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Computer-aided detection of wall motion abnormalities in cardiac MRI

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**AUTOMATED DETECTION OF REGIONAL WALL
MOTION ABNORMALITIES BASED ON A STATISTICAL
MODEL APPLIED TO MULTI-SLICE SHORT-AXIS
CARDIAC MR IMAGES**

Abstract

In this section, a statistical shape analysis method for myocardial contraction is presented that was built to detect and locate regional wall motion abnormalities (RWMA). For each slice level (base, middle and apex), 44 short-axis MR images were selected from healthy volunteers to train a statistical model of normal myocardial contraction using independent component analysis (ICA). A classification algorithm was constructed from the ICA components to automatically detect and localize abnormally contracting regions of the myocardium. The algorithm was validated on 45 patients suffering from ischemic heart disease. Two validations were performed; one with visual wall motion scores (VWMS) and the other with wall thickening (WT) used as references. Accuracy of the ICA-based method on each slice level was 69.93% (base), 89.63% (middle) and 72.78% (apex) when WT was used as reference, and 63.70% (base), 67.41% (middle) and 66.67% (apex) when VWMS was used as reference. From this observation, it is concluded that the proposed method is a promising diagnostic support tool to assist clinicians in reducing the subjectivity in VWMS.

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All the knowledge I possess everyone else can
acquire, but my heart is all my own.

Die Leiden des jungen Werther
(The Sorrows of Young Werther)
JOHANN WOLFGANG VON GOETHE

ASSESSMENT of wall motion is important to determine cardiac function in rest, in stress-induced ischemia (with high dose dobutamine echocardiographic protocols) and in the assessment of viability (with low dose dobutamine protocols). In practice, dobutamine stress echo is often applied, but there are some difficulties to image the heart properly in patients with a bad acoustic window. The analysis is also subjective, with moderate reproducibility, and quantification is not very accurate. Dobutamine MRI is an alternative method to assess regional wall motion abnormalities (RWMA). MRI has a higher resolution and does not depend on acoustic window and therefore enables more accurate quantification.

In clinical practice however, RWMA assessment mainly relies on visual analysis and interpretation of wall motion. Visual Wall Motion Scoring (VWMS) is commonly performed by following a standard issued by the American Heart Association (AHA) [1], where seventeen myocardial segments are graded by an expert from cine-MR images. Segments are graded on a five point scale: normo-kinetic, mild-hypokinetic, severe hypokinetic, akinetic and dyskinetic.

The main problem with VWMS is the high interobserver variability. The subtle differences in cardiac motion abnormalities are difficult to score, which makes VWMS less reproducible and less objective. Also, the segment boundaries are often decided based on qualitative criteria, and may vary depending on the location of the diseased myocardium. In two studies, the interobserver agreement to assess RWMA has been investigated. Paetsch et al. [2], assessed interobserver agreement of RWMA from stress studies and their kappa coefficient (κ) is 0.59. Hoffmann et al. [3] compared 3 different modalities: echocardiography ($\kappa = 0.41$ without contrast agent and $\kappa = 0.77$ with contrast agent), MRI ($\kappa = 0.43$) and cineventriculography ($\kappa = 0.56$). In conclusion, there was no modality that achieved a near perfect agreement and reader differences continue to exist even with high quality images [3]. Both studies underscore that VWMS is very subjective, not to mention that it requires an elaborate training of the observer.

The goal of the present study is to develop an automated tool to detect and localize myocardial regions that show an abnormal contractile behavior based on statistics trained from healthy wall motion. Such an automated tool would have the advantage that it would reduce the inter- and intra observer variability and subjectivity in the analysis, and as subsequently it may assist less experienced readers to arrive at a reliable assessment of regional wall motion abnormalities.



6.1 Introduction

6.1.1 Automated RWMA detection methods

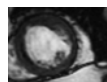
There have been prior studies aimed at developing an automatic detection of wall motion abnormalities. These studies are mainly based on shape statistics, that are described using a point distribution model (PDM) [4]. In a PDM, myocardial shapes are subsampled into a number of landmark points. A statistical model is then estimated from the set of landmark points, expressing the training population as a linear combination of an average shape and a set of characteristic eigenvariations. PDMs have been used extensively, particularly for segmentation purposes, because the model has been restricted to search such a statistically plausible shape in the image, e.g. [5, 6].

Shape parameterization using PDMs for the diagnosis of cardiac shape abnormalities was first explored by Mitchell et al. [7]. A mixed model of patients and healthy volunteers is created by taking myocardial contours only from end-diastole (ED) phase. Principal component analysis (PCA) is then used to parameterize the model. The classification between normal and abnormal shapes was evaluated by leave-one-out validation using three classification techniques: linear discriminant analysis (LDA), kernel LDA and nearest neighbor classifier. A comparable performance was found for all three classifiers. In spite of that, the model was based on static ED images, therefore solely based on shape, not incorporating any motion or contraction.

Remme et al. [8] developed a 3D left ventricle (LV) model using a fitted finite-element mesh onto the ED LV surface and selected nine clinically-termed deformation modes that were calculated by PCA. The LV deformation was estimated using tagged MR images. Two models from normal and patient subjects were investigated and the statistical inference on each nine PCA modes were estimated independently. Five out of nine PCA modes showed significant differences between normal and patient subjects. The method is useful to make a global classification between normal and patients, but not to locate the RWMA.

The first attempt to make a statistical model to quantify RWMA was proposed by Bosch et al. [9]. Only infarct patients from echocardiographic images were included to build the statistical model. The classification performance was tested by randomly splitting the data into training and test sets. PCA was used to parameterize the shape. To perform regional classification, multivariate linear regression was used to select principal components that have good correlation with the corresponding VWMS values. Bosch et al.'s study showed that VWMS correlated to the global PCA modes, although only weak correlations were found.

The drawbacks of the previous automatic wall motion abnormality studies lie on two main issues of their shape modeling. First, the typical PCA modes of shape variation affect global shape. Classifying different shape groups can only reveal global shape differences [10]. There is no information on the exact location of shape differences through PCA components. Second, the model generalization ability is limited because both patients and normal subjects are mixed in the training set (Mitchell study [7]), or only patients are included (Bosch et al. study [9]). These models are biased towards the trained pathology and they may not generalize well towards other pathologies.



6.1.2 Sparse decomposition in statistical shape analysis

Recently, an extension of PCA, which exploits sparseness by adding constraints of the number of nonzero loadings [11], has gained interest in shape analysis. Local variations of landmark position, as well as texture, can be achieved from Sparse PCA [12]. Applied to *corpus callosum* shapes, Sparse PCA reveals some position preferences of a local shape variation over a certain physiologically meaningful clinical outcome [13]. A preliminary report of Sparse PCA for characterizing myocardial wall motion abnormality from echocardiograms has also been reported [14].

Sparsity in Sparse PCA is induced deliberately with the additional constraint. Rather than imposing some regression techniques to enforce sparsity, an assumption of statistical independency can be applied to get a sparse decomposition. Here, Independent Component Analysis (ICA) is applied in the shape domain. ICA was originally developed in signal processing to separate mixing signals into sources without any knowledge, except the mixing signals themselves [15, 16]. The only assumption that can be made is that the source signals are independent. Typically, a mixture of signals is observed and the independent source signals can be estimated either by maximizing non-Gaussianity (the FastICA method [16]), maximizing entropy (the infomax principle [17]), or by using fourth-order cumulant matrix (the JADE algorithm [18]), among other ICA algorithms.

In shape analysis, the observed mixed signals are the training shapes. Since these signals are taken from the same group, all signals have similar characteristics and after ICA, the independent sources exhibit sparse regional spikes. Regional spike signals appear because these signals maximize statistical independency between each other for similar source signals. This phenomenon is what drives sparse decomposition for shape modeling with ICA. Unlike Sparse PCA, sparsity comes directly from ICA without additional constraints.

