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Automatic segmentation of the left ventricle cavity and myocardium in MRI data

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Abstract

A novel approach for the automatic segmentation has been developed to extract the *epi-cardium* and *endo-cardium* boundaries of the left ventricle (lv) of the heart. The developed segmentation scheme takes multi-slice and multi-phase magnetic resonance (MR) images of the heart, transversing the short-axis length from the base to the apex. Each image is taken at one instance in the heart's phase. The images are segmented using a diffusion-based filter followed by an unsupervised clustering technique and the resulting labels are checked to locate the (lv) cavity. From cardiac anatomy, the closest pool of blood to the lv cavity is the right ventricle cavity. The wall between these two blood-pools (*interventricular septum*) is measured to give an approximate thickness for the myocardium. This value is used when a radial search is performed on a gradient image to find appropriate robust segments of the epi-cardium boundary. The robust edge segments are then joined using a normal spline curve. Experimental results are presented with very encouraging qualitative and quantitative results and a comparison is made against the state-of-the art level-sets method.

Keywords: MRI; Left ventricle; Segmentation; Myocardium; Clustering; Level-set

1. Introduction

According to the World Health Organisation's [1] 2002 Report, 29% of deaths in their 191 members states were a result of cardiovascular disease (CVD), 32% in women and 27% in men. These alarming

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statistics have spurred the increase in research into the diagnosis and prevention of CVDs. The size and structure of the left ventricle is a primary indicator for the diagnosis and treatment monitoring of many CVDs. For example, left ventricle contraction and thickening plays a key role in the assessment of deficient blood supply to the cardiac tissue (ischaemia) [2] while a fall in left ventricle output or the ejection fraction can be a late complication of elevated vascular resistance (hypertension). Diagnostic imaging is set to play a vital role in the future fight against heart disease.

Traditional methods of cardiac imaging include cardiac ultrasound and angiography. Cardiac ultrasound is a tomographic imaging system, it is relatively cheap, non-invasive and can image on arbitrary planes. It gives low contrast when compared to MR and X-ray and hence cannot image through gaseous mediums and has a low signal-to-noise ratio (SNR) due to frequency attenuation in the tissue. Also, it has a low SNR in cases where the patient presents obesity. 3D ultrasound [3,4] has been introduced to analyse the heart function but currently does not have the resolution to accurately distinguish between the epi-cardium border and other organs in the thoracic cavity [5]. In angiography, X-ray projection images are used. The quality of the image can suffer when the heart muscle is overlapped by the diaphragm or the ribs. A contrast agent is injected into the heart cavity by means of a pigtail catheritor threaded through the arteries. This may cause complications like *arrhythmias* (irregular heartbeat) or *embolism* (by dislodging plaque from the wall) and may even result in death. This contrast agent also has difficulty reaching the apex of the heart [6].

Cardiac magnetic resonance imaging (CMRI), which is used in this study is a well established and rapidly advancing imaging modality in analysing heart disease. It is considered by some authors [7,8] to be the reference standard. MR has proved to be more accurate than echo-cardiology in the calculation of the ejection fraction and also shown superior results in endo-cardium border segmentation [8]. It has a wide topographical field of view and high contrast between soft tissues without the need for a contrast agent. This means there is a high discrimination between the flowing blood and the myocardium muscle. It is non-invasive with high spatial resolution and can be gated using an *electrocardiogram* (ECG) at different phases during the hearts pulse. However, it can suffer from noise and grey scale variation between adjacent slices [6,9–13].

All of these modalities are providing increasing amounts of information in higher dimensions, spatially and temporally. Such an increase in data produced from the different modalities makes it much more laborious and time-consuming for the cardiologist to hand-annotate and measure the myocardium. Recent research projects have moved from a manual segmentation toward a fully automated segmentation of the left ventricle [14–16,9].

Computer aided diagnostic (CAD) tools have been developed to aid cardiologists with the manual delinearisation of the myocardium [17,18]. Measurements are taken using geometric approximations of the left ventricle (lv). While these geometric models are fair approximations for healthy patients, they are not as accurate when compared to the actual MR image data [7]. Manual segmentation also suffers from inter- and intra-observer variability.

Semi-automated methods have been developed in order to further aid the cardiologist in the segmentation process [19–21]. These methods require user intervention by placing an initial contour around the lv or moving the cursor around the lv wall while the border attaches itself to the high gradient points. Although these approaches considerably reduce the time taken to manually segment the myocardium boundary it is still subject to inter- and intra-observer variability.

Traditional methods of segmentation such as thresholding, region-growing, edge-detection and watershed [22–24] (reviewed in [6]) are also used in the evaluation of the left ventricle cavity and wall.

These methods on their own have difficulty dealing with noise, grey scale variations and low gradients associated with most medical images and a high degree of supervision is required from the user.

Snakes or active contours [25] are curves that move toward the sought-for shape in a way that is controlled by internal forces such as rigidity, elasticity, and an external image force. The external force should attract the contour to certain features, such as edges in the image [26–29]. Initialisation of the contour is the key to its success. Bad initialisation can draw the curve away from the left ventricle to edges that best fit its predefined parameters. Snakes and active contours have difficulty working on images with low contrast and may not be able to flag important features such as wall thinning.

Level-set [30] methods have become well established methods for segmentation. Level-sets have also become a prevalent method in medical image segmentation [31–33]. Level-sets have gained popularity due to their implicit nature and ability to perform well in noisy data. They also have the ability to split and re-join throughout the deformation without the need for re-parameterisation. Similar to active contours, they rely on the first initialisation step and can fall into the trap of local minima.

Recently, in the field of medical image processing, many model-based segmentation approaches have been studied (reviewed in [10,34]). Geometrically deformable models [35–37] are parametric representations of the desired shape to be segmented. These parametric models can enhance the local properties of an image such as grey level or texture to aid the delinerisation in poor quality images.

