Assessment of Kidney Function Using Dynamic Contrast Enhanced MRI Techniques

Melih S. Aslan  
*University of Louisville, USA*

Hossam Abd El Munim  
*University of Louisville, USA*

Aly A. Farag  
*University of Louisville, USA*

Mohamed Abou El-Ghar  
*University of Mansoura, Egypt*

Abstract

Graft failure of kidneys after transplantation is most often the consequence of the acute rejection. Hence, early detection of the kidney rejection is important for the treatment of renal diseases. In this chapter, authors introduce a new automatic approach to classify normal kidney function from kidney rejection using dynamic contrast enhanced magnetic resonance imaging (DCE-MRI). The kidney has three regions named the cortex, medulla, and pelvis. In their experiment, they use the medulla region because it has specific responses to DCE-MRI that are helpful to identify kidney rejection. In the authors’ process they segment the kidney using the level sets method. They then employ several classification methods such as the Euclidean distance, Mahalanobis distance, and least square support vector machines (LS-SVM). The authors’ preliminary results are very encouraging and reproducibility of the results was achieved for 55 clinical data sets. The classification accuracy, diagnostic sensitivity, and diagnostic specificity are 84%, 75%, and 96%, respectively.

**Keywords:** Renal failure, acute rejection, dialysis, biopsy, kidney transplantation, allograft survival, kidney segmentation, the level sets method, segmentation of the medulla and the cortex region, renograms, classification of normal and rejected kidneys, DCE-MRI.
INTRODUCTION

According to National Kidney Foundation, patients with renal diseases have increased from 100,000 to 400,000 over the last two decades (Tu, 2004). The patients with renal failure have three choices: 1) dialysis treatment, 2) medication, and 3) renal transplantation (Hamilton, 1999). Dialysis therapy is used for removing fluid, potassium, and uremic toxins to relieve symptoms of diseases. However, dialysis therapy may not prevent kidney failure (Tu, 2004). Patients who have acute renal disease can be treated with drugs. However, treatment with drugs has some side effects such as infections, and increasing incidence of cancer. Since the first successful organ transplantation was made in 1954 (Tu, 2004), renal transplantation has been applied for treatment of renal failure. However, patient might have some problems such as acute rejection, delayed-appearing antibody-mediated rejection, and acute tubular necrosis after kidney transplantation (Solez, 1999). In order to detect acute rejections, molecular diagnostic strategies have been investigated by the National Institutes of Health and the Immune Tolerance Network (Tu, 2004). However, this field still needs more experimentation and improvement.

Long-term renal allograft survival is dependent on the early detection of acute rejection. Currently, the diagnosis of rejection is done via biopsy, but biopsy has the negative effect of subjecting the patients to risks like bleeding and infections. Moreover, the relatively small needle biopsies may lead to over or underestimation of the extent of inflammation in the entire graft (Farag, 2006). Also, transplanted kidneys face a number of surgical and medical complications. These cause a decrease in kidneys functionality (Yuksel, 2005). Therefore, a noninvasive and repeatable technique is not only helpful but also needed in the diagnosis of acute renal rejection.

In DCE-MRI, a contrast agent called Gd-DTPA is injected into the bloodstream, and as it perfuses into the organ, the kidneys are imaged rapidly and repeatedly. During the perfusion, Gd-DTPA causes a change in the relaxation times of the tissue and creates a contrast change in the images (Yuksel, 2005). As a result, the patterns of the contrast change give functional information, while MRI provides good anatomical information which helps in distinguishing the diseases that affect different regions of the kidneys (Yuksel, 2007). The kidney has mainly three regions: 1) medulla, 2) cortex, and 3) pelvis. In our experiment, they use the medulla and cortex regions. A typical protocol using dynamic MRI involves the following steps: 1) collect a sequence of images from the kidney region as the contrast agent perfuse through the kidney; 2) follow the contrast difference in the kidney with time (image intensity information from the cortex and the medulla regions vary with time as the contrast agent perfuse through the kidney); and 3) establish a correspondence between change of contrast in the image sequence and the status of the kidney.

Even with an imaging technique like DCE-MRI, there are several problems such as, (i) the spatial resolution of the dynamic MR images is low due to fast scanning, (ii) the intensity of the kidney changes non-uniformly as the contrast agent perfuse into the cortex and medulla which complicates the segmentation procedures, and (iii) the medulla region could not be distinguished from the cortex region approximately after the first 25 slices because of low contrast difference. Therefore, the segmentation method is a very important process in our experiment which we will discuss further in this chapter.

