MD #1 comprise of 28 data sets, due to an error in saving one of the studies.

Although all studies were calibrated 4 times (before manual analysis and before automated analysis, by 2 MDs), the average calibration factor of 0.273 mm/pixel was used for comparison purposes.

6.3.1 Ejection Fraction and Volumetric Accuracy

To asses the clinical validity of the proposed automated method, the calculated ED and ES volumes and the calculated ejection fractions were compared with the manual contour analysis results.

Excellent correlation was found when comparing the manual and edited automatic results, with all correlation coefficients larger than $R^2 = 0.95$ (Table 6.1). All comparisons were found statistically insignificant: $p = 0.19$ (ED) and $p = 0.08$ (ES) when analyzed by expert cardiologist #1 and $p = 0.57$ (ED) and $p = 0.05$ (ES) for expert cardiologist #2. Bland-Altman plots showed a slight but statistically non-significant overestimation of ES volumes, when using the automated method. For

ED no clear over- or underestimation could be observed (Figure 6.2). Bland Altman analysis did not show dependence of the error on LV volume.

Also for the ejection fractions good correlation was achieved, with correlation coefficients $R^2 = 0.92$ for expert cardiologist #1 and $R^2 = 0.94$ for expert cardiologist #2 (Table 6.1, Figure 6.3). In a paired samples t-test, differences were found to be statistically insignificant ($p = 0.06$) for expert #1 and significant ($p = 0.02$) for expert #2. The good correlation is supported by the small difference in the derived ejection fraction between manual and edited contours, which is approximately 2% ejection fraction for both experts (Table 6.2).

6.3.2 Workflow Speed

In 23 out of 29 cases, MD #1 was able to analyze a patient in a shorter time period with the presented automated algorithm than by drawing contours by hand. For MD #2 this figure was 23 out of 28 cases, since the audit trail showed discontinuity in the workflow in one case. The speed gain in terms of LV function analysis duration was 15.7%. The average total study duration even decreased with 26.1% when using the automated method (Table 6.3).

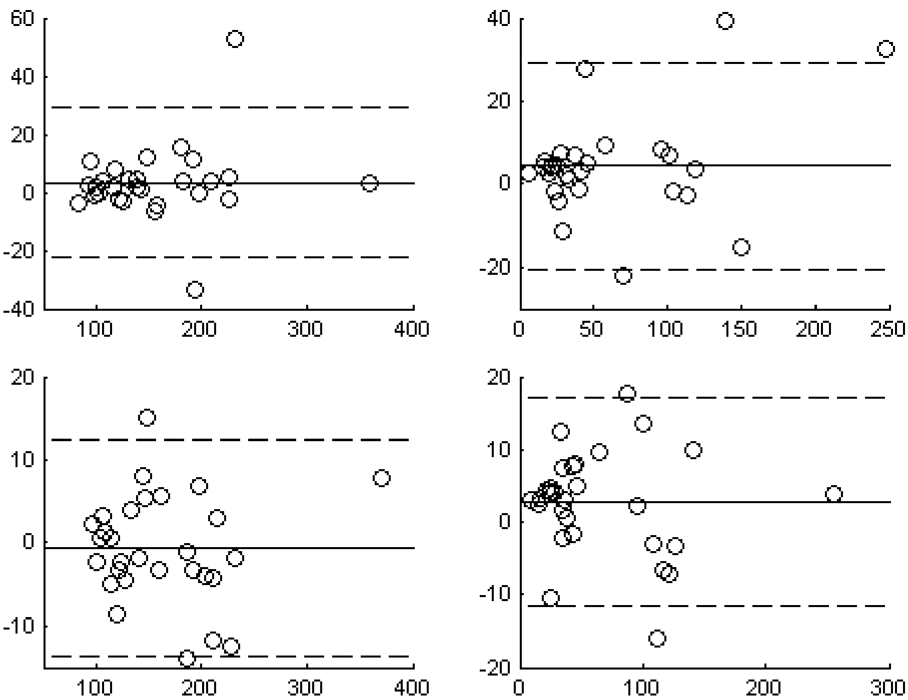

Figure 6.2: Bland-Altman analysis of manual and edited automatic volumes. The top row shows the results for expert #1, the bottom row shows expert #2 results. The ED results are shown on the left-hand side, the ES results are shown on the right. y-axes denote edited minus manual, x-axes denote averages.