Active shape models (ASMs) [38–40] are a model driven segmentation approach. The model is built up using a priori knowledge about the left ventricle shape, usually hand-annotated segmentations from a training set of data. This shape model is then compressed, usually using principle component analysis (PCA), to find the common modes of shape variation. The mean shape then searches an unseen image and converges over the most likely set of features. The mean shape is then deformed using the PCA modes. The accuracy of the segmentation relies heavily on the amount and variation of images in the training set. If the training set is too small with low variation, there is a limited number of unseen images that the model is applicable too. On the other hand, if the model is large with large variation it may easily choose some erroneous points. The hand annotation of the training set can also be very time consuming and introduce bias.

Active appearance models (AAM) [16,38] are similar to ASMs but texture of the shape is added to the model and they perform a combined shape-appearance statistical analysis. Stegmann [41] showed how these active appearance models could be applied to analyse short axis MR images of the heart. Mitchell [42] addresses the problems that AAMs have with attaching the model with the gradient information by formulating a hybrid approach which combines ASMs and AAMs. Lelieveldt [43] introduces a time factor into his active appearance motion models and minimises the appearance-to-target differences. Again all AAMs suffers the same limitations as the shape models with regards to the variation and building of the training sets.

We present a two-phase approach to address these issues. A diagram for the segmentation scheme is illustrated in Fig. 3. In the first stage we automatically locates and segments the lv cavity. It is invariant to changes in scale and changes in grey scale through the volume image. It performs a true segmentation of the endo-cardium boundary including the papillary muscles attached to the myocardium. The inclusion or exclusion of the papillary muscles in the calculation of the ejection fraction is usually dependent on the radiologist who can make this decision once the automatic segmentation is performed. In the second phase, we use the thickness of the interventricular septum (the myocardium between the left and right ventricle) as a guide for segmenting the remainder of the epi-cardium, using edge information. The epi-cardium boundary is closed using a spline.

This paper is organised as follows: Section 2 discusses the preprocessing with a short description of the segmentation algorithm. Section 3 focuses on the automatic detection of the lv cavity where we perform the segmentation of the lv cavity on both the end-systole and end-diastole phases and calculate the ejection fraction subsequently [44]. Section 4 moves onto the heuristics involved in segmenting the outer wall of the myocardium. The results are shown and evaluated in Section 5 with concluding remarks in Section 6.

2. Smoothing and clustering algorithms

Each image slice is smoothed to remove the noise which occurs in MR images [23]. The image is then clustered using an adapted *k*-means algorithm. The clustering of MRI data using different clustering techniques has being documented in [45,46].

2.1. Edge-preserving smoothing

In this preprocessing step, noise is filtered out of the image while maintaining the important edge information using an edge preserving filter. The use of diffusion-based filters has also been performed in MRI data [47–50,52]. The algorithm for adaptive smoothing implemented in this paper is adapted from Chen [51]. The technique measures two types of discontinuities in the image, local and spatial. From these two measures a less ambiguous smoothing solution is found. In short, the local discontinuities indicate the detailed local structures while the contextual discontinuities show the important features (Fig. 1).

In order to measure the local discontinuities, four detectors are set up as shown

$$\begin{aligned} E_{H_{xy}} &= |I_{x+1,y} - I_{x-1,y}|, \\ E_{V_{xy}} &= |I_{x,y+1} - I_{x,y-1}|, \\ E_{D_{xy}} &= |I_{x+1,y+1} - I_{x-1,y-1}|, \\ E_{C_{xy}} &= |I_{x+1,y-1} - I_{x-1,y+1}|, \end{aligned} \tag{1}$$

where $I_{x,y}$ is the intensity of the pixel at the position (x, y). We can then define a local discontinuity measure E_{xy} as

$$E_{xy} = \frac{E_{H_{xy}} + E_{V_{xy}} + E_{D_{xy}} + E_{C_{xy}}}{4}. \tag{2}$$

In order to measure the contextual discontinuities, a spatial variance is employed. First, a square kernel is set up around the pixel of interest, $N_{xy}(R)$. The mean intensity value of all the members of this kernel is calculated for each pixel as follows:

$$\mu_{xy}(R) = \frac{\sum_{(i,j)\in N_{xy}(R)} I_{i,j}}{|N_{xy}(R)|}. \tag{3}$$

From the mean the spatial variance is then calculated to be

$$\sigma^2_{xy}(R) = \frac{\sum_{(i,j)\in N_{xy}(R)} (I_{i,j} - \mu_{xy}(R))^2}{|N_{xy}(R)|}. \tag{4}$$

