Automated image analysis techniques for cardiovascular magnetic resonance imaging

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CHAPTER

9

Summary and conclusions

Over the period, in which the work described in this thesis was carried out, cardiovascular magnetic resonance (CMR) imaging has developed from an imaging modality primarily used for research into a routinely used clinical imaging modality which is applied every day in many hospitals worldwide. CMR has become the accepted gold standard for quantification of ventricular volumes. However, an MR scanner does not automatically generate quantitative results. It requires image segmentation, i.e. definition of object boundaries in the images, which is a time-consuming and tedious procedure when done manually. The availability of automated contour detection techniques that can accurately detect the myocardial boundaries in clinical CMR imaging studies would be of enormous value for routine clinical use of CMR.

The aim of this thesis was to investigate image processing techniques for automated and semi-automated assessment of quantitative parameters from cardiovascular magnetic resonance imaging studies.

Chapter 1 presents a general introduction to this thesis and defines the scope of the work.

In **Chapter 2** an overview is presented of image processing techniques which are used for quantitative analysis of various CMR acquisition protocols.

Chapter 3 describes an image segmentation method that was developed for the semi-automated detection of endocardial and epicardial contours for all slices and phases in short-axis cine MR imaging studies. Goal of this study was to evaluate the newly developed semi-automated contour detection algorithm.

The segmentation procedure presented in this chapter is based on multiple image processing steps including low-level techniques such as thresholding and edge detection using dynamic programming. Several constraints are incorporated in the various processing steps in order to increase the accuracy and robustness of the method. The segmentation algorithm is performed slice by slice, starting with the detection of the epicardial contour in the end-diastolic time-frame. A frame-by-frame detection of the epicardial contours in the remaining time-frames is performed by using the available epicardial contour of the ED frame as a model and deforming it such that the local image characteristics near the contour are similar to the corresponding location in the ED phase. Only a small deviation from the model contour is allowed, as it is known that the shape of the epicardial contour only shows little movement over the cardiac cycle.

Once the epicardial contours are available, the search for endocardial contours can be restricted to the region within the epicardial contour. The first step performed is finding an optimal threshold value separating the LV blood pool from the surrounding myocardium. The contour around the extracted blood pool serves as a first approximation of the endocardial contour. Concave sections in this contour are often caused by papillary muscles or trabecularization of the LV endocardial wall. Therefore a smooth convex hull around the extracted region is used as a better approximation of the endocardial contour. This contour is then used as input for dynamic programming, resulting in a locally more accurate contour.

A main ingredient of the developed contour detection procedure is the incorporation of available contours as *a priori* information when detecting other contours in the MR study. Since any automatically detected contour may be inaccurate, the use of such information may also lead to error propagation. Therefore, for each contour also the status was recorded and only those contours which are known to be valid are used as model information. A valid contour can either be a contour that was edited manually, or a contour that was initially detected automatically and then accepted by the operator. Using this concept, it was shown that the presented contour detection approach could be used to obtain accurate contours in all slices and phases of a study with minimal amount of contour

editing. For endocardial contours no manual editing was used at all. For epicardial contours, only in 1.4% of the images manual editing was performed. However, in this study, in the most basal slice level where no complete circumference of myocardium is present, both endo- and epicardial contours were traced manually.

Chapter 4 describes an automated contour detection method for the assessment of aortic flow from velocity-encoded cine MR imaging studies of the ascending aorta. Quantification of flow in the aorta can be used to derive the left ventricular stroke volume. In addition, by comparing aortic flow with pulmonary flow, the severity of shunts between the left and right heart chambers can be quantified.

Instantaneous aortic flow can be obtained by tracing a contour around the aortic cross-section and multiplying the cross-sectional area with the average blood flow velocity. To correct for the significant in-plane and through-plane motion as well as changes in cross-sectional shape over the cardiac cycle of the aorta, during manual image analysis the user is required to trace the vessel border in each individual image of the multi-phase MR examination, thereby carefully avoiding the inclusion of flow in adjacent regions from other vessels. Since this is a time consuming and tedious procedure which introduces observer variabilities, the automation of this process is desirable. The developed automated contour detection algorithm performs the segmentation in three separate steps. In the first step the user is required to identify an approximate center point of the aorta in one of the time frames. A contour around the aorta is detected and used as first approximation for the remaining time frames. To correct for in-plane motion of the aorta, the contour location is adjusted for each individual time frame, thereby enforcing a time-continuous motion pattern. Finally for each contour an edge based contour detection is performed to account for shape changes of the aortic cross-section.