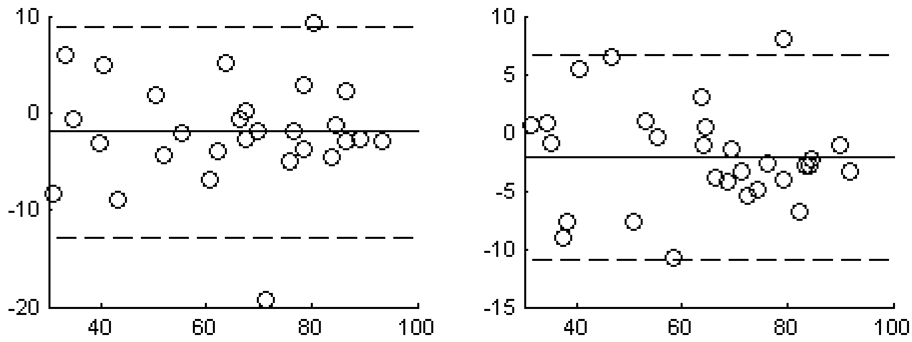

Figure 6.3: Bland-Altman analysis of manual and edited automatic ejection fractions, for expert #1 (left) and expert #2 (right). y-axes denote edited minus manual, x-axes denote averages.

	MD	Regression Equation	R^2	p
Edit vs. Man ED	1	y = 1.01x + 1.38 [ml]	0.96	0.19
Edit vs. Man ES	1	y = 1.06x + 0.99 [ml]	0.96	0.08
Edit vs. Man EF	1	y = 0.96x + 0.74 [%]	0.92	0.06
Edit vs. Man ED	2	y = 0.99x + 0.57 [ml]	0.99	0.57
Edit vs. Man ES	2	y = 0.98x + 4.21 [ml]	0.98	0.05
Edit vs. Man EF	2	y = 0.95x + 1.13 [%]	0.94	0.02
Auto vs. Edit ED	1	y = 0.99x + 4.13 [ml]	0.98	0.12
Auto vs. Edit ES	1	y = 0.97x + 6.59 [ml]	0.98	0.01
Auto vs. Edit ED	2	y = 1.05x – 7.34 [ml]	0.98	0.47
Auto vs. Edit ES	2	y = 0.93x + 4.73 [ml]	0.98	0.94
Auto vs. Man ED	1	y = 1.01x + 3.99 [ml]	0.96	0.03
Auto vs. Man ES	1	y = 0.98x + 9.70 [ml]	0.93	0.01
Auto vs. Man ED	2	y = 1.04x – 5.48 [ml]	0.95	0.80
Auto vs. Man ES	2	y = 0.91x + 9.13 [ml]	0.98	0.06

Table 6.1: Correlation statistics.

6.3.3 Manual Correction Effort

The majority of the automatically generated ED contours was accepted without further manual editing. Expert #1 accepted 15 out of 28 contours directly, expert #2 accepted 19 out of 29 contours. For the ES contours these numbers were 2 and 4 for expert #1 and expert #2 respectively.
When editing was required, on average 18.7% of the total ED contour length was corrected manually (14.6% for MD #1 and 22.9% for MD #2). For ES on average 25.3% of the total contour length was adjusted (26.0% for MD #1 and 24.6% for MD #2).

6.3.4 Inter- and Intra-Observer Variability

For both ED and ES the difference between edited automatic and automatic contours on average is smaller than the difference between manual and automatic

	Auto vs. Edit [%]	Man vs. Auto [%]	Man vs. Edit [%]
MD #1	-4.6 ± 11.8	6.6 ± 12.2	2.0 ± 5.4*
MD #2	-0.7 ± 7.8*	2.8 ± 7.9*	2.1 ± 4.4

Table 6.2: Signed differences in ejection fraction in comparing manual, automatic and edited automatic results. Numbers denote average ± standard deviation, asterix marks statistical significance.

	LV function analysis duration			Total study duration		
	Man [s]	Auto [s]	Gain [%]	Man [s]	Auto [s]	Gain [%]
MD #1	146.7	135.3	7.7	251.2	201.9	19.6
MD #2	166.1	127.9	23.0	254.6	171.3	32.7
Average	156.2	131.7	15.7	252.9	186.9	26.1

Table 6.3: Average LV function analysis duration and average total study duration.