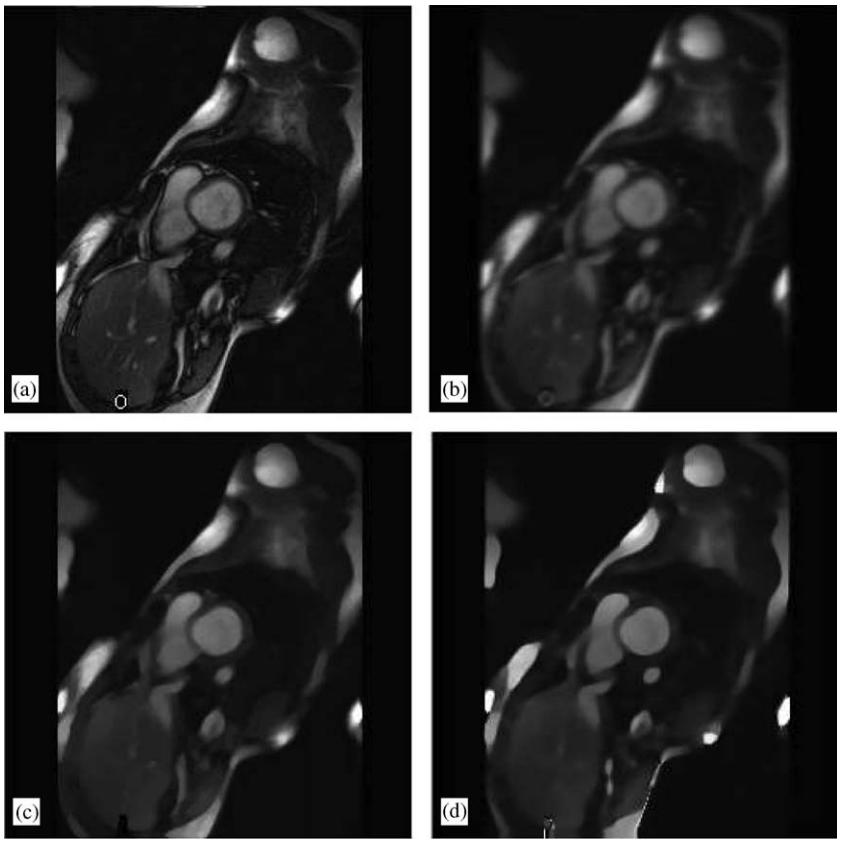

Fig. 1. Figures show the filtering of the short axis view: (a) the original image of the short axis view; (b) results after a single pass of a 5 × 5 average filter; (c) shows the results after a single pass of a 5 × 5 fifth-largest median filter; (d) the results from the adaptive filtering using a 5 × 5 neighbourhood mask, note the preservation of the edge features.

This value of sigma is then normalised to $\tilde{\sigma}^2_{xy}$ between 0 and 1 in the entire image. A transformation is then added into $\tilde{\sigma}^2_{xy}$ to alleviate the influence of noise and trivial features. It is given a threshold value of $\theta_\sigma = (0 \leqslant \theta_\sigma \leqslant 1)$ to limit the degree of contextual discontinuities.

Finally, the actual smoothing algorithm runs through the entire image updating each pixels intensity value I^t_{xy}, where t is the iteration value.

$$I^{t+1}_{xy} = I^t_{xy} + \eta_{xy} \frac{\Sigma_{(i,j)\in N_{xy}(1)/\{(x,y)\}} \eta_{ij} \gamma^t_{ij} (I^t_{i,j} - I^t_{x,y})}{\Sigma_{(i,j)\in N_{xy}(1)/\{(x,y)\}} \eta_{ij} \gamma^t_{ij}}, \tag{5}$$

where

$$\eta_{ij} = \exp(-\alpha \Phi(\tilde{\sigma}^2_{xy}(R), \theta_\sigma)), \tag{6}$$

$$\gamma^t_{ij} = \exp(-E^t_{ij}/S). \tag{7}$$

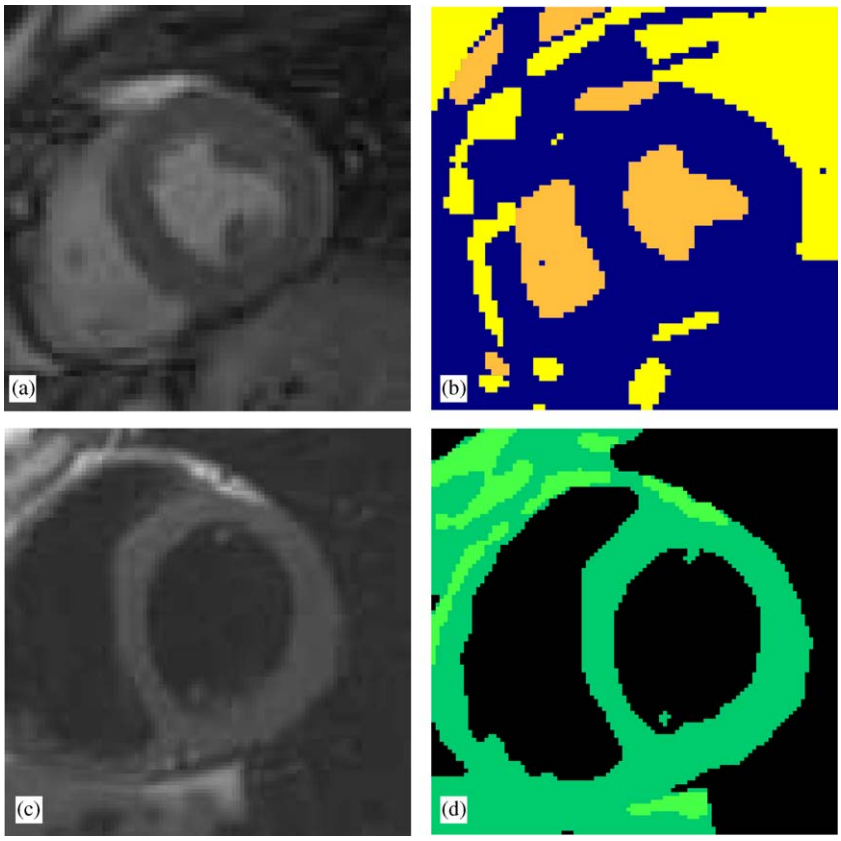

Fig. 2. Figure shows four images, two gradient-echo images before (a) and after clustering (b), and two spin-echo images before (c) and after clustering (d).

The variables S and α determine to what extent the local and contextual disontinuities should be preserved during smoothing. If there are a lot of contextual discontinuities in the image then the value of η_{ij} will have a large influence on the updated intensity value. On the other hand, if there are a lot of local discontinuities then both γ_{ij} and η_{ij} will contribute, as η_{ij} is used for gain control of the adaption.

2.2. *Clustering*

The smoothed images are then clustered using an adaptation of the k-means algorithm proposed by Duda and Hart [53,54]. This algorithm has four steps to find the image clusters.

(i) Initialise the position of the means $m_1 \rightarrow m_k$.
(ii) Assign each of the k-items to the cluster whose mean is nearest.
(iii) Recalculate the mean for the cluster gaining the new item and the mean for the cluster loosing the same item. Recalculation is made using the variance.
(iv) Loop through steps (ii) and (iii) until there are no movements of items.