The statistical independency property gives an advantage of ICA over Sparse PCA for classification purposes. It allows a simple joint probability density function estimation from all components. Consequently, a probability density function can be defined for each landmark point, as will be explained in details in Section 6.2. One limitation of ICA compared to PCA (and Sparse PCA) is that the ICA components are not necessarily linked to any anatomical or physiological meaning of the training shapes. For some ICA algorithms, such as FastICA, the source signal results can even vary between different estimations due to its stochastic nature. In this study, however, anatomically meaningful sparse decomposition is not the main interest. ICA is used only for feature extraction rather than for anatomical description.

ICA has been previously used for statistical shape analysis [19, 20]. The sparseness characteristic of ICA has been exploited for an automated detection of tissue disorders in 3D aortic vessels [21] and for image segmentation [22]. In a comparison study of statistical shape analysis between different non-Euclidean metrics, it is reported that a method equivalent with ICA (Maximum Autocorrelation Factors) is one of the superior methods to decompose large shape variations [23].

6.1.3 Contribution of this chapter

In Chapter 3, it has been demonstrated that ICA has an advantage over PCA for local shape classification, because ICA decomposes shapes into local shape descriptors [10]. Therefore ICA is suitable to be used as a local feature classifier compared to PCA. In Chapter 4, ICA has been applied in cardiac shapes to locate abnormal regions in mid-ventricular slice level of myocardium [24]. By selecting ‘abnormal’ independent components, an ICA-based classifier gives good visual correspondence with infarcted regions indicated by delayed-enhancement MR images.

In this chapter, the ICA-based detection method is improved and quantitative validations are presented. The contribution of this chapter is twofold:

1. Proposing a statistical method to extract local myocardial contraction patterns from multi-slice short-axis MRI by ICA, and a method to detect and to localize regional wall motion abnormalities based on the ICA shape parameterization.
2. Quantitative validations of the proposed statistics-based method are presented with 45 patients suffering from ischemic heart disease.

This chapter is further organized as follows. Section 6.2 describes the methodology in-depth from building the statistical model of healthy cardiac contraction until the construction of RWMA detectors. In Section 6.3, the method is quantitatively validated, followed by a discussion in Section 6.4 and conclusions in Section 6.5.

6.2 Methodology

This section starts off by introducing the cardiac contraction modeling from a set of myocardial contours, such that all pose and shape variations, including shapes at the starting point of contraction (end-diastolic phase), are eliminated. In Section 6.2.2, the model is decomposed into local shape descriptors using ICA. The ICA algorithm requires the number of independent components as a parameter. A robust estimation method to estimate this parameter is given in Section 6.2.3. After the ICA model is constructed, distributions of model’s coefficient can be estimated, as described in Section 6.2.4. Finally, Section 6.2.5 explains the RWMA detection method by propagating probability density functions from ICA domain into shape domain.

6.2.1 Statistical Shape Modeling of Cardiac Contraction

Landmark-based statistical shape analysis was introduced in 1980s as a method to investigate the geometrical statistics of a set of shapes and their relative positions [25]. Landmarks are homologous points with point-to-point correspondences between shapes, that can be defined either mathematically, anatomically or manually. Let (x_i, y_i) be a 2D Cartesian coordinate of the i -th landmark point. A shape vector $\mathbf{x} \in R^{2P}$ with P landmarks is defined by

$$\mathbf{x} = [x_1, y_1, x_2, y_2, \dots, x_P, y_P]^T. \quad (6.1)$$

Shapes are aligned by using Procrustes alignment [26] to eliminate variations in location, size and shape orientation. This is given by

$$\mathbf{x}^p = \frac{\mathbf{x}^T \hat{\mu} \mathbf{x}}{\mathbf{x}^T \mathbf{x}}, \quad (6.2)$$

where $\mathbf{x}^p$ is the shape $\mathbf{x}$ aligned to the mean shape $\hat{\mu}$. The aligned shapes are invariant under scale, translation and rotation transformations.

The mean shape $\hat{\mu}$ is estimated from a training set $\{\mathbf{x}_i\}$, $i = 1, \dots, N$. Let $\mathbf{S}$ be a matrix defined as

$$\mathbf{S} = \sum_{i=1}^N \frac{\mathbf{x}_i \mathbf{x}_i^T}{\mathbf{x}_i^T \mathbf{x}_i}. \quad (6.3)$$

The mean shape $\hat{\mu}$ can be found as the eigenvector corresponding to the largest eigenvalue of $\mathbf{S}$, provided that $\{\mathbf{x}_i\}$ are centered to its origin, i.e. $\mathbf{x}_i \cdot \mathbf{1} = 0$. It has been proven that $\hat{\mu}$ is unique up to rotation [26]. All rotations of $\hat{\mu}$ are also solutions, which correspond to the same mean shape.

The aligned shape $\mathbf{x}^p$ can be expressed in a linear generative model, given as

$$\mathbf{x}^p = \hat{\mu} + \Phi \mathbf{c}, \quad (6.4)$$

where $\Phi \in \mathbb{R}^{2P \times M}$ is the component matrix with $M \leq 2P$ number of components and $\mathbf{c} \in \mathbb{R}^M$ is a coefficient vector. The matrix Φ decomposes the training set $\{\mathbf{x}_i\}$ into M components.

In Chapter 4, four contours (endocardial and epicardial contours at end-diastole (ED) and end-systole (ES)) were combined serially to form a shape vector [24]. This sufficed to capture myocardial contraction. However, since the main focus is to statistically compare ‘contraction shapes’ between two individuals, geometrical variation of shapes at the beginning of contraction must be removed. Consequently, all training samples start the contraction from the same shape, providing a *unit contraction model*. This is similar to Bookstein’s coordinate system [27], where two landmark points are sent to a fixed position (known as *baseline landmarks*) allowing $P - 2$ non-zero variation of landmark point distributions.

However, instead of using a rigid similarity transformation, thin-plate splines are applied [28] to allow deformation of the heart shape. This is necessary in particular for patients because their myocardial shapes are dissimilar from normal subjects. As an example, the effect of thin-plate spline warping on a patient shape is shown in Figure 6.1 (light gray arrows) and it is noticeable on the lower part of myocardium. On the contrary, only moving contraction vectors from the patient shape to the mean shape (dark gray arrows in Figure 6.1) does not compensate for deformation.

With the unit contraction model, the linear generative model (6.4) can be estimated only from the ES shape part. This gives an advantage of reducing half the dimension during ICA computation while preserving the contraction information. Figure 6.2 shows comparison of the point distribution model between serially combined vectors (Figure 6.2(a)) and the unit contraction model (Figure 6.2(b)).

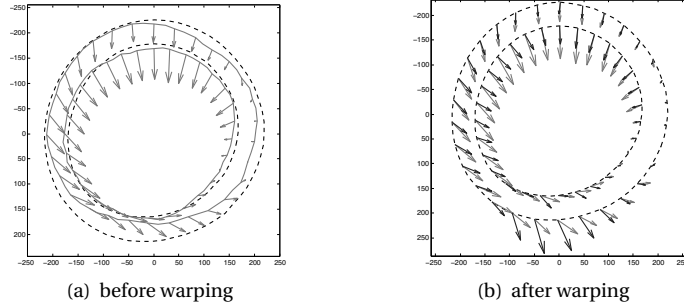


FIGURE 6.1: An example of the effect of thin-plate splines warping to the mean shape (dashed lines) during the unit contraction modeling. Light gray arrows show original contraction vector from ED to ES, while dark gray arrows show unit contraction vector from ED to ES.

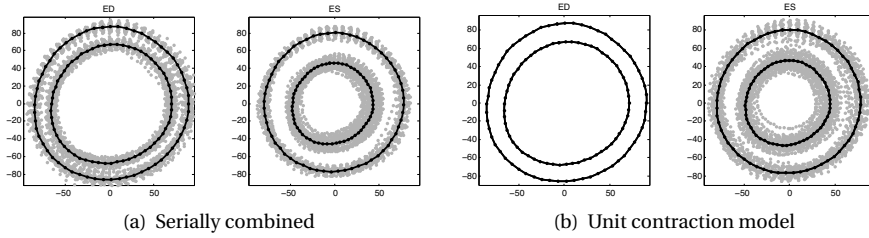


FIGURE 6.2: Shapes of endocardial and epicardial contours from 50 healthy volunteers after the Procrustes fit. The mean shapes are depicted as black thick solid lines.