	Inter-Obs, Man	Inter-Obs, Edit	Intra-Obs, Expert #1	Intra-Obs, Expert #2	Auto vs. Edit
ED	0.74 ± 0.21	0.64 ± 0.45	0.80 ± 0.23	0.84 ± 0.32	0.46 ± 0.83
ES	1.48 ± 0.60	1.33 ± 0.95	0.93 ± 0.21	1.24 ± 0.46	1.06 ± 0.85

Table 6.4: Point-to-curve differences [mm].

contours (Table 6.2). Hence, this indicates that the automatic method introduces a bias on the (ratified) edited automatic contours, which reduces the inter-observer variability. Furthermore, the average point-to-curve differences between expert cardiologists #1 and #2, for the manual contours and the edited automatic contours were evaluated (Table 6.4, first two columns). For both ED and ES the inter-observer variability is lower for the edited automatic contours. For ED the variability is 0.64 mm (vs. 0.75 mm for the manual contours), for ES it is 1.33 mm (vs. 1.48 mm for the manual contours).
When comparing the manually drawn contours with the edited automatic contours for both experts, the average intra-observer variability is 0.82 mm for ED and 1.08 mm for ES (Table 6.4, columns three and four).
All results for inter- and intra-observer variability are based only on comparisons of studies in which exactly the same ED or ES frame was selected for analysis.

6.3.5 Accuracy of the Automatic Contours

The fully automatic contours for ED and ES LV delineation, generated by the presented algorithm, are the base for the clinically approved edited automatic contours. As the previous section suggests, these automatic contours introduce a

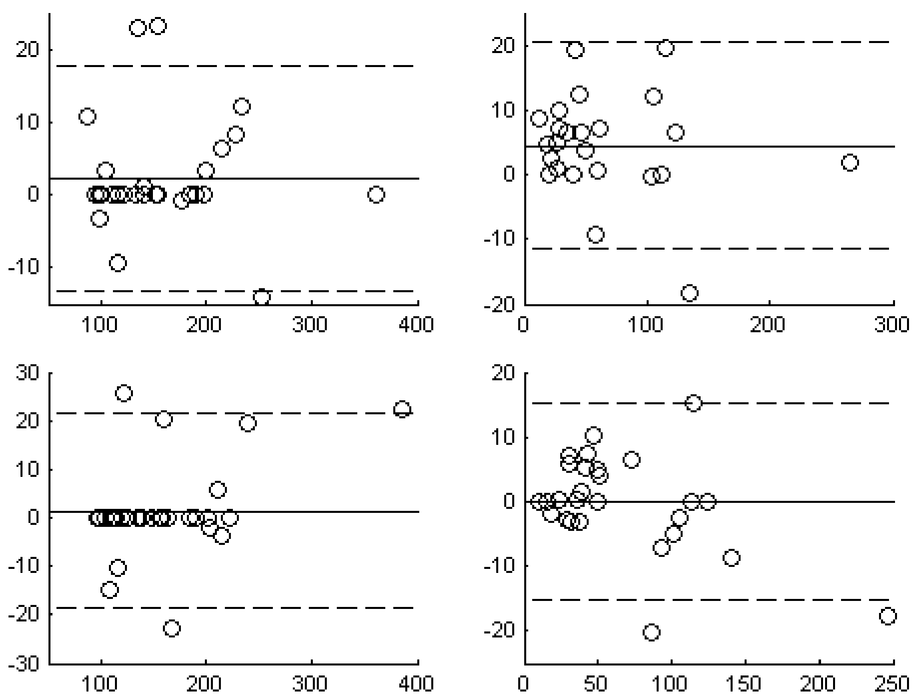

Figure 6.4: Bland-Altman analysis of automatic and edited automatic volumes. The top row shows the results for expert #1, the bottom row shows expert #2 results. The ED results are shown on the left-hand side, the ES results on the right. y-axes denote automatic minus edited, x-axes denote averages.

bias. It is therefore essential that the quality of the contours presented by the algorithm approximate the level of clinical acceptance.
The success rate for automatic segmentation was 100% for ED for both experts and 86% (expert #1, 4 failures) and 93% (expert #2, 2 failures) for ES. A segmentation failure was defined as when the volume difference was above 30% and the point-to-curve difference was more than 3 mm.
Corresponding volumetric differences between the automatically generated contours and both ratified contours were low (Table 6.1, Figure 6.4, Figure 6.5). Overall correlation coefficients between automatic and edited automatic results were high (R^2 = 0.98 for all results), with p-values of 0.12 (ED MD #1), 0.01 (ES MD #1), 0.47 (ED MD #2) and 0.94 (ES MD #2). Bland-Altman plots showed a slight overestimation of the automatic volumes of approximately 2 ml for both ED and ES, with respect to the edited volumes (Figure 6.4).
When comparing the automatic results with the manual contours, the correlation coefficients dropped somewhat (R^2 = {0.98; 0.93; 0.95; 0.98} for ED MD #1, ES MD #1, ED MD #2, ES MD #2 respectively), yet the correspondence still was good, with p-values of 0.03 (ED MD #1), 0.01 (ES MD #1), 0.80 (ED MD #2) and 0.06 (ES MD #2). A slight overestimation of the automatic volumes of approximately 3 ml (ED) and 6 ml (ES) could be derived from the Bland-Altman analysis (Figure 6.5).

