# HeAT: A Software Assistant for the Analysis of LV Remodeling after Myocardial Infarction in 4D MR Follow-Up Studies

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Abstract: Spatio-temporal Cine-MR image sequences of the heart contain information about shape and motion changes, spatial delayed-enhanced (DE)-MR enables identification of pathological structures after myocardial infarction. In this paper the Heart Analysis Tool (HeAT) for the quantitative analysis of 4D MR image sequences of infarct patients is used to analyze the characteristics of left ventricular (LV) remodeling extracting regional and global parameters in the acute (base-line) and approximately 15 months past acute (follow-up) phase. The software assistant HeAT provides the combined evaluation of Cine- and DE-MR image data. Partitioning of the myocardium in segments enables the analysis with high local resolution. Corresponding segments are generated and used for intra patient comparison. First results of 10 infarct patients indicate an exact analysis of morphological and functional characteristics of the infarcted myocardium. Based on the visualization and statistical interpretation of these analysis LV remodeling can be quantified. Quantitative analysis can help to find predictive parameters describing LV remodeling having an impact on further therapy.

## 1 Introduction

Myocardial infarction causes the development of myocardial necrosis. The necrotic area loses its ability to contract and the remaining heart muscle needs to compensate for that weakened area. Loss of contractile function is attributed to left ventricular remodeling. LV remodeling is an important element in the progression of cardiac insufficiency. Remodeling is characterized by wall thinning, chamber dilation and increased end-diastolic and end-systolic volumes  $[J^+03]$ . It is an important clinical problem to get quantitative parameters characterizing LV remodeling.

New magnetic resonance (MR) imaging techniques provide the means for a non-invasive evaluation of anatomic and functional parameters of the beating heart. In this paper, 4D Cine-MR and 3D delayed enhancement (DE)-MR image sequences are used for this pur-

pose. Cine-MR with high spatial and temporal resolution enable accurate measurements of the myocardial shapes. DE-MR is effective in identifying the presence and extent of myocardial infarction. DE-MR also has the potential to allow identification of microvascular obstruction (MO). Presence of MO is associated with greater myocardial damage, with LV remodeling and increased risk of mortality and morbidity [W<sup>+</sup>98]. Analyzing myocardial variation, e.g. infarct shrinkage, revitalization of shocked tissue, requires detailed evaluation of the transition from healthy myocardium to diseased myocardium (borderzone). Thus, anatomical information from Cine-MR and pathological information from DE-MR images have to be combined.

Due to the quantity of MR image data, analyzing 4D MR data by hand is time-consuming and in most cases not reproducible. The computer-assisted extraction of these measurements is reproducible and fast. Several approaches for assessing LV wall motion are published e.g. [SRD94]. In contrast to these approaches the Heart Analysis Tool (HeAT) incorporates myocardial shape and motion information derived from 4D Cine-MR, as well as acute infarction information (e.g. MO) from DE-MR. Local analysis in high user-defined resolution is enabled by dividing the myocardium into small myocardial segments. Furthermore a unique labeling of these segments enables inter/intra patient comparison. Derived quantitative parameters can be stored and analyzed by medical experts.

# 2 Methods

In the Department of Diagnostic and Interventional Radiology, University Medical Center Hamburg-Eppendorf, two MR techniques are used to acquire spatio-temporal image data of patients after myocardial infarction and approximately 15 months later. Generally, these images are generated in 4D MR short axis studies (Cine-MR) and 3D DE-MR. All images are acquired with a 1.5T system by using electrocardiographic triggering and during breath-hold sequences. The Cine-MR images have a resolution of 224 x 256 x Z (Z differs between 7 and 12) voxels. These sequences usually contain 16 up to 20 time frames per R-R interval. The DE-MR was performed in all short-axis LV sections by using T1-weighted turbo fast low-angle shot sequence. The inversion time was 220-300 msec and the resolution is 224 x 256 for each slice. About 200 Cine-MR images and 7-12 DE-MR images for each patient were acquired.

The software assistant HeAT enables the import of 4D Cine-MR, 3D DE-MR and XML contour files. First, a segmentation of anatomical structures (e.g. endocard, epicard, papillaries, right ventricle) at endiastolic and endsystolic phase in 4D Cine-MR is provided. Selection of corresponding slices in Cine- and DE-MR using Mutual Information provides automatic comparative visualization of both modalities. Registration of corresponding slices enables direct myocardial contour overlay on DE-MR to support the data-driven segmentation of pathological structures (infarct area, MO).

In addition to the extraction of global parameters (e.g. LV ejection fraction (LVEF), stroke volume (SV)) a segment model dividing the myocardium in a variable number of myocardial segments enables extraction of local parameters with high resolution.

HeAT was executed on a standard PC with Intel Pentium 4 CPU 3.00 GHz, 2 GB memory and NVIDIA Quadro4 graphic card. To avoid re-implementing of state-of-the-art methods we implemented HeAT in C++ utilizing ITK and VTK with a problem-oriented adaptation.