6.2.2 Myocardial Shape Decomposition with ICA

Independent component analysis (ICA) is then applied to estimate Φ and $\mathbf{c}$ in (6.4) by maximizing the statistical independency. In ICA terminology, the mixed signals are $\{\mathbf{x}_i^p - \hat{\mu}\}$ vectors, the source signals are $\{\mathbf{c}_i\}$ vectors and the mixing matrix is Φ .

The k -th mode of shape variation, $\mathbf{z}_k \in \mathbb{R}^{2P}$, is defined by

$$\mathbf{z}_k = \hat{\mu} + \Phi \delta \mathbf{e}_k, \quad \mathbf{e}_k^{(i)} = \begin{cases} 1 & i = k, \\ 0 & i \neq k. \end{cases} \quad (6.5)$$

The modes of shape variation describe variation of the landmark point's location, triggered only by one component. The value of δ determines the distance of the generated shape $\mathbf{z}_k$ from the mean shape. It is usually determined from the variance of the k -th coefficient values σ_k^2 from the model, e.g. $-3\sigma_k \leq \delta \leq 3\sigma_k$.

Four examples of ICA modes of variation from the myocardial contraction shape are shown in Figure 6.3, which clearly show local shape variations associated with a certain

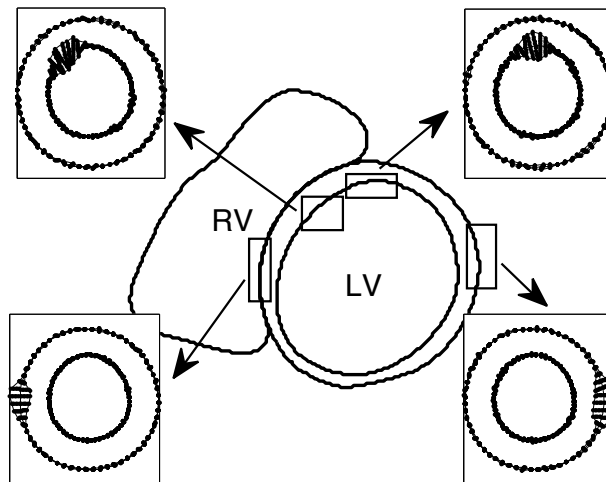


FIGURE 6.3: ICA modes of shape variation applied for myocardial contraction with their associated regions in the myocardium.

region in the myocardium. The modes of shape variation are useful to inspect a statistical shape model or to generate a new shape. In this study, the component matrix Φ is going to be exploited for classification purposes.

6.2.3 Robust Estimation of Independent Components

The main difficulty in ICA is to determine the number of independent components (ICs) into which the source signals should be decomposed. Any number can be given between 1 and N . It is straightforward for a case where the number of source signals is a priori known, however, in many cases, the number of real ICs that constitute the dataset is unknown.

The number of ICs can be estimated by selecting ICs that are reliable. An IC is said to be reliable if the source signal passes a test based on specific criteria. There have been several approaches to such a reliability test, i.e. by using mutual information [29], neural networks [30], a Bayesian approach [31] or clustering techniques [32].

The clustering technique, proposed by Himberg et al. [32], is chosen in this work, because this approach is suitable for the FastICA algorithm [16]. Reliable ICs are calculated from a certain number of different ICA estimations. At each realization, ICs are collected and mapped onto a cluster space. Strong ICs are shown by their clusters that are compact and well separated from the other clusters. One disadvantage of this technique is that it needs to perform the ICA algorithm several times to estimate the number of reliable components. However, in model construction, computation time is not a critical issue, because building the ICA model is only performed once.

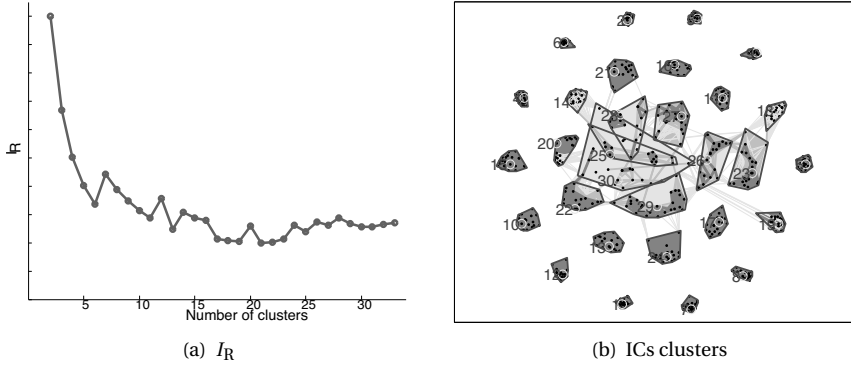


FIGURE 6.4: The I_R vs number of clusters plot (left) and the clusters of ICs from the unit contraction model (right). The model was reduced first by PCA to eliminate noise by retaining 99% of the total variance. Note that the left figure only to show relative I_R values, therefore the y-axis units are not given.

To indicate strong ICs, the ratio between the within-cluster and between-cluster scatter matrices is used. It is defined as

$$I_R = \frac{1}{M} \sum_{k=1}^M \frac{S_k^{\text{in}}}{S_k^{\text{ex}}}. \quad (6.6)$$

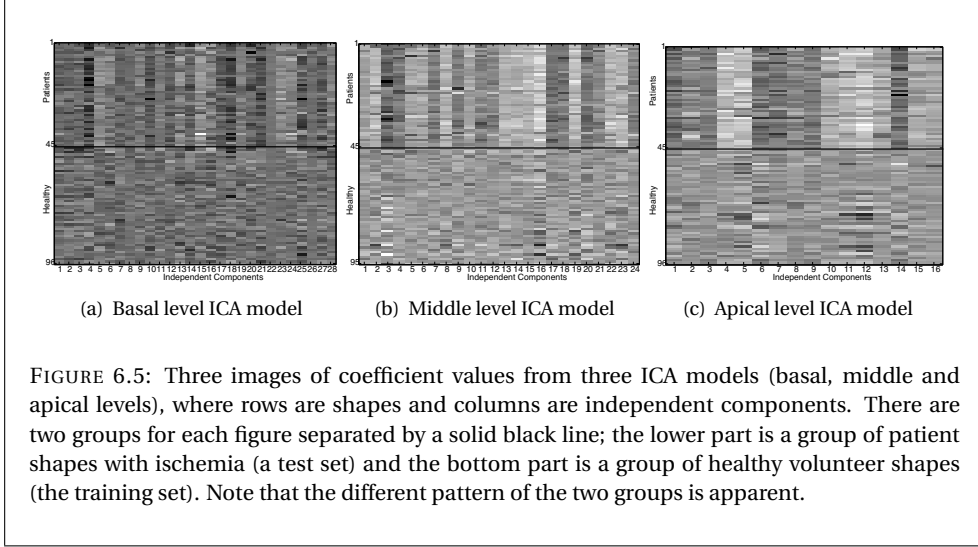
where S_k^{in} and S_k^{ex} are the within-cluster and between-cluster scatter matrices respectively, defined by

$$S_k^{\text{in}} = \frac{1}{|C_k|^2} \sum_{i,j \in C_k} (1 - \alpha_{ij}),$$

$$S_k^{\text{ex}} = \min_{k' \neq k} \frac{1}{|C_k||C_{k'}|} \sum_{i \in C_k} \sum_{j \in C_{k'}} (1 - \alpha_{ij}),$$

with C_k and $C_{k'}$, $k = 1, \dots, M$ are two sets of indices that belong and do not belong to the k -th cluster, respectively. The α_{ij} is a similarity measurement between the i -th and j -th clusters, using the absolute value of their mutual correlation coefficient. A compact cluster has a high S_k^{ex} value and an isolated cluster shows a low S_k^{in} value. A minimal I_R value is preferred. An example of an I_R plot over the number of ICs is shown in Figure 6.4(a). The corresponding cluster space is shown in Figure 6.4(b).