The presented automated contour detection method fulfills the clinical requirements, as it requires minimal user interaction, it provides results which are in close agreement with results derived from manual contour tracing and has low inter- and intra-observer variability.

In **Chapter 5** a new method is presented to obtain more accurate measurements of left ventricular wall thickness using a 3D extension of the Centerline method. The method takes advantage of the available 3D geometrical information of the acquired imaging planes. Conventional 2D approaches may result in overestimation of the true wall thickness in regions where the ventricular wall does not intersect at an exact 90° angle

Chapter

9

with the imaging plane. This situation commonly occurs near the apex of the left ventricle. However, such overestimation may also be the result of inaccurate planning of the short-axis stack of images. Additionally, the extent of overestimation may vary over the cardiac cycle in case the left ventricle exhibits a significant change in orientation during contraction and relaxation.

Evaluation of the method using a data set of synthetic phantoms mimicking the geometry of the left ventricle, demonstrates the validity of the new approach. It is shown that over-estimation in wall thickness that typically occurs near the ventricular apex using the standard 2D Centerline method, is strongly reduced by applying the new 3D method. In addition, the 3D method is able to correct errors in wall thickness measurements that occur in case of inaccurate planning of the orientation of the stack of short-axis images. Using MR studies of normal volunteers, it is also shown that the 3D method results in less variability in wall thickness from base to apex and between different regions of the left ventricle. It should be noted that application of the 3D wall thickness calculation method requires multi-slice short-axis acquisitions with correct 3D alignment. In case the short-axis slices are acquired during separate breath-holds, image co-registration may be needed as a preprocessing procedure.

Chapter 6 describes a study evaluating an image processing algorithm for the automated detection of endocardial and epicardial boundaries of the left ventricle in time series of short-axis MR images based on an Active Appearance Motion Model (AAMM). In previous work the usefulness of AAM contour detection for the segmentation of the left and right ventricular boundaries in individual short-axis MR images had already been demonstrated. In this work an extension of the AAM contour detection was developed which performs modeling and contour detection for complete time-series of short-axis MR images. The rationale for this new approach is that by modeling the image information contained in a time-series of images, the automated segmentation procedure is expected to be more robust since all image data are used during the detection of a globally optimal time-continuous segmentation result. Poor image quality in particular time-frames will therefore not result in outlier contours.

In the AAMM, the appearance of the left ventricle is modeled for the systolic phase of the cardiac cycle by considering the image frames from ED to ES. For application of the AAMM contour detection method, for each study the ES time frame needs to be identified manually; the first time frame is assumed to represent ED. Using an iterative procedure the gray value difference between the synthetic AAMM image and the actual pixel

data is minimized by adjusting the pose parameters and the AAMM model parameters. This matching process results in the endocardial and epicardial contours for the complete time-series.

For the evaluation of the performance of the AAMM contour detection method a leave-one-subject-out approach is used. In three out of twenty studies the contour detection was not successful. For the remaining 17 studies a good agreement was found between manually derived and automatically derived global LV function parameters. Differences between manually and automatically derived results were 0.3±12% for the end-diastolic volume; 2±23% for the end-systolic volume; 0.1±6.7% for ejection fraction and for 0.7±15% for LV mass. These results compare favorably with the computed inter-observer variability for manual contour tracing.

Despite the good results, the study also shows a shortcoming of the AAMM contour detection method. In three studies the obtained contours do not fit to the actual endocardial and epicardial boundaries. Further inspection of these three studies reveals the presence of particular features in these studies that could explain the poor performance. Using a more extended training set of CMR exams including more pathological cases may alleviate this problem.

In **Chapter 7** an automated contour detection technique is described which is based on tracking of landmark points over the cardiac cycle. The landmarks are positioned at the myocardial boundary and are tracked over the cardiac cycle using a multi-dimensional dynamic programming (ND-DP) technique. As input, the method requires an existing contour in one of the time frames. In this study, the method is initialized using a manually traced contour in the mid-systolic time frame and 32 landmarks are defined at evenly spaced intervals along the contour. Image information around the defined landmarks is used to find likely locations for the landmark in other time frames. Within the ND-DP framework constraints are imposed on the allowed motion of a landmark, i.e. 1) the maximal excursion should be less than a certain threshold; 2) the maximal displacement from frame to frame is limited; and 3) since the image sequence describes a complete cardiac cycle, the path described by a landmark must be cyclic.