### 2.1 Pre-processing of the MR image sequences

Pre-processing is necessary before the automatic algorithms for parameter extraction can be applied to evaluate the effect of LV remodeling. The analysis is based on the segmentation of myocardial and infarct structures. Furthermore the registration of corresponding Cine- and DE-MR slices enables the combined analysis of the outlined structures.

#### 2.1.1 Segmentation of anatomical and pathological structures

The automatic segmentation of anatomical structures in cardiac MR images is a difficult task due to artifacts caused by turbulent blood flow, which leads to a loss of signal and temporary occlusion of object boundaries. In recent years, several methods with different approaches for segmentation of the left ventricle were developed, e.g. model-based segmentation [Par03]. At the moment the focus of the development of HeAT is the quantitative analysis. Therefore, a basic tool for manual contour drawing was used for identifying endocard and epicard in different phases of the heart cycle in HeAT. Additionally, 3D visualization of the segmented structures is generated in real-time. Unfortunately, in Cine-MR image sequences the localization and quantification of pathological areas like the infarct area and MO is not possible. But in DE-MR data these structures can be distinguished using a data-driven segmentation approach described in [G<sup>+</sup>02]. Outlined contours are stored in XML-files.

#### 2.1.2 Registration of Cine- and DE-MR data

One objective of HeAT is to combine Cine- and DE-MR contour information. Direct transfer of myocardial contours to the DE-MR image sequences causes two problems. *Correspondence:* DE-MR sequences contain only one frame per cardiac loop. In order to minimize heart-moving artifacts this frame is acquired in a neutral cardiac phase (end-diastolic phase). DE-MR imaging requires approximately 220 ms. Cine-MR image sequences usually contain 16 to 20 time frames, each frame is acquired in about 10 - 50 ms. Thus, for each DE-MR image several temporal Cine-MR images of the same spatial position exist. For combination of anatomical and pathological information the definition of corresponding Cine- and DE-MR data is required. In this paper we address the correspondence problem using Mutual Information (MI) as similarity measure for the entire images. The corresponding image pair is selected automatically by the maximum MI value. *Alignment:* The imaging of Cine- and DE-MR data requires different settings, e.g. inversion time. Generally, these settings leads to different field of views and/or different patient positions. So, an alignment of corresponding Cine- and DE-MR silces is necessary. To address this problem a semi-automatic rigid registration using MI is ap-

plied. After pre-registration, the user can manually adjust shifting and scaling of DE-MR. Thus, information of both datasets is combined by transferring the Cine-MR contours to the corresponding registered DE data.



Figure 1: Visualization of the results of direct contour overlay (Cine-MR myocardial contours on DE-MR image data) before (a), and after (b) registration. Segmentation of the infarct area is presented in (c).

#### 2.2 Automatic computation of quantitative parameters

Detailed cardiac analysis of patient image data after myocardial infarction requires a high local resolution. Therefore, a standardised arrangement in 17 segments was proposed by the American Heart Association  $[C^+02]$ . For analyzing the characteristics of LV remodeling, local resolution of the 17 segment model is insufficient. So, HeAT supports a segment model with a variable number of segments in dependence on the centerline method [S+86]. Based on the endocardial and epicardial contours a centerline was computed and thereafter the myocardium was divided in even spaced segments. Unified segment numbering according to significant anatomical structures (wall position of the right ventricle in anteriorseptal section) enables identification of corresponding segments (Fig.2(a)). Manual selection of the anatomical structure is time-consuming and user-dependent. Therefore, the starting point is automatically defined at  $45^{\circ}$  to a horizontal line from the geometrical midpoint of the ventricle in anterolateral direction. Provided that all images are equal oriented, segments of different phases and different patients but with the same segment number can be identified as corresponding. Thus, these segments are usable for inter- and intra-patient comparison. The local quantitative parameters are computed automatically for each myocardial segment. Additionally, global parameters (e.g. LVEF, myocardial mass LVDM) were calculated. For evaluation of LV remodeling 13 regions of interest were automatically selected, e.g.

- infarct-center  $(inf_{center})$  (central one-third of the infarct circonverge)
- infarct-periphery  $(L_{in}, R_{in})$  (border one-third of the infarct circonvergence)

• peri-infarct zone  $(L_{out}, R_{out})$  (10% of the myocardial circonverence adjacent to the infarct border).

Each region is defined as a set of segments (see Fig.2(b)). Union of infarct-periphery and peri-infarct zone represents the border zone.



Figure 2: Schematically representation of anatomical and pathological structures as well as segment lines and segment numbering (a). Definition of ROIs in the infarct surrounding area (b).

## **3** Results

In HeAT Cine- and DE-MR datasets of 10 patients after myocardial infarction (base-line (BL), follow-up (FU)) were analyzed by two medical experts in all slices for each patient. Based on the segmentation with HeAT one dataset can be analyzed in about 10 minutes. For the acquirement of the local parameters, e.g. endocardial movement or infarct transmurality a myocardial partitioning in 100 segments was used. The automatically computed parameters were displayed in tables (Fig.4) and as curves in a datasheet (Fig.3). This enables a clinical interpretation of characteristics describing LV remodeling at the first glance. Main results of the first 10 patients are discussed in the following.