This clustering method is applied to determine two FastICA parameters: the number of computed ICs and the initial guess position. The number of computed ICs is selected from clusters that give a low I_R from (6.6). The initial guess parameter value is defined from the *centroid* of the IC clusters.



The modes of shape variation in ICA are not ordered, because all independent components are equally important. This is not a problem in this study, because all independent components are used as local shape detectors for abnormal shape components.

6.2.4 Estimating Density Functions of Independent Components

Let $\mathbf{y} \in \mathbb{R}^{2P}$ be a new shape that is not in the training shapes $\{\mathbf{x}_i\}$, and it is aligned by (6.2). Using the Moore-Penrose pseudo-inverse, the projection of $\mathbf{y}$ onto Φ can be calculated by

$$\mathbf{c}_y = (\Phi^T \Phi)^{-1} \Phi^T (\mathbf{y} - \hat{\mu}). \quad (6.7)$$

If shape $\mathbf{y}$ is similar to the training shapes $\{\mathbf{x}_i\}$, then $\mathbf{c}_y$ resembles any one of $\{\mathbf{c}_i\}$ in (6.4). On the contrary, if $\mathbf{y}$ comes from a different group, for example $\mathbf{y}$ is a pathological shape and $\{\mathbf{x}_i\}$ is normal (healthy) shapes, then the coefficient values of $\mathbf{c}_y$ lie outside the distribution of $\{\mathbf{c}_i\}$. This is shown in Figure 6.5, which displays the coefficient values from the control group (healthy volunteers) and ischemic patient group from basal, middle and apical ICA models.

Classification is then performed by specifying which elements of $\mathbf{c}_y$ lie outside the distribution of the model. Since an IC is related to a certain segment in a shape (an ICA mode of variation exhibits local shape variation as seen in Figure 6.6(d)), detecting the i -th element of $\mathbf{c}_y$ as an outlier yields a segment in the shape that deviates from the model.

Let $W_k, k = 1, \dots, M$, be random variables, each corresponds to the k -th component. By the independency, the joint probability density function of the ICA model coefficient values is defined by

$$f_{W_1, W_2, \dots, W_M}(w_1, w_2, \dots, w_M) = \prod_{k=1}^M f_{W_k}(w_k). \quad (6.8)$$

Hence, the distribution of the ICA model coefficient values can be simplified by estimating the density function of each component separately.

ICs have non Gaussian distributions, or at most only one component with a normal distribution [16]. Consequently, the normal density assumption cannot be used to estimate the density functions. Non-parametric kernel density estimation [33] is more suitable, because it does not assume a particular distribution. The density function for the k -th component can be estimated by

$$\hat{f}_{W_k}(w) = \frac{1}{Nh} \sum_{i=1}^N K\left(\frac{w - \mathbf{c}_{i,k}}{h}\right), \quad (6.9)$$

where w is a real value, h is the bandwidth of a kernel function $K(u)$ and $\mathbf{c}_{i,k}$ is the k -th element of the model coefficient vector $\mathbf{c}_i$.

Kernel density estimation method uses a mixture of N kernel functions, where N is the number of samples. Notice that in (6.9), each kernel is centered on each sample. The specific choice of kernel function is not critical [33], so the unit Gaussian kernel function is chosen, as defined below

$$K(u) = \frac{1}{\sqrt{2\pi}} \exp\left(-\frac{u^2}{2}\right). \quad (6.10)$$

However, the selection of bandwidth h is the important factor [33]. The bandwidth controls the amount of smoothing. A small difference in h can yield a big difference in the density function. The Sheather-Jones solve-the-plugin method [34] is applied to estimate the optimal bandwidth, which solves unknown functional parameters directly from the sample distribution.

6.2.5 Detecting Abnormal Regions

Based on the combination of the localized ICA model of myocardial contraction and the estimated density functions, a classification boundary separating normal and abnormal subjects can be developed. 'Abnormal components' can be defined from parameters that yield low probability values from the corresponding density functions. By selecting only these abnormal components, and due to the local nature of the ICA modes, the spatial location of the wall motion abnormality can be located, and thus RWMA assessment can be automatically carried out.

Classifying a component as abnormal does not directly identify abnormal regions. The abnormal components need to be mapped to the shape domain to identify abnormal regions. Therefore, propagation of the estimated M density functions $\{\hat{f}_{W_k}(w)\}$ to the shape domain is needed, resulting in a density function for each element in the shape vector.

The propagation of density functions can be calculated by using the inverse relation of (6.7), which transforms values in the component domain to the shape domain with the same form as in (6.4). Let $\hat{\mu}$ in (6.7) be defined as $\mathbf{0}$. For notational simplicity, let us focus only on a single element in a shape vector and define Y as a random variable for the

element. From the inverse of (6.7), the random variable Y is defined as

$$Y = \phi_1 W_1 + \phi_2 W_2 + \dots + \phi_M W_M = \sum_{k=1}^M \phi_k W_k, \quad (6.11)$$

where $\phi_1, \dots, \phi_M$ are elements of the corresponding row of Φ for the shape vector element.

Let $U_1, \dots, U_M$ be M new random variables, each defined as

$$U_k = \phi_k W_k. \quad (6.12)$$

It is obvious that U_k is independent from U_l for $(k \neq l)$, and its density function can be defined as

$$f_{U_k}(u_k) = \frac{1}{|\phi_k|} f_{W_k}\left(\frac{u_k}{\phi_k}\right). \quad (6.13)$$

Substitute (6.9) with (6.13) yields

$$f_{U_k}(u_k) = \frac{1}{|\phi_k| N h} \sum_{i=1}^N K\left(\frac{u_k - \mathbf{c}_{i,k} \phi_k}{\phi_k h}\right). \quad (6.14)$$

The density function of the sum of two independent random variables U_k and U_l is given by the convolution of $f_{U_k}(u_k)$ and $f_{U_l}(u_l)$ [35]. By introducing another M auxiliary random variables

$$\begin{aligned} Y_1 &= U_1 \\ Y_2 &= Y_1 + U_2 \\ &\vdots \\ Y_{M-1} &= Y_{M-2} + U_{M-1} \\ Y_M &= Y_{M-1} + U_M, \end{aligned} \quad (6.15)$$

the joint density function of Y in (6.11) can be recursively solved as follows

$$\begin{aligned} f_Y(y) &= f_{Y_M}(y_M) \\ &= \int f_{U_M}(y_M - y_{M-1}) f_{Y_{M-1}}(y_{M-1}) dy_{M-1} \\ &= \iint f_{U_M}(y_M - y_{M-1}) f_{U_{M-1}}(y_{M-1} - y_{M-2}) \\ &\quad f_{Y_{M-2}}(y_{M-2}) dy_{M-2} dy_{M-1} \\ &= \int \dots \int f_{U_M}(y_M - y_{M-1}) f_{U_{M-1}}(y_{M-1} - y_{M-2}) \\ &\quad \dots f_{U_1}(y_1) dy_1 \dots dy_{M-2} dy_{M-1} \\ &= f_{U_M} * f_{U_{M-1}} * \dots * f_{U_1}. \end{aligned} \quad (6.16)$$

Equation (6.16) defines the density function of an element of a shape vector. It is given as the series of convolutions of M density functions $\{f_{U_i}(u_i)\}$ in (6.14), which are defined for each element IC.