The image is clustered using an initial guess of 15–20 independent cluster centres which is sufficient to capture all the relevant features. The pixels are clustered together using the strategy explained before. The number of clusters is then optimised by merging clusters with similar attributes. This is repeated until there are no more clusters to be merged [44] (Fig. 2).

3. Automatic detection of lv cavity

The image has now been segmented into separate clustered regions. The next step is to automatically detect which of these clusters represents the lv cavity on the first slice. To allow for different imaging parameters the lv cavity is located using shape descriptors only and not using the grey scale values. The images are short axis, therefore we assume that the lv cavity approximates a circular shape and that the lv feature is continuous in successive slices. Approximation to a circle is calculated as the error between the shape and the least squares approximation to the circle (see Appendix A). It is also assumed that the lv is not located on the peripheral of the image.

The volume of the left ventricle is then extracted using two criteria:

(i) Overlapping area of the regions contained in successive slices.
(ii) Grey scale value of the regions under investigation.

The regions cannot be connected using just grey scale values due to the variation in the intensity values through the volume caused, to some extent, by coil intensity falloff. The lv regions are then connected in 3D and the volumes are then rendered (see Fig. 5). The ejection fraction is calculated using the volumes. The ejection fraction is defined as "the proportion, or fraction, of blood pumped out of your heart with each beat" [55] and can be represented by

$$\mathrm{EF} = \frac{V_{\mathrm{endo}}(t_{\mathrm{D}}) - V_{\mathrm{endo}}(t_{\mathrm{S}})}{V_{\mathrm{endo}}(t_{\mathrm{D}})}, \tag{8}$$

where V_{endo} is the volume of the inner walls of the heart, $V_{\mathrm{endo}}(t_{\mathrm{D}}) = \max_t[V_{\mathrm{endo}}(t)]$ is the end-diastolic volume and $V_{\mathrm{endo}}(t_{\mathrm{S}}) = \min_t[V_{\mathrm{endo}}(t)]$ is the end-systolic volume.

4. Segmentation of epi-cardium border

The procedure for segmenting the epi-cardium is illustrated in Fig. 3. The position of the lv cavity is already known for each slice as explained in the previous section. In order to determine the epi-cardium border a region of interest is defined around the lv cavity. Two copies of this region of interest are taken. The first image Image 1 is used to find a value for the approximate radius of the myocardium and the second image Image 2 is used to find real borders around the myocardium. The two are combined to find the true value of the epi-cardium around the lv.

Image 1 is again clustered using a predefined low number of clusters around the region of interest. A low number of clusters is chosen because of the scarcity of important features around the lv cavity. Anatomically, the closest blood pocket to the lv cavity is the right ventricle cavity, it is also known that the

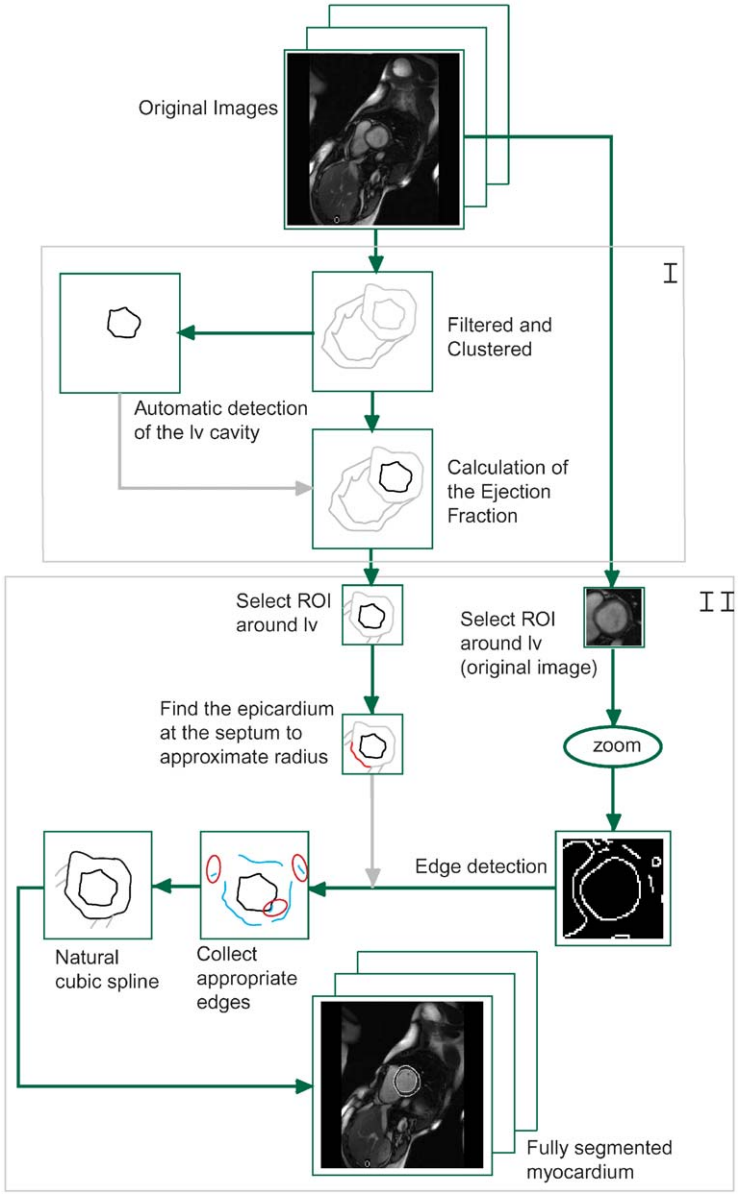

Fig. 3. A schematic representation of the two phases involved in the segmentation of the endo- and epi-cardium border. Stage I shows the preprocessing and segmentation processes, the automatic detection of the lv cavity and the connection of the cavity through the volume. Stage II shows the method for segmenting the epi-cardium border in each image.

thickness of the myocardium will not change drastically over the entire circumference. The thickness of the *interventricular septum* between the two blood pockets can give a reliable estimate for the thickness of the rest of the myocardium.