The analysis of the global parameters shows at BL an inverse correlation between the infarct size and left ventricular ejection fraction (LVEF) (r = 0.65, P < 0.05), reflecting that patients with large infarction had worse left ventricular function. Mean infarct size decreased from  $25 \pm 11$  gr at BL to  $17 \pm 7$  gr at FU (P < 0.01). Mean LV mass also decreased from  $118 \pm 25$  gr at BL to  $103 \pm 19$  gr at FU (P < 0.05). There was a



Figure 3: Regression plot (infarct size change to base-line infarct size) of 10 patients(a).

strong correlation between the initial infarct size at BL and reduction of infarct size at FU (r = 0.80, P < 0.01), indicating that infarct shrinkage is determined by the BL infarct size.

Lout	Lin	INF	Rin	Rout	HEALTH
0,00	1,00	3,00	1,00	0,00	-3,00
-1,02	-1,50	-1,87	-2,81	-3,64	-3,27
2,03	1,15	-0,45	-0,01	4,93	3,48
0,00	-1,04	-0,92	-0,72	-0,07	-0,01
0,00	0,00	1,01	1,03	0,00	0,00
-1,88	-2,84	-3,50	-5,30	-7,58	-6,26
-0,41	2,97	6,39	2,37	1,18	-3,71
1,82	2,56	8,23	2,42	0,21	0,51
0,61	1,41	-1,19	-1,88	-0,87	0,26
0,00	0,02	0,10	0,26	0,00	0,00
0,00	0,00	0,23	0,22	0,00	0,00
	Lout 0,00 -1,02 2,03 0,00 0,00 -1,88 -0,41 1,82 0,61 0,00 0,00	Lout     Lin       0,00     1,00       -1,02     -1,50       2,03     1,15       0,00     -1,04       0,00     0,00       -1,88     -2,84       -0,41     2,97       1,82     2,56       0,61     1,41       0,00     0,00	Lout     Lin     INF       0,00     1,00     3,00       -1,02     -1,50     -1,87       2,03     1,15     -0,45       0,00     -1,04     -0,92       0,00     0,00     1,01       -1,88     -2,84     -3,50       -0,41     2,97     6,39       1,82     2,56     8,23       0,61     1,41     -1,19       0,00     0,02     0,10	Lout     Lin     INF     Rin       0,00     1,00     3,00     1,00       -1,02     -1,50     -1,87     -2,81       2,03     1,15     -0,45     -0,01       0,00     -1,04     -0,92     -0,72       0,00     0,00     1,01     1,03       -1,88     -2,84     -3,50     -5,30       -0,41     2,97     6,39     2,37       1,82     2,56     8,23     2,42       0,61     1,41     -1,19     -1,88       0,00     0,02     0,10     0,26       0,00     0,02     0,10     0,26       0,00     0,00     0,23     0,22	Lout     Lin     INF     Rin     Rout       0,00     1,00     3,00     1,00     0,00       -1,02     -1,50     -1,87     -2,81     -3,64       2,03     1,15     -0,45     -0,01     4,93       0,00     -1,04     -0,92     -0,72     -0,07       0,00     -1,04     -0,92     -5,30     -7,58       -0,41     2,97     6,39     2,37     1,18       1,82     2,56     8,23     2,42     0,21       0,61     1,41     -1,19     -0,87     -0,87       0,00     0,02     0,10     0,26     0,00       0,03     0,23     0,22     0,00

Figure 4: Datasheets of global (b) and local (c) parameters of pat #6

The analysis of the regional parameters shows the mean diastolic wall thickness of the infarcted tissue decreased from  $7.7 \pm 1.4$  mm at BL to  $6.7 \pm 1.5$  mm at FU (P < 0.05), indicating wall thinning of the infarcted myocardium. Mean infarct transmurality decreased from  $71 \pm 13$  % at BL to  $65 \pm 11$  % at FU (P < 0.05). The number of the infarcted segments showed no significant change from BL ( $39 \pm 17$  segments) to FU ( $43 \pm 22$  segments, P = not significant), indicating that thinning and not stretching occurs in the infarcted myocardium.

## 4 Discussion

For cardiac analysis and visualization a huge range of tools, e.g. IDL exist. In contrast to these tools HeAT enables a combined analysis of anatomical and functional information in

infarct regions and healthy tissue based on registered Cine- and DE-MR image sequences. Furthermore, computation of parameters in user-defined regions of interest with high local resolution enables a detailed evaluation of LV remodeling. The manual segmentation is time-consuming and its results are user-dependent. Therefore automatic or semi-automatic methods will be integrated to improve the segmentation process.

Data analysis using the software assistant HeAT quantifies significant shrinkage of the infarcted area from BL to FU. The initial infarct size determines the later reduction of infarct size. The shrinkage of the infarction is mainly characterized by thinning of infarct transmurality. In this study additional 20 patient datasets will be evaluated concerning LV remodeling in the next step.

Intra-patient comparison of parameters in corresponding local areas (BL to FU) can be useful to predict the course of disease (e.g. regeneration of shocked tissue can be identified by an increased endocardial movement and myocardial thickening). These results of inter-patient comparisons can be useful for predicting the course of disease for an acute myocardial infarct patient.

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