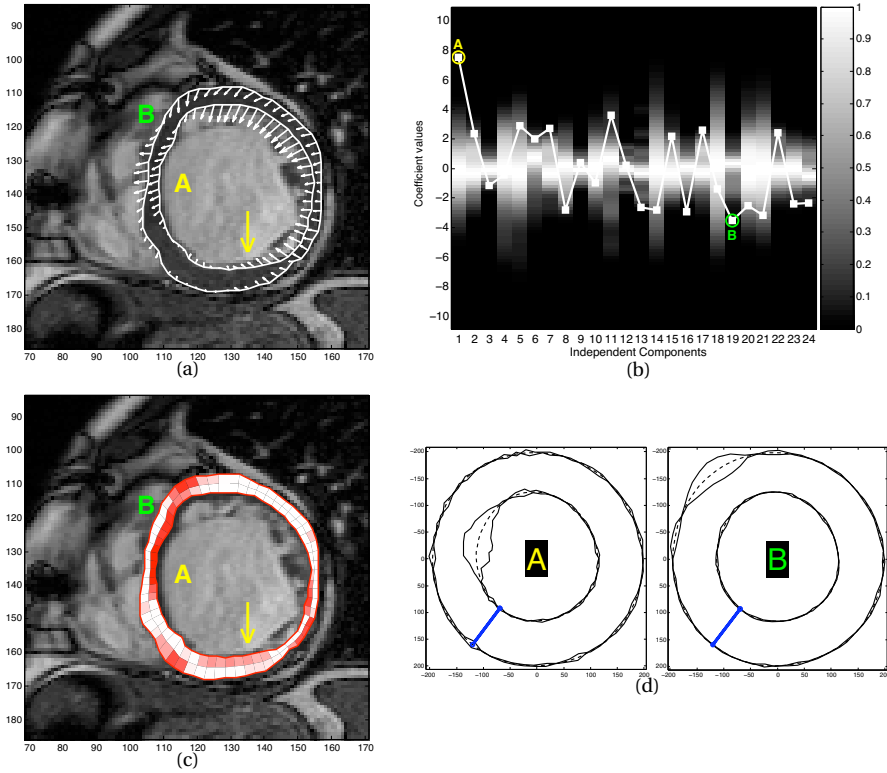


FIGURE 6.6: An example of an automatic RWMA detection on a patient dataset. The septal (label A and B) and the inferior (arrow) regions show reduced wall motion. (a) Raw patient contours (as vectors from ED to ES) projected on the patient's MR image at ED. (b) Coefficient values for the same patient (solid line) after projection onto the ICA model, superimposed on the model parameter distributions. Each column shows one distribution of an independent component. The values in the greyscale bar indicate probability values of a healthy wall motion. Two components (label A and B) are specially noted that have the two lowest probability values. (c) The detection result. Dark areas indicate abnormal wall motion based on the estimated density functions (6.15) on each landmark point. (d) Shape variations from the first IC (label A) and the 19th IC (label B), both of which show local shape variations (dashed line is the mean shape, and solid lines are ± 3 times standard deviation of the component's coefficients). The lines crossing myocardium indicate the first landmark points at endo and epicardial contours.

An example of how the density function propagation works is shown in Figure 6.6, which uses the mid-ventricular ICA model. The input contours are shown in Figure 6.6(a) as vectors from ED to ES contours that represent the myocardial contraction. The detection result is given in Figure 6.6(c), which is shown as probability values of having an abnormal shape at each landmark point. Note also how hypokinetic motion in the inferior region (the small arrow in Figure 6.6(a)) points to regions with high probability values of being abnormal (the small arrow in Figure 6.6(c)).

In Figure 6.6(b), two independent components (the 1st and the 19th ICs), which have the largest deviations of coefficient values from the model coefficient values, were labeled as A and B, respectively. When the ICA modes of variations from these two ICs are inspected (see Figure 6.6(d)), the local shape variations correlate with regions with abnormal motion. The first IC (label A) detects a reverse contraction motion in the septal region, while the 19th IC (label B) detects small wall thickening in the upper part of the septum.

6.3 Experimental Results

6.3.1 Data description and preprocessing

TABLE 6.1: Patient and Control Groups Statistics.

	Patients	Controls
Samples	45	44
Males/females	42/3	33/11
Ejection fraction (%)	36.30 ± 10.7	61.99 ± 6.4
Stroke volume (ml)	75.57 ± 19.6	94.94 ± 21.5

Myocardial contours of short-axis MR images were collected from two groups: a control group for model training and a patient group for classification testing. The control group consists of healthy volunteers, whereas the patient group consists of patients suffering from chronic coronary artery disease, with a depressed LV function. Baseline statistics of both groups are shown in Table 6.1, which also shows that ejection fraction and stroke volume is significantly different between the two groups.

MR images were acquired by 1.5T Gyroscan ACS-NT MRI scanner (Philips Medical Systems, Best, The Netherlands) and only short-axis view datasets were used that cover the LV from apex to base. End-diastole (ED) and end-systole (ES) phases from basal, mid-ventricular and apical levels were selected. Epi- and endocardial contours were manually drawn by an expert.

Visual wall motion scores (VWMS) for the patient group were performed for each segment by an experienced cardiologist on a 5-point scale: normokinetic, mild-hypokinetic, severe-hypokinetic, akinetic and dyskinetic. During the scoring process, cine-MRI viewing of the short-axis views was used and the observer was blinded to the result of the proposed method. VWMS was performed on 6 segments at the basal level, 6 segments at the mid-ventricular level, and 4 segments at the apical level. To determine the segment

TABLE 6.2: RWMA validations using WT (top) and VWMS (bottom) as reference

Validation using WT as a reference (WT benchmarking)						
	ICA-based Method			VWMS		
	acc. (%)	sens. (%)	spec. (%)	acc. (%)	sens. (%)	spec. (%)
base	69.63	76.92	66.67	66.67	69.23	65.62
middle	89.63	85.48	90.87	76.30	56.45	82.21
apex	72.78	72.97	72.73	63.33	54.05	65.73

Validation using VWMS as a reference (VWMS benchmarking)						
	ICA-based Method			WT		
	acc. (%)	sens. (%)	spec. (%)	acc. (%)	sens. (%)	spec. (%)
base	63.70	60.83	66.00	70.00	65.83	73.33
middle	67.41	65.12	69.50	68.52	60.47	75.89
apex	66.67	59.42	71.17	62.22	60.87	63.06

Each percentage value was computed with all segments included after determining the optimal cut-off boundary value.

locations, the American Heart Association (AHA) standard for myocardial segmentation was adopted [1]. Wall thickening (WT) was calculated by using dedicated quantitative MR measurement software MR Analytical Software System (MASS v5.0, Medis, Leiden, the Netherlands) [36]). WT is defined in term of percentage systolic thickening, calculated per landmark point as defined by

$$WT = \frac{w_{es} - w_{ed}}{w_{ed}} \times 100\%, \quad (6.17)$$

where w_{es} and w_{ed} are myocardial wall thickness (the distance from endocardial and epicardial contours) at end systolic and end diastolic respectively.

For ICA modeling, landmarks were defined by equi-angular sampling of epi- and endocardial contours from the center of myocardium. The number of landmarks per segment was set to 10, producing 60 landmarks per contour for basal and middle slices and 40 for apical slices. To ensure point-to-point correspondence between subjects, a fixed anatomical reference point was defined at the intersection between the left and right ventricle at the inferior region. The ICA model was calculated with FastICA algorithm [16], implemented in Matlab (Matlab v6.5, The Mathworks, Natick, MA, USA). The non-linear objective function parameter in FastICA was $g(y) = 3y^2$ and the symmetric orthogonalization parameter was used.

6.3.2 Validation Method

As described before, VWMS is sensitive to high subjectivity and variability [2, 3]. Therefore, to enable an objective performance assesment of the proposed method, two validations were performed by establishing two types of benchmarking. The first one is by selecting

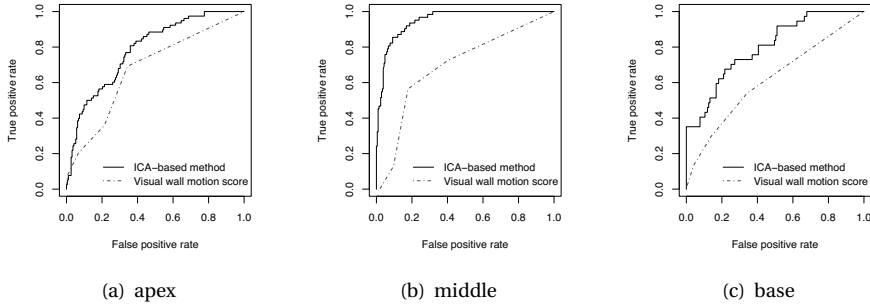


FIGURE 6.7: The performance of the ICA-based method compared with VWMS from the WT benchmarking.