The proposed method has a number of important advantages. First, the contour detection result is relatively insensitive to individual image frames with poor image quality. Second, since an image matching strategy is used to find the likely locations of a landmark, the tracking results are also reliable in case part of the contour is defined in an area without clear edges. This advantage is especially of importance near the papillary

Chapter

9

muscles for the endocardial boundaries and regions of poor contrast or epicardial fat during the detection of epicardial contours.

Quantitative evaluation of the method was performed on 20 CMR data sets of 18 patients with several pathologies and 2 normal volunteers. Compared to results derived by manual tracing, errors in end-diastolic volume, end-systolic volume and ejection fraction were smaller than 5%. Border position errors were in the order of one pixel.

The general applicability of the ND-DP method is further demonstrated in another segmentation problem. ND-DP is applied to a temporal series of MR phase-contrast images of the ascending aorta. A six-dimensional implementation was tested using four radii and the x,y position of the aorta center. By imposing a temporal continuity constraint on all six parameters, temporal tracking of the contour describing the aortic cross-section was performed successfully.

The motivation for the work described in **Chapter 8** is that image characteristics are highly dependent on the MRI scanner used and the applied scanning protocol. Therefore for optimal performance, the parameter settings of an automated contour detection method, such as the one described in Chapter 3, needs to be fine-tuned for a specific MR acquisition protocol. Since the optimal value of a parameter can be dependent on the values of other parameters, finding the optimal values for all parameters is a non-trivial task. Searching for the optimal settings can be seen as a high-dimensional optimization problem. In this study the value of genetic algorithm based parameter optimization is studied for this particular problem. To this end the automated endocardial contour detection algorithm as described in Chapter 3 is tested on MR image data acquired with either a gradient-echo (GRE), or a Steady State Free Procession (SSFP) protocol. Based on earlier experience, 15 parameters are selected for the optimization. It is demonstrated that compared to the default setting of the parameters a significant improvement in detection performance is obtained after parameter optimization. This study also reveals that the contour detection algorithm, although originally developed for GRE MR image data, is also applicable for images acquired using a SSFP protocol. It can be concluded that parameter optimization using genetic algorithms is a practical technique for optimization of the performance of a contour detection method for a particular type of image data.

9.1 GENERAL CONCLUSIONS

Cardiac Magnetic Resonance Imaging (CMR) has become an important clinical imaging modality for cardiac evaluation. Reliable computer

algorithms for quantitative image analysis, including automated contour detection, are therefore of enormous clinical importance. The purpose of this thesis, as described in the first chapter, was to develop and validate automated contour detection techniques for quantitative evaluation of cardiac MR examinations that can be used in a routine clinical setting.

The automated contour detection techniques described in the thesis were all applied to clinical CMR data and the results of automated contour detection were compared to manually traced contours as gold standard. A high agreement with manual image analysis was demonstrated for the presented contour detection techniques. For all algorithms developed it was attempted to make effective use of available *a priori* information. The algorithms described in chapter 2 and 7 use information from manually traced or edited contours as *a priori* information to guide the contour detection in other frames. This however implies that these algorithms are dependent on manual interaction. The AAMM contour detection technique described in Chapter 6 only requires the manual definition of the end-systolic phase, while the contour detection itself runs fully automatically. The *a priori* information used in this algorithm is derived from a training set of CMR exams with available contours.

A possible direction in realizing the ultimate goal of accurate and robust fully automated contour detection in clinically acquired CMR imaging studies is by combining several components of the algorithms described in this thesis. The large variability in image characteristics and inter-patient differences requires the use of *a priori* information. The segmentation of the apical and basal short-axis slices, which are more difficult to process automatically, can be supported by taking advantage of available images acquired in the long-axis orientation. While fully automated contour detection seems attractive, also the use of more efficient methods of user-interaction is worth investigating. The combination of advanced automated contour detection techniques, optimal visualization and advanced user interaction may result in the most viable solution.

In conclusion, in this thesis we have developed and validated various automated contour detection techniques and image analysis approaches for quantitative analysis of cardiac MR imaging studies. The developed methods have also been integrated into analytical software packages that are being used in many clinical centers worldwide. Based on the work described in the thesis and the large quantity of clinical journal papers in which the developed approaches have been applied for clinical research, we may conclude that we have realized the goals that were set at the start of the thesis.

Chapter

9