The chapter is organized as follows. The background section gives an overview of the previous kidney segmentation and classification works. The procedure section illustrates a brief outline of the proposed algorithm. The methods section presents the level sets segmentation algorithm and the classification methods. In the experiments section, they illustrate the
experimental results. The discussion section compares all methods implemented in this work. The last section presents the conclusion and future work.

BACKGROUND

In this section they briefly give an overview of the previous kidney segmentation and classification works. Kidney segmentation and analysis methods can be classified into three categories: 1) region and threshold based approaches; 2) knowledge-based models, and 3) deformable methods.

Pohle & Toennies (2001) proposed a region-growing algorithm which updated its homogeneity criterion automatically from features of the region to be segmented. Kim & Yoo (2000) developed a kidney segmentation method based on the pixel value distribution of the organ and the mesh operation using CT images. First, they found the location of the kidney using the backbone. Then, they extracted the kidney region by using a template. Mavromatis et al. (2001) described image segmentation using tissue texture analysis and distribution of directional maximums. They defined a window that produced a local view of this location, and a set of measurements. Wang et al. (2004) proposed a constrained optimization approach that created a deformable contour computed within the contour energy minimization framework. Tsagaan & Shimizu (2001) developed a deformable model approach which was represented by grey level appearance of the kidney and its statistical information of the shape for automatic kidney segmentation. They used Non-Uniform Rational B-splines surface to represent the deformable model. Prior knowledge of subject’s shape was introduced as an energy function for model fitting process. They represented kidney shape using statistical information such as average and covariance. Lin et al. (2006) proposed computer-aided kidney segmentation on abdominal CT images by using adaptive growing region and the location of the spine as landmark. They tried to combine the advantages of the region-based and model-based methods. Xie & Jiang (2005) proposed kidney segmentation from ultrasound images based on texture and shape priors. Texture features were obtained by applying Gabor filters on images through a two-sided convolution strategy. Chevaillier & Ponvianne (2008) proposed a semi-automated method to segment internal structures from a DCE-MRI registered sequence. They segmented cortex, medulla, and pelvis regions using the k-means partitioning algorithm. Pixels were classified according to their time-intensity curves. Marcuzzo & Masiero (2007) segmented kidneys using the Expectation Maximization (EM) algorithm. They proposed 5 different classification methods to distinguish normal kidneys from rejected kidneys. They used symmetry of two kidney images, shape, relative position, boundaries, and radiopharmaceutical information in DRE-MRI. They used 20 training kidney subjects to build reference information for these classification methods. For shape information they averaged 20 left and 20 right kidneys and determined a reference mean shape for a normal kidney. Koh & Shen (2006) suggested a segmentation procedure based on a generated rectangular mask and edge information to overcome the problem that no prior information about location or appearance exists. They also used threshold values in segmentation step. However, organs in DRE-MRI have similar gray level information. Also cortex, medulla, and pelvis regions of kidneys have similar gray level value in some scans. Therefore, segmentation based on threshold will not work to segment cortex and medulla regions in our case. In this paper, they use the level set function proposed by Farag & Hassan (2004) to segment the kidney from its surroundings in DCE-MRI scans.

The next section gives a brief explanation of the proposed algorithm.
In this paper, they use the level set function proposed by Farag & Hassan (2004). There are 72 slices for each kidney sequence of DCE-MRI. The medulla region could not be distinguished from the cortex region approximately after first 25 slices in DCE-MRI because of low contrast difference as shown in Figure 1. To solve this problem, one slice of each kidney subject is segmented into its cortex and medulla regions using the level sets method (as will be discussed in the methods section). Hence, each kidney subject has its own cortex and medulla masks (see the last two rows of Figure 2) which are used to segment the other 71 slices. These masks are propagated to all slices.

After the segmentation is completed, the renograms (feature vectors) that are based on the mean (average) and maximum gray level information are obtained. They use these renograms in the classification steps. Finally, classification methods which are described in the methods section are applied to classify normal and rejected kidneys.