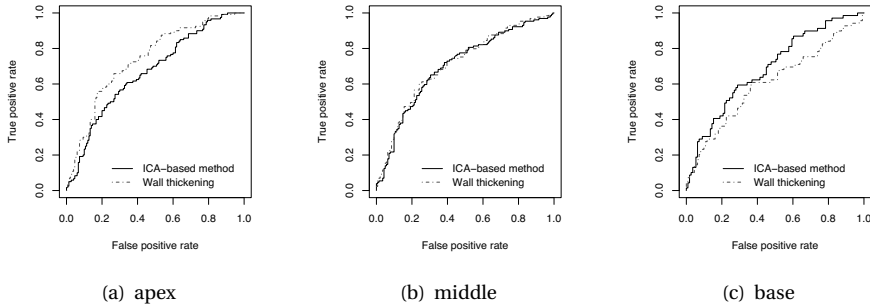


FIGURE 6.8: The performance of the ICA-based method compared with WT from the VWMS benchmarking.

WT as a point of reference to compare the ICA-based method with VWMS (WT benchmarking) and the second one is by selecting VWMS as another point of reference to compare the ICA-based method with WT (VWMS benchmarking). In the WT benchmarking, a threshold value of 10% was determined as the boundary between normal and reduced WT [37]. In the VWMS benchmarking, the classification boundary is converted into binary values: 0 for normokinetic region and 1 for other dyskinetic regions.

To evaluate the performance of the diagnostic methods in both benchmarking tests, receiver operating characteristics (ROC) curves were used. ROC graph is a standard graphical tool to visually compare different classification methods [38]. The optimal cut-off value to define classification boundary can also be estimated by using ROC curve, which is defined by minimizing $(1 - \text{sensitivity})^2 + (1 - \text{specificity})^2$. The optimal cut-off value was

then used to calculate the performance of a method in terms of accuracy, sensitivity and specificity, as given by

$$\text{acc} = \frac{T_P + T_N}{P + N}, \quad \text{spec} = \frac{T_N}{N}, \quad \text{sens} = \frac{T_P}{P}, \quad (6.18)$$

where T_P and T_N are true positive (the number of segments that are correctly identified as abnormal) and true negative (the number of segments that are correctly identified as normal) values, respectively. The total number of abnormal (positive) and normal (negative) segments are P and N . The ROC package developed by [39] was used to generate ROC graphs.

6.3.3 Classification performance

Five examples of the automated detection result are presented in Figure 6.9, side-by-side with the corresponding MR image sequences. Corresponding RWMA areas (white arrows) are found in the same place with the estimated abnormal wall motion from the automated method. Table 6.2 shows the classification performance using the WT and the VWMS benchmarking tests. Compared to VWMS in the WT benchmarking, accuracy of the ICA-based method is significantly higher. This is also the case for sensitivity and specificity measurements. The highest performance was achieved in the mid-ventricular slice model with the average of almost 89.6% for accuracy, 85.5% of sensitivity and 90.9% of specificity. During the VWMS benchmarking, the ICA-based method performance is comparable with WT.

ROC curves from each ventricular slice level are given in Figure 6.7 and Figure 6.8. In all cases, the area under ROC curves of the proposed method are larger than VWMS, indicating that the ICA-based method gives a higher performance. The area under ROC curve of the ICA-based method for the basal slice is slightly smaller than WT, while it is slightly larger for the apical slice. Interestingly, the area under the ROC curve of the proposed method for the mid-ventricular slice is almost the equal with WT, but this does not imply that the results of both methods are equal (see Section 6.3.5).

6.3.4 Disagreement with visual wall motion score

A common disagreement between the ICA-based method with VWMS lies in the extend of abnormal landmark points that cross segment boundaries. Observers score on segments, instead of points. Boundaries between segments can be visually repositioned according to the observer's interpretation while looking at the cine images. Therefore it is often the case that the automated method detected abnormal points only in a partial myocardial segment as pointed by arrows in Figure 6.10(a). The false positive result in Figure 6.10(a) belongs to the same abnormal motion of the inferior segment marked by VWMS. The visual score assigned the abnormal motion only to one segment, while the automated method detected all the abnormal points preserving the wall motion continuity.

Another problem of the proposed method in the current study is the lack of full cardiac cycle information in the shapes that are defined only by ED and ES phases. In a few cases, as one given in Figure 6.10(b), the observer detected a wall motion peculiarity from the

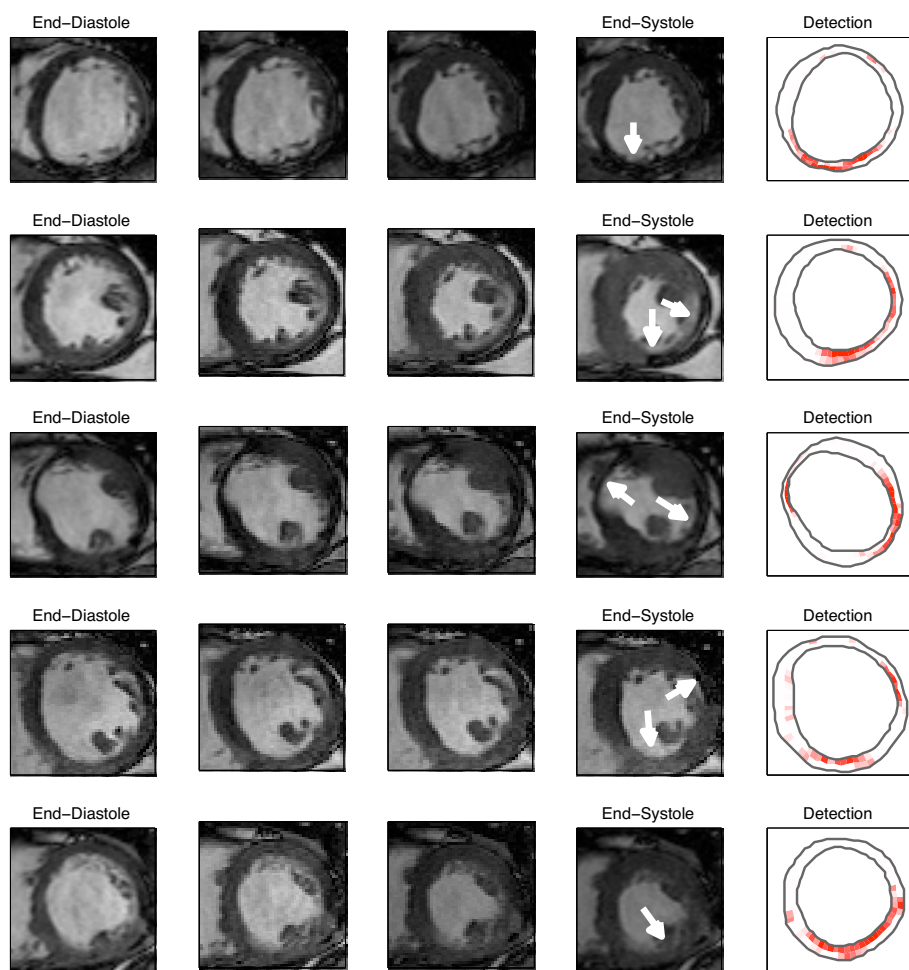
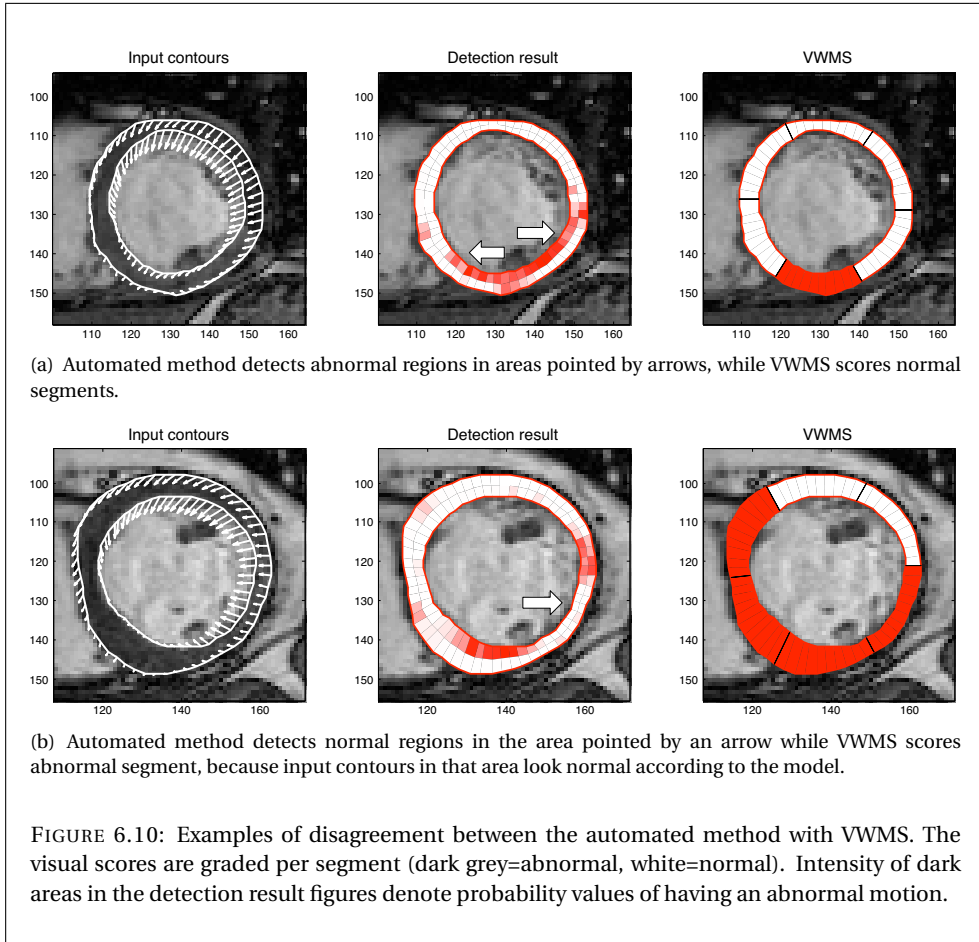