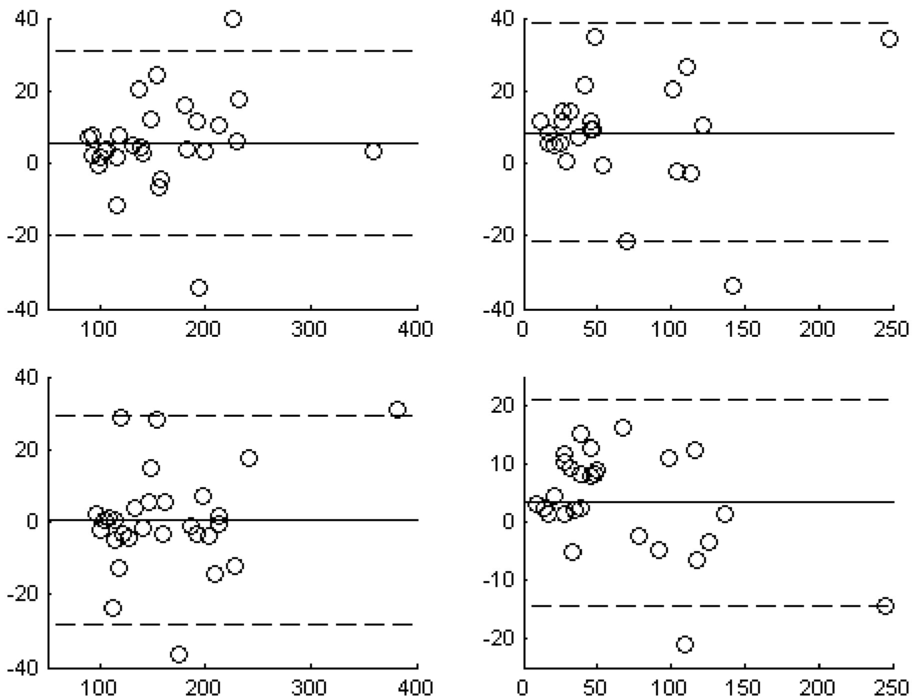

Figure 6.5: Bland-Altman analysis of automatic and manual volumes. The top row shows the results for expert #1, the bottom row shows expert #2 results. The ED results are shown on the left-hand side, the ES results are shown on the right. y-axes denote automatic minus manual, x-axes denote averages.

The average point-to-curve differences between the automatic and the edited automatic contours, combined for both expert cardiologists is an additional measure to determine the accuracy of the automated method. These differences (0.46 mm for ED and 1.06 mm for ES) are generally equal to or smaller than the reported inter- and intra-observer variability results (Table 6.4, right column).

6.4 Discussion

6.4.1 Accuracy of the Volumetric Measurements

The experiments presented in this chapter provide two reference standards for delineation of the left ventricle in X-ray angiograms. First, the manually drawn contours by the expert cardiologists and second, the edited automatic contours. Both types of contours were approved by the expert cardiologists as valid LV delineation.
For the most relevant clinical parameter, the ejection fraction, there is an excellent correlation between the manual results and the results based on the approved edited automatic contours (Table 6.1, Figure 6.3). This holds for the calculated ejection fractions by both cardiologists. For cardiologist #1, there was no statistically significant difference between the two approaches, meaning that the edited automatic contours could be regarded as an equally reliable gold standard as the manual contours. The p-value of 0.02 for expert cardiologist #2 does not directly support this conclusion.
Nonetheless, when concentrating on the correspondence between the calculated ED and ES volumes, from which the ejection fractions are derived, the correlation coefficients were even higher than the ones found for the ejection fraction (Table 6.1, Figure 6.2). Specifically the results for cardiologist #2 ($R^2 = 0.99$ for ED and $R^2 = 0.98$ for ES) were excellent. Since in the paired samples t-test differences between manually and semi-automatically calculated ED and ES volumes were found statistically insignificant for both expert cardiologists, the edited automatic contours can be regarded as an equally reliable gold standard as the manual contours.

6.4.2 Workflow Optimization

The previous section shows that the presented method provides robust, accurate and clinically acceptable performance. However, aspects such as the speed of the workflow and the amount of manual effort are equally important for clinical acceptance.
The proposed method dramatically reduces the amount of manual contouring. 60% of all automatically generated ED contours and 11% of all automatically generated ES contours did not need any further manual editing. Furthermore, when editing was required, the average amount of manual editing was 18.7% of the total contour length for ED and 25.3% of the total contour length for ES.