Image 2 is zoomed using an area averaging technique around the area of interest. The zooming operation is applied to increase the edge separation. The image is then segmented using a thresholded edge-based

algorithm [56]. The largest connected segments within certain bounds of the estimated thickness found from Image 1 are taken as potential border segments. There is an angular restraint placed on the transition of these segments around the epi-cardium to eliminate stepping into the endo-cardium border or stepping out to other organs.

A closed natural cubic spline is fitted around the points on the epi-cardium [57] (see Appendix A). The spline is used to close the epi-cardium contour by connecting all the points on the curve in a smooth way. Splines are piecewise polynomials of degree n ($n = 3$ in the case of cubic splines) with the pieces smoothly joined together. The joining points of the polynomial pieces are called control points which need not be evenly spaced.

5. Results

In order to assess the performance of the automatic segmentation, results were compared against those obtained by manually segmenting 25 volume image sequences for the endo- and epi-cardium borders. The manual segmentation was assisted by an experienced cardiologist. Each volume includes 5–12 images containing the lv, transversing the length of the cavity and includes the papillary muscles. The imaging device used was a Siemens Magnetom Sonata, 1.5 T, TR = 3.2 ms, TE = 1.6 ms, flip-angle 60° and resolution ($1.37 \times 1.37 \times 8$ mm) for the bright blood sequence and a Siemens Vision 1.5 T, T1-weighted scan used in the dark blood sequence. The automatic segmentation results can be seen in Fig. 4. The method shows good visual results for bright blood images 4(a)–(f) and dark blood images 4(g)–(i). The errors are calculated on volumes, endo and epi contours areas, myocardium thickness and finally point correspondence. The latter is measured against a level-set segmentation (see Appendix A).

Table 1 shows the signed average and root mean square error of the ejection fraction from eight volumes from the sequence. The ejection fractions were worked out using pairs of volumes, not necessarily the end-systole and end-diastole and compared with the ejection fraction calculated from the manually segmented volumes. We can see in Table 1 low errors between the manual and automatic results.

The errors for the manually segmented endo-cardium area and the automatically traced area are given in Table 1. The signed average and root mean square error are shown. Errors around the apex have a significant effect because a low number of pixels is a high proportion of the overall manually traced area. Linear regression analysis was also performed in Fig. 6(a) and high correlation value of $r = 0.98$ is obtained. Reproducibility is assessed using the Bland–Altman plot, Fig. 6(c) [58]. Note that the graphs are relatively zoomed to show the detailed distribution and the plots are graphed in units of mm^2.

The epi-cardium area was assessed using the same techniques. It shows a slightly lower percentage error for both the average signed and the rms errors. This can be attributed to the increased overall area of the manually traced contours. Linear analysis, Fig. 6(b), gives a value of $r = 0.94$ which is slightly lower than that produced for the endo-cardium. This lower correlation is a result of low contrast on the lateral side of the heart making the segmentation of the epi-cardium border difficult. In this case our algorithm connects two end-points of robust segments, how the ends are connected can incorporate a priori information [59]. Manual segmentation is also problematic in areas of low gradient and is dependent on the user's own interpretation of 'what looks appropriate'. Reproducibility was again assessed with the Bland–Altman plot, Fig. 6(d).

Tables 2 and Fig. 7 gives the Euclidean point to curve error in mm's for > 150 images through a heart sequence. It gives the minimum and maximum distance between the manual and automatic segmentation

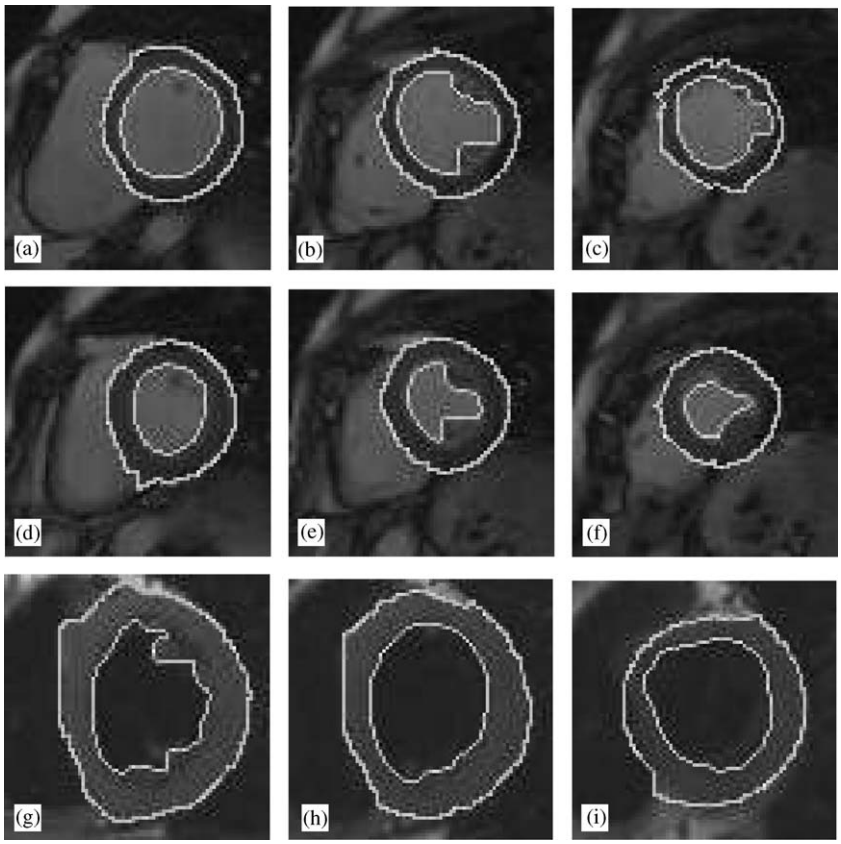

Fig. 4. The left ventricle contours obtained using our automatic segmentation method in short axis cardiac MR images. (a)–(f) show images taken at both the end-diastolic phase and end-systolic phase of a gradient-echo sequence. (g)–(i) show images from a spin-echo study.