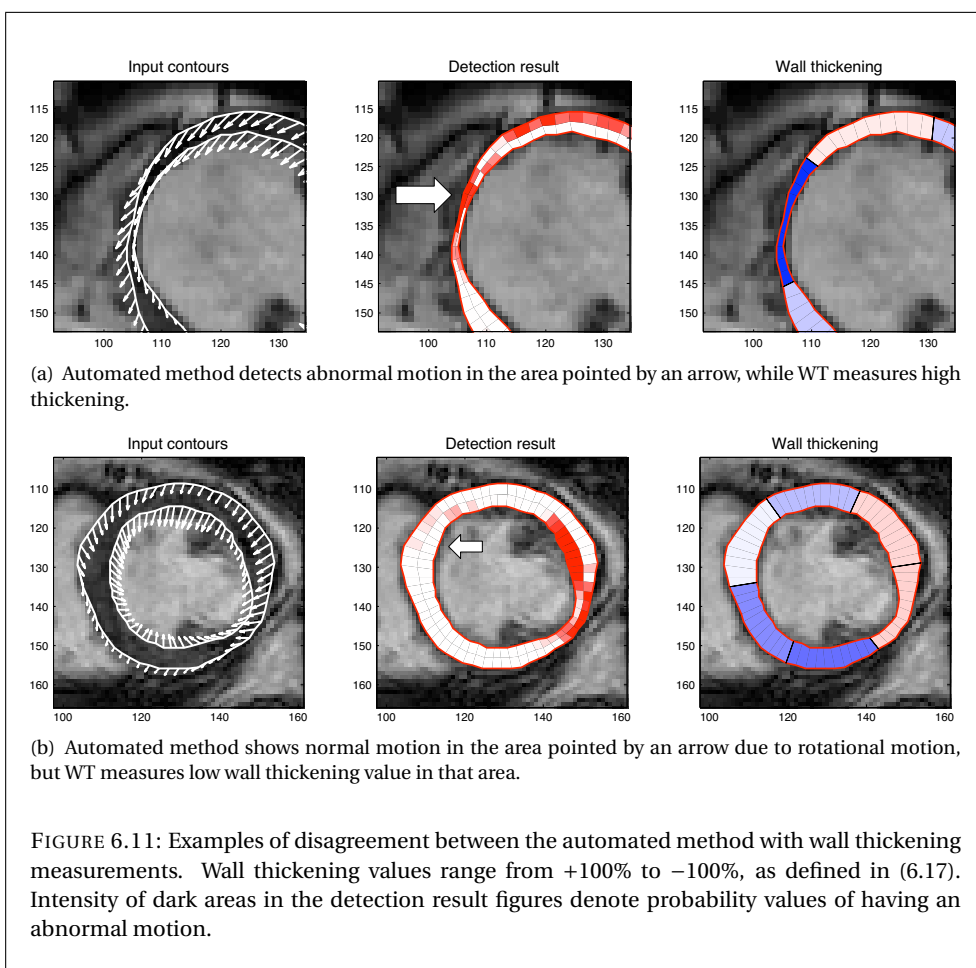
FIGURE 6.9: Five automated detection results compared to the associated myocardial motion taken from MR image sequences (four frames from End-Diastole to End-Systole). Dark color in the rightmost column indicates high probability of having an abnormal motion. White arrows in the End-Systole images show corresponding RWMA areas with the automated detection.



cine images, while the automated method detected normal contraction because shapes at ES looks normal according to the statistics of the model. The arrow in Figure 6.10(b) shows a good ED to ES contraction. In this case, the automated method missed the abnormal wall motion because it did not include the information of the contour positions between ED and ES phases.

6.3.5 Disagreement with wall thickening

ROC curves of the ICA-based method and wall thickening during the VWMS benchmarking in Figure 6.8 show high degree of similar performances. The main reason is that statistical shapes in the ICA-based method was constructed from ED and ES contours, which are the same phases to define the wall thickening value (see (6.17)). However there are substantial differences between the ICA-based method and wall thickening results.



WT measurement does not consider geometry of the contours. It only subtracts myocardial thickness from ES to ED, regardless whether the contraction movement performs in an unusual way. An example of this case is shown in Figure 6.11(a), where the myocardium at the anteroseptal region (pointed by an arrow) is moving towards the right ventricle. It means that the myocardium at that region is dilating instead of contracting. The ICA-based method however is still capable to detect this kind of movement as abnormal. This shows that the statistical model does not merely imitate wall thickening, but it also includes wall motion information implicitly.