![Figure 1: Two sample slices of same clinical data set, (a) the cortex and medulla regions can be easily distinguished in the 6th slice, (b) the cortex and medulla region cannot be distinguished in the 60th slice because of low contrast between two regions. Hence, they obtain a mask (see the last two rows of Figure 2) for each region and propagate it to whole slices. This step is iterated for each subject.](image-url)
Figure 2: Three segmented kidney images. (a)-(c) show three different subjects. First row shows the original DCE-MRI image, second row shows segmented kidney image (binary), third row shows segmented cortex region (binary), and the last row shows the segmented medulla region (binary).
Figure 3 shows the schematic of our algorithm applied to both training and testing dataset.

**METHODS**

**Segmentation**

Segmentation is an important method for feature extraction, image measurements, and image display. Segmentation has been used in many applications such as detection of coronary border in angiograms, multiple sclerosis lesion quantification, surgery simulations, surgical planning, measuring tumor volume, functional mapping, automated classification of blood cells, studying brain development, detection of micro calcifications on mammograms, image registration, atlas-matching, heart image extraction from cardiac cineangiograms, and detection of tumors. In some applications it may be used to classify image pixels into anatomic regions. In some studies it is used to classify the entire image into sub regions such as the white matter, gray matter, and cerebrospinal fluid spaces of the brain (Bankman, 2000).
There are many segmentation methods that work well with a specific image modality. However, there is no standard method that could work well with all medical image modalities, and produce satisfactory results for all imaging applications. The objective of segmentation methods varies according to the goal of the study and the type of the image data (Bankman, 2000).

Segmentation methods can be divided into classes in many ways such as: 1) Manual, semiautomatic, and automatic, 2) Pixel based (local methods) and regions-based (global methods), 3) Classical (edge-based and region based techniques), statistical, fuzzy, and neural network methods, and 4) Model-based and low-level segmentation methods (Bankman, 2000).

Level set methods were first introduced by Osher & Sethian (1988). Their goal is to handle topological merging and breaking, to work in any number of space dimensions. Also their algorithm is used in Hamilton-Jacobi type problems. Active contours were introduced by Kass, Witkins, & Terzopoulos (1987) for segmenting objects in images. Geometrical active contours were independently introduced by Casellas et al. (1993) and Malladi et al. (1995), respectively. These algorithms were based on curve evolution and level set method. The basic idea is to represent contours as the zero level set of an implicit function defined in a higher dimension, referred to the level set function, and to evolve the level set function according to a partial differential equation (PDE). This method presents several advantages (Sethian, 1999) over the traditional parametric active contours. The contours represented by the level set function may break or merge naturally during the evolution, and changes are automatically handled. Another advantage is that the level set function always remains a function on a fixed grid, which allows efficient numerical schemes. Geometric active contour models (Caselles, 1993; Malladi, 1995) are derived using a Lagrangian formulation that yields a certain evolution PDE of a parameterized curve. This PDE is converted to another PDE for a level set function using the related Eulerian formulation from level set methods. Also, the evolution PDE of the level set function can be directly derived from the problem of minimizing certain energy functional defined on the level set function. This type of variation methods is called variational level set methods (Chan & Vese, 2001; Vemuri & Chen, 2003; Zhao, 1996). The variational level set methods are more convenient than pure PDE driven level set methods because region-based information and shape-prior information are directly formulated in the level set domain. Hence, variational level set methods produce more robust results. For instance, Chan & Vese (2001) proposed an active contour model using a variational level set formulation. Vemuri & Chen (2003) proposed another variational level set formulation that is able to perform joint image registration and segmentation (Li, 2005).

In DCE-MRI kidney images, many organs have similar grayscale values. In many cases, segmentation process is performed using deformable models. Deformable models have had great success in medical imaging and computer vision. However, the disadvantage of this method is that the initial contour should be close to the final one.

Level sets method is invariant to transformations. Farag & Hassan (2004) and Sussman (2004) introduced a new level function defined as a vector distance rather than a scalar method. The level set function $\Phi$ is used to represent the evolving region, where $\Phi(X,t) = [\phi(X,t)]^T$. It is defined as the minimum Euclidean distance between the point $X = [x,y,z]^T$ and a curve/surface $V$.