Table 1
Mean percentage errors ±1SD for manual versus automatic

	Average signed error	RMS error
Ejection fraction	1.593 ± 0.82	3.176
Endo-cardium areas	-3.623 ± 5.14	4.765
Epi-cardium areas	-0.556 ± 4.29	3.75

contours. The average distance, standard deviation (SD) and root-mean-square (RMS) are also given. The results are compared to those obtained using the level set technique, detailed in the Appendix A, where the user selects the lv cavity for each image. The large maximum errors taken from the level-set approach are mainly due to the level-set encountering local minima due to the variation in blood intensity in the image. The results for the epi-cardium boundary point to curve errors are shown in Table 3 and illustrated in Fig. 8.

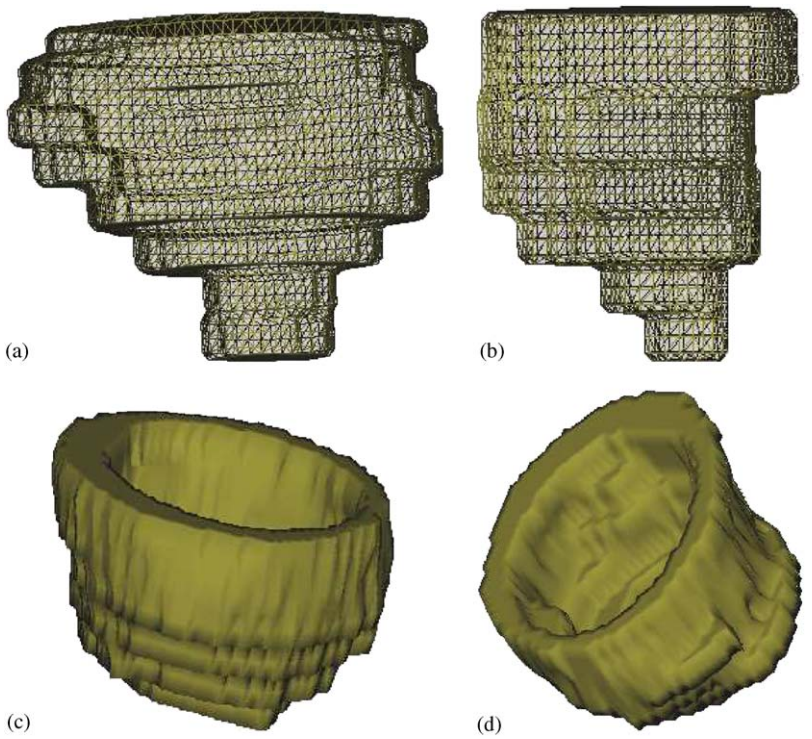

Fig. 5. The rendered images of: (a) the end-diastole lv cavity: (b) the end-systole lv cavity; (c) and (d) the diastolic myocardium. These volumes are constructed from the true segmentation of the images excluding fat and papillary muscles.

Table 2
Point to curve errors between manual and computer segmentation for both the clustering and level-set techniques for the endocardium boundary (mm)

Method	Endo				
	Min (mm)	Max (mm)	Average (mm)	SD (mm)	RMS (mm)
Clustered	0.0	7.07	0.69	0.88	1.12
Level-set	0.0	10.296	1.08	1.36	1.73

Table 3
Point to curve errors between manual and automatic segmentation for the epi-cardium boundary (mm)

Method	Endo				
	Min (mm)	Max (mm)	Average (mm)	SD (mm)	RMS (mm)
Robust arc	0.0	13.45	1.31	1.86	2.14