As the statistical model contains wall motion, the automated method sometimes detects regions with low thickening as normal, because the contraction shape is still normal according to the model. Figure 6.11(b) shows this case of disagreement. The myocardial region pointed by an arrow in Figure 6.11(b) shows rotational movement while contracting

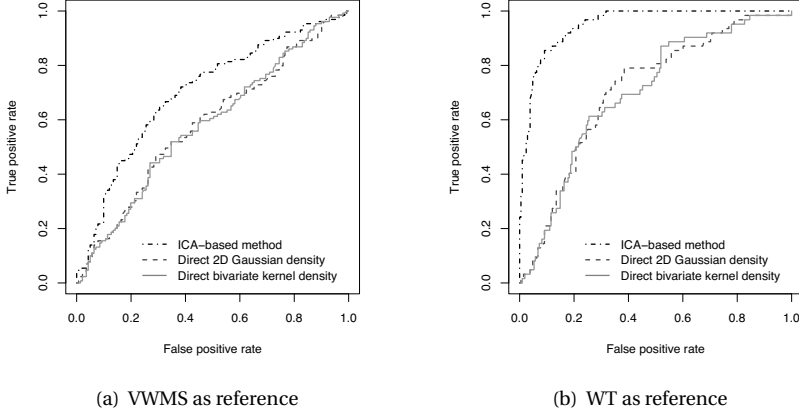


FIGURE 6.12: Comparisons between the ICA-based detection method with the direct landmark density estimation using a bivariate normal (2D Gaussian) density model. Both ROC curves were calculated from mid-ventricular slice level.

with low wall thickening.

6.3.6 Comparison with direct landmark density estimation

The proposed method starts off by modeling statistics of training shapes with ICA. The estimated density functions in the IC domain are then propagated into the shape domain (6.16), resulting a density function for each landmark point. Having density functions at the level of landmark points may raise some issues over the benefit of using ICA modeling instead of directly estimating probability density functions at each landmark point, e.g. by using a bivariate normal distribution model, which would reduce the complexity.

In this study, ICA is particularly used as a feature extraction to model the shape of myocardial contraction. The contraction shape at one landmark is not only determined by the distribution of that particular landmark, but is also affected by its neighbors. The closer the neighbor landmark, the higher its contribution. Density functions for each landmark point have been calculated based on all independent components, which means that all other point distributions contribute to estimating it. This is different from direct landmark point density estimation which only estimates a distribution model of a particular landmark point without considering its spatial context.

To perform a comparison between ICA and direct landmark density estimation, two bivariate density functions were estimated directly at each landmark point [40]: one with a gaussian function and the other with a non-parametric kernel density function. Only the

mid-ventricular slice level was used because the contraction motion is most pronounced in this level. All the three methods received the same input points, which are the landmark points from End-Systole contours after unit contraction (see Figure 6.2(b)). Hence, they only differ in how the probability density functions are estimated.

Figure 6.12(a) and Figure 6.12(b) show the ROC curves of the three methods during the WT and VWMS benchmarking tests, respectively. The ROC curves show that the ICA-based method gives much better performance compared to the direct landmark density estimations, especially in Figure 6.12(b). This proves that direct landmark density estimation is not enough to capture motion contraction, and that modeling landmarks in their shape context is thus necessary. ICA was chosen because it gives local shape variation and it allows the propagation of the density functions to the shape domain.

6.4 Discussion

6.4.1 Method performance

From both benchmarking tests, the mid-ventricular slice level gives the highest performance (almost 90% in WT benchmarking and 67% in VWMS benchmarking). This is due to fact that wall motion in the mid-ventricular level is well defined and more stable compared with basal and apical levels; thus regional wall motion abnormalities can be well separated from the control group.

In the basal level, there are large shape variations in the septal region due to the close proximity of the valve opening which gives a lower accuracy for abnormal motion in that region. This conforms with the lowest accuracy outcome in the basal level compared with the other levels in both benchmarking tests. In the apical level, the ICA-based method is still capable to detect abnormal motion (73% and 67%). However, the method's sensitivity reduced significantly (59% in VWMS benchmarking).

6.4.2 Study limitations

Both the ICA model and the RWMA detection method are sensitive to the quality of the myocardial contours. To construct a good ICA model, high quality myocardial contours are required. This requires a low inter- and intraobserver variation in the contours (if they are manually drawn), or a low segmentation error (if the contours are segmented automatically). This issue is not specific to the proposed method, but it is inherent to any quantitative regional LV function measurement.

In the present study, a binary classification between normal and abnormal motion is proposed. Classification of a specific type of abnormal motion, i.e. hypokinetic, akinetic and dyskinetic, are not presented yet. As yet, the method therefore only serves as a computer-aided tool to draw the clinician's attention to the suspected abnormal motion areas in the myocardium; staging of the wall motion abnormality may still be performed visually.

The current automated method works by modeling contractility patterns for each ventricular slice level. Therefore the method does not capture the three dimensional heart

motion. It is natural to extend the ICA model into 3D but we decided to model 2D cardiac contraction based on two reasons. During visual scoring, observers assess RWMA by looking at planar motion on multi-slice cine-MR sequences. Therefore by modeling multi-slice 2D ICA model, VWMS is emulated. Another reason is the dimensionality problem. Increasing the shape dimensionality also increases the necessary amount of training shapes required to generate a representative model.

The main benefit of the proposed method over previously described work on automatic wall motion classification (Bosch et al. [9], Mitchell et al. [7] and Remme et al. [41] studies) is that the method does not only distinguish between normals and patients, but also localizes the anomalies. Furthermore, the model is trained on normal subjects, therefore it is not biased towards a specific pathology, and can be deployed to other disease processes that manifest themselves in regional contraction anomalies.

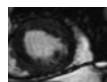
6.4.3 Clinical utility

The accuracy of the automated method in comparison with visual observers' scores ranges from 63.70%–67.41%. This disagreement still hinders the application of the proposed method in clinical routines. Even VWMS is often difficult to be applied in clinical settings due to high intra- and interobserver variations [2, 3]. Hoffmann et al. study [3] found that the accuracy of RWMA assessment from cine MRI from three independent observers is 62%, 55% and 86%. In the current validation, only one observer performed the scoring. To make a better quantitative validation, it may therefore be needed to set a consensus reading from more than one independent observer.

Nonetheless, there is still room for improving the proposed method to reach the agreement with visual observers. The most prominent difference between visual observers with the automated method is the temporal resolution. This problem has been addressed in Section 6.3.4. There are two possibilities to enhance the statistical model with respect to this problem. First is to include more shapes taken from in between ED and ES frames. Interpolation might be needed in this case, because the number of images per one cardiac cycle is different between subjects. Second is to enhance point correspondences between time frames. In the current implementation, there is no particular verification of point correspondences between ED and ES. This solution can improve the statistical model particularly in basal slice where valve opening causes a lot of shape variations in the septum.

6.5 Conclusion

A statistical model-based method to automatically detect RWMA in cardiac MR short-axis views of the myocardium has been presented. The model can capture the myocardial contractility pattern in a framework where all shapes contract from the same shape. This leads to a direct statistical analysis of the contraction by eliminating the shape variations at the ED phase. Furthermore, the automated process does not depend on a specific segmentation algorithm to produce the diagnostic results. The idea behind this approach is to construct a full pipeline of automated cardiac MRI analysis from segmentation to diagnosis, aimed to help clinicians in their daily routines.



Modeling by ICA proved very suitable in this study, because ICA produces local shape variations that are needed by the detection method to locate RWMA segments. The statistical independence property of ICA gives a benefit of an easy derivation of local probability density functions from the component domain to the shape domain.

The validation showed an almost similar performance compared to WT during the VWMS benchmarking, and a higher accuracy performance than VWMS during the WT benchmarking. Two advantages of this method over VWMS are (1) given myocardial contours, the detection method is automatic, and (2) the method does not require a specialized rater, as VWMS does, to arrive to a clinically meaningful interpretation.

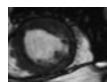
Having a reference of normal cardiac contraction has another advantage. The same model can be used for follow-up studies, for instance the stress MR study or post-operative MRI, to investigate whether the same patient exhibits improvement in the cardiac function towards the normal behavior reference. This opens the path towards an automated viability assessment, an important diagnosis in the clinical routines. With the same concept of detecting RWMA regions, viability can be analyzed from stress MR studies by comparing RWMA regions in the corresponding rest MR studies. The functional improvement can be detected by measuring the direction of the patient's coefficient value from rest to stress. A pilot study to assess functional improvement has been presented in [42], as well as linking this method with an automated segmentation of cardiac MR images [43, 44], enabling a full pipeline of automated cardiac MR image analysis.

6.6 References

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