When using the proposed method, the average speed gain in LV function analysis duration was recorded at 15.7%. The speed gain in total study duration even amounted to 26.1%, reducing the total amount of time spent on analyzing one patient from, on average, 253 seconds (= 4 minutes and 13 seconds) to 187 seconds (3 minutes and 7 seconds). The additional gain in total study analysis is difficult to explain. Possibly the initially generated automatic contours influence the interpretation of the experts such that it results in a faster analysis: because they are immediately dealing with a set of contours, they are converging towards an image interpretation in an earlier stage of the workflow.
Given the fact that both expert cardiologists were fully familiar with the manual workflow, while the automated workflow was new to them, it is likely to expect an even further decrease in patient analysis time in routine clinical practice.

6.4.3 Inter- and Intra-Observer Variability Decrease

Compared to manual analysis, introducing an automated method that is dedicatedly trained on delineating anatomical structures in medical images should theoretically reduce the inter- and intra-observer variability in patient analysis.
Regarding the inter-observer variability, the average point-to-curve difference between both expert cardiologists dropped from 0.75 ± 0.23 mm to 0.64 ± 0.45 mm for ED and from 1.48 ± 0.60 mm to 1.33 ± 0.95 mm for ES.
Furthermore, the introduction of a bias can evidently be derived: the differences between automatic contours and edited automatic contours generally are smaller than differences between automatic contours and manual contours (Table 6.2). This bias supports the suggestion that the presented automated algorithm does reduce the inter-and intra-observer variability.
Finally, one can argue that the introduction of a bias is not necessarily a good development. Nevertheless, the generated contours are edited and/or ratified by an expert and the resulting clinical parameters are not significantly affected.
The intra-observer variability was measured by comparing the manual results with the edited automatic results, but this could only be used to assess the quality of the automatically generated contours. Nonetheless, given the fact that the inter-observer variability did decrease when using the automated algorithm, a similar trend can be expected for the intra-observer variability.

6.4.4 Accuracy of the Automatic Contours

The previous sections show that the results of the presented automated algorithm are of clinically acceptable quality, can be generated faster in comparison with manual contour drawing and have the capacity to reduce the inter- and intra-observer variability. These results are a combination of automatically generated contours and, possibly, additional manual editing. Since there is a large automatic component in the presented method that evidently influences the expert cardiologists, a more thorough investigation of the accuracy of the automatically generated contours is desired.

The described method is incorporated in the QAngio® XA package marketed by Medis medical imaging systems B.V. and has been subject to a thorough technical validation by Oost *et al.* [16]. Another available commercial package for automated contouring of ventriculograms, the CAAS LVA package, is marketed by Pie Medical Imaging B.V. The methodology used in the CAAS LVA package is mainly based on Dynamic Programming [8]. The methodology described by Oost *et al.* is a hybrid algorithm in which statistical modeling and Dynamic Programming are combined. It has been proven that this hybrid approach outperforms the individual application of Dynamic Programming alone [16]. The high degree of accuracy of the hybrid approach by Oost *et al.* is corroborated by the results in this clinical validation study. Good agreement was found between the automatically derived ED and ES volumes and both reference standards (Table 6.1, Figure 6.4, Figure 6.5).

Looking at the point-to-curve difference between automatic contours and edited automatic contours, the quality of the automatic contours is even more apparent. Both the ED and the ES results (0.46 mm and 1.06 mm) are well within the measured ranges for inter-observer variability (0.64 - 0.74 mm for ED and 1.33 - 1.48 mm for ES) and within the ranges of the averaged intra-observer variability for expert #1 and expert #2 (0.82 mm for ED and 1.09 mm for ES).

Furthermore, the presented results for inter-observer variability are based on study comparisons in which the frame selection was identical. However, in clinical practice different MDs will select different frames to be analyzed, either because they have a different judgment on the exact time point for ED or ES, or because they consider a different cardiac cycle to be optimal for patient analysis. Hence, numbers on inter- and intra-observer variability will be higher in practice than those reported in this study.

6.5 Conclusions

An automated methodology was presented to delineate the left ventricular contours in the ED and ES phases in X-ray LV angiograms. The method proved to be accurate and the results were highly similar to the manually traced outlines, which were regarded to be the gold standard. The method significantly reduced the analysis workload by diminishing the necessary amount of manual contouring and by considerably reducing the average time required for a patient analysis. Moreover, the algorithm reduced the inter- and intra-observer variability. The presented results indicate that this automated approach has the potential to optimize the analysis workflow for X-ray LV angiography in clinical practice.

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