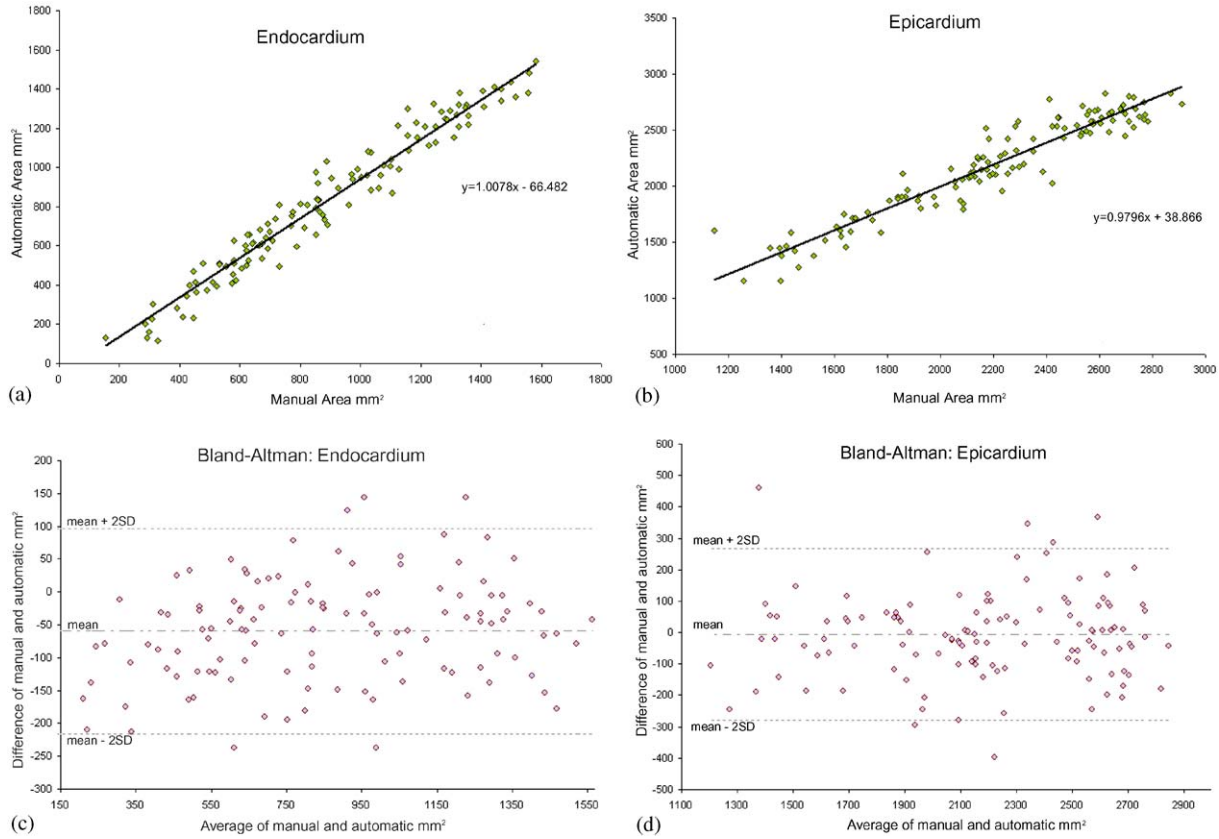

Fig. 6. (a) and (b) shows scatterline plot of manual segmentation against the automatic segmentation for both the endo- and epi-areas and figures (c) and (d) shows Bland–Altman plot for the same.

6. Conclusion

A fully automatic detection and segmentation of the left ventricle myocardium has been detailed in this paper. An edge preserving filter followed by an unsupervised clustering to successfully segment the left ventricle cavity from short axis MR images of the heart. Once the cavity volume is extracted the ejection fraction can be calculated. The edge-point accuracy is compared with level-set segmentation of the blood pool.

In the second part of the paper the epi-cardium border is successfully segmented using an edge-based technique. The thickness of the wall is approximated by measuring the thickness of the interventricular septum. The interventricular septum is an anatomically sound feature of the heart and because it is surrounded by blood on both sides it can be robustly segmented. This measurement is then used as an initial estimate for the thickness of the complete wall. A gradient image of the area around the lv is computed and the use of the approximate wall thickness, gradient points potentially belonging to the epi-cardium border are selected. If there are no viable gradients found on the epi-cardium border then the outer wall is estimated using the approximation found using the interventricular septum.

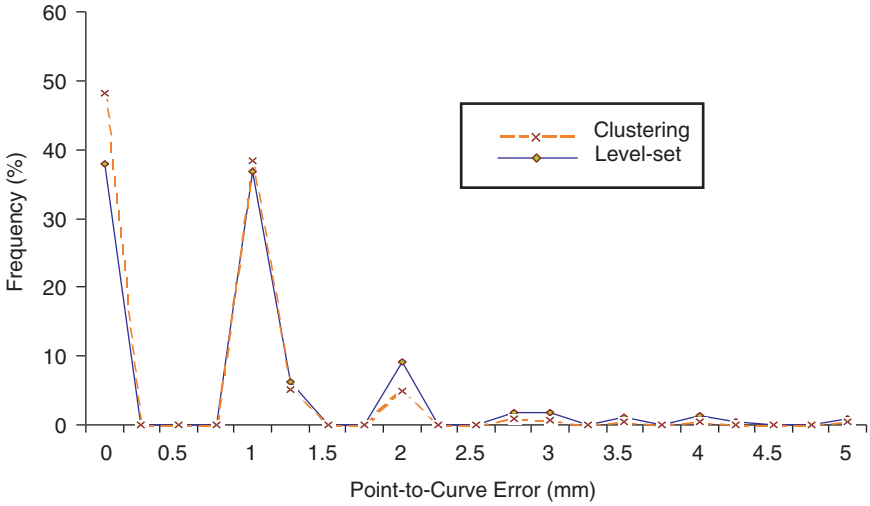

Fig. 7. Plot of the average thickness of the myocardium over 34 slices with both the manual segmentation and the automatic segmentation shown. Values are taken at evenly spaced radial positions around the endo-cardium border.

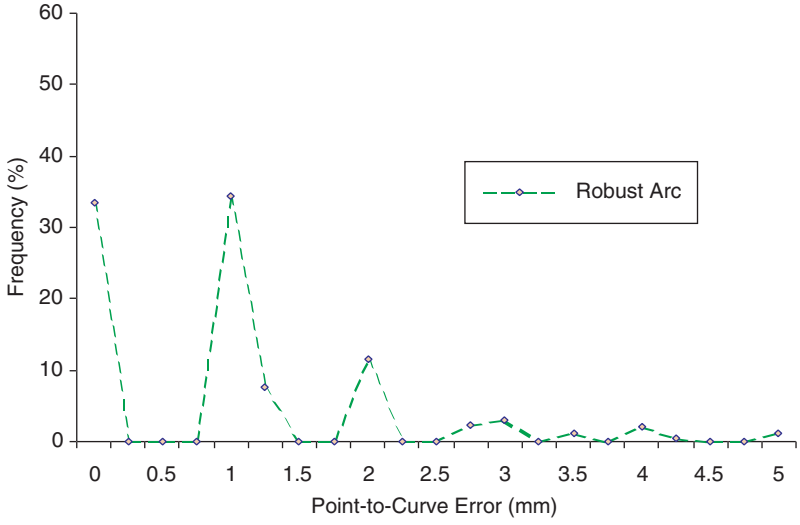

Fig. 8. Plot of the average thickness of the myocardium over 34 slices with both the manual segmentation and the automatic segmentation shown. Values are taken at evenly spaced radial positions around the endo-cardium border.

We believe that general models in ASMs\AAMs built up from training sets are limited in their application to the variety of heart shapes. Abnormalities in the image data can indicate disease. Model based approaches approximate to the closest plausible instance shape from the training set point distribution model (PDM), but this may not be sufficiently accurate. Also AAMs cannot deal well with the

changes in texture. This paper presents a robust, fully automated method to identify the endo-cardium and epi-cardium borders that does not rely on a priori knowledge nor does it use constraints to find the left ventricle cavity.

Left ventricle segmentation is primarily motivated by the need to clinically diagnose a feature of the heart with potential problems. Models that approximate left ventricular boundaries try to fit variations of boundaries that have already been segmented. The left ventricle is anatomically variant, the scanners are inconsistent and the variations of pathologies found in patients is vast. To build a model to accommodate such diversity would be an immense task. Our algorithm makes no approximations but produces a true evaluation of the heart structure by segmenting the true borders in the image. We should remember that the aim is not to segment hearts that are part of a model but to assist the cardiologist in the prognosis by delineating the true anatomical features present in the image.

Evaluating the endo-cardium and epi-cardium borders using this approach could provide a more appropriate technique for flagging problems like wall thinning and low ejection fraction.

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Appendix A.

A.1. LMS circle

Using the least squares solution a circle is fitted around a collection of points, P_i, with images coordinates, (x_i, y_i) for $i = 1, 2, \ldots, N$.

A circle is defined by three parameters. These parameters are the coordinates of its centre (x_0, y_0) and its radius r. The equation of a circle can be written isolating these three parameters as follows:

$$(2x_i \;\; 2y_i \;\; 1) \begin{pmatrix} x_0 \\ y_0 \\ r^2 - x_0^2 - y_0^2 \end{pmatrix} = (x_i^2 + y_i^2).$$

In order to find these three unknowns a linear least squares solution is obtained, where

$$A = \begin{pmatrix} 2x_1 & 2y_1 & 1 \\ 2x_2 & 2y_2 & 1 \\ 2x_3 & 2y_3 & 1 \\ & \cdots & \\ 2x_N & 2y_N & 1 \end{pmatrix}, \quad b = \begin{pmatrix} x_1^2 + y_1^2 \\ x_2^2 + y_2^2 \\ x_3^2 + y_3^2 \\ \cdots \\ x_N^2 + y_N^2 \end{pmatrix}.$$

The best fitting circle for the points P_i is the least squares solution to $[x_0 \;\; y_0 \;\; r^2-x_0^2-y_0^2]^{\mathrm{T}}=(A^{\mathrm{T}}A)^{-1}A^{\mathrm{T}}b$ where $(A^{\mathrm{T}}A)^{-1}A^{\mathrm{T}}b$ can be written as

$$\begin{pmatrix} 4\sum x_i^2 & 4\sum x_i y_i & 2\sum x_i \\ 4\sum x_i y_i & 4\sum y_i^2 & 2\sum y_i \\ 2\sum x_i & 2\sum y_i & N \end{pmatrix}^{-1} \begin{pmatrix} 2\sum x_i^3 + 2\sum x_i y_i^2 \\ 2\sum y_i^3 + 2\sum x_i^2 y_i \\ \sum x_i + \sum y_i^2 \end{pmatrix}.$$

The errors of this least squares solution can be calculated with $e_{\mathrm{circle}} = \|A[x_0 \quad y_0 \quad r^2 - x_0^2 - y_0^2] - b\|$

A.2. Splines

A spline fits a smoothed curve around a collection of points P_i where $i = 1, 2, 3, \ldots, N$. It works by fitting a cubic curve between each pair of points in the collection. Smoothness of the curve is maintained by forcing the first and second derivative of the end point of one curve to equal the start of the next curve. This is achieved by solving a system of simultaneous equations. The equation is illustrated below

$$f_i(x) = a_i + b_i u + c_i u^2 + d_i u^3,$$
$$0 \leqslant u \leqslant 1,$$
$$1 \leqslant i \leqslant n,$$

where i is the amount of points on the curve and u is the number of steps in between each point. The coefficients of the cubic equation are

$$a = x_n,$$
$$b = \frac{\mathrm{d}x_n}{\mathrm{d}P},$$
$$c = 3(x_{n+1} - x_n) - 2\frac{\mathrm{d}x_n}{\mathrm{d}P} - \frac{\mathrm{d}x_{n+1}}{\mathrm{d}P},$$
$$d = 2(x_n - x_{n+1}) + \frac{\mathrm{d}x_n}{\mathrm{d}P} + \frac{\mathrm{d}x_{n+1}}{\mathrm{d}P}.$$

A.3. Level-set formulation

The formulation of the problem is straight forward. The evolving curve or front Γ, evolves as the zero level-set of a higher dimensional function ϕ. This function deforms with a force F that is dependent on both curvature of the front and external forces in the image. The force acts in the direction of the normal to the front.

$$\phi_t + F|\nabla\phi| = 0,$$
$$\phi(x, y, t = 0) = \text{given}. \tag{9}$$

Our implementation is a standard two step approach which includes a fast-marching initial step to speed up the segmentation. Fast marching is a special case of the above equation where $F(x, y) > 0$. Let $T(x, y)$ be the time that the front Γ crosses the point (x, y). The function $T(x, y)$ then satisfies

$$|\nabla T|F = 1 \tag{10}$$

which simply says that the gradient of the arrival time is inversely proportional to the speed of the surface. The T function is evaluated using the diffusion and attraction to pixels within the front. The front grows out from its initial position to points with the smallest value of $T(x, y)$. The $T(x, y)$ function is then updated and continued until the front does not grow.

The fast-marching step is then followed with a fine tuning step using a narrow-band level-set method. Here the shape model is implicitly represented as the zero level-set of a function ϕ. Where $\phi=$ signed distance to the Γ, negative if inside the front and positive if outside. ϕ is iteratively updated as

$$\phi_{t+1} = \phi_t + k_I(1 - \varepsilon\kappa)|\nabla\phi| + \beta\nabla I \cdot \nabla\phi \tag{11}$$

where ε and β are user parameters, κ is the curvature term and equal to $\nabla \cdot \nabla\phi/|\nabla\phi|$ and k_I is an image dependent speed term and is given by $(1/1 + \nabla I)$. The third term, $\nabla I \cdot \nabla\phi$ represents the attractive force vector normal to the front. The updates were performed efficiently within a narrow-band around the front.

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