The evolving region is a propagating front embedded as the zero level or a higher dimensional function $\Phi$ (Farag & Hassan, 2004). The continuous change of the projections of $\Phi$ is described as
\[
\frac{d}{dt} \phi + |\nabla \phi| F = 0 \quad i = 1,2,3.
\]  

where  \( F \) is a vector velocity function depending on the local curvature of the front and on the external features related to the input image (Farag & Hassan, 2004). The parameter  \( \Phi \) deforms iteratively according to  \( F \). The position of the front is given at each iteration step by using the eq.2.

\[
|\Phi(x, y, z, t)| = 0
\]  

\( F \) can be defined as

\[
F = [v - \epsilon k] \nabla
\]  

where  \( v = 1 \) or  \( v = -1 \) for contracting or expanding the front, respectively,  \( \epsilon \) is a smoothing coefficient smaller or equal to 1, and  \( k \) is the local curvature defined for the corresponding projection function  \( \Phi \) (Farag & Hassan, 2004).

The intensity segmentation is described by the function  \( \Phi \) which changes based on eq.1. If the point belongs to the associated object, the front region expands, otherwise it contracts. The point classification is based on the Bayesian decision at point at  \( X \) (Farag & Hassan, 2004). The parameter  \( v \) for each point is replaced by the function  \( v(X) \) can be defined as follow:

\[
v(X) = \begin{cases} 
-1 & \text{if } \pi_o p_o I(X) \geq \pi_b p_b I(X) \\
+1 & \text{otherwise}
\end{cases}
\]  

where  \( \pi \) is the region prior probability,  \( p() \) is the probability density function (pdf) for the object  \( o \) and the background  \( b \), and  \( I \) is the image data. Each region is defined by a Gaussian distribution with adaptive parameters (Farag & Hassan, 2004) as follows:

\[
\pi_o = \frac{\int_{\Omega} H(-\phi^g) d\Omega}{\int_{\Omega} d\Omega}, \quad \pi_b = \frac{\int_{\Omega} H(\phi^g) d\Omega}{\int_{\Omega} d\Omega}
\]

\[
\mu_o = \frac{\int_{\Omega} H(-\phi) I d\Omega}{\int_{\Omega} H(-\phi) d\Omega}, \quad \mu_b = \frac{\int_{\Omega} H(\phi) I d\Omega}{\int_{\Omega} H(\phi) d\Omega}
\]
\[
\sigma_a^2 = \frac{\int_{\Omega} H(-\phi_g) (l - \mu_a)^2 \, d\Omega}{\int H(-\phi_g) \, d\Omega}, \quad \sigma_b^2 = \frac{\int_{\Omega} H(\phi_g) (l - \mu_b)^2 \, d\Omega}{\int H(\phi_g) \, d\Omega}
\]

(7)

where \( H \) is Heaviside step function.

\( \Phi \) is the projection of the distance in the coordinates directions negative inside the curve/surface, positive outside and zero on the boundary (see (Farag & Hassan, 2004) for details).

By evolving the level sets method, the cortex and medulla masks of each subject are obtained. The segmented cortex and medulla masks are propagated over all slices (frames) of the corresponding subject. They repeat this step on all training and testing subjects. After this step, they obtain the mean (average) and the maximum intensity values of the cortex and medulla regions. Then, these intensities are plotted as renograms. More information is given in the experiments section.

**Classification**

In our experiment, three classification methods are used to classify normal and rejected kidneys. The Least square support vector machine (LS-SVM), Mahalanobis distance and Euclidean distance methods are used.

**The Least Squares Support Vector Machine**

Support vector machines have been introduced in (Vapnik, 1995) in order to solve nonlinear function estimation and pattern recognition problems. In our method, they used the Least square support vector machine (LS-SVM) proposed by Suykens, 2002. The LS-SVM expresses the training in terms of solving a set of linear equations instead of quadratic programming as for the standard SVM case (Suykens, 2002).

Given a training set of \( N \) data points \( \{y_k, x_k\}_{k=1}^N \), \( x_k \in \mathbb{R}^n \) is the \( k \)-th input and \( y_k \in \mathbb{R} \) is the \( k \)-th output pattern. The main aim is to construct a classifier of the form:

\[
y(x) = \text{sign} \left[ \sum_{k=1}^N \alpha_k y_k \psi(x, x_k) + b \right]
\]

(8)

Where \( \alpha_k \) are support values and \( b \) is a real constant. \( \psi(,,) \) has the following choices:

\[
\psi(x, x_k) = \begin{cases} 
    x^T x & \text{For Linear SVM} \\
    \left( x^T x + 1 \right)^d & \text{For polynomial SVM of degree} \ d \\
    \exp \left\{ -\frac{\|x - x_k\|^2}{\sigma^2} \right\} & \text{For RBF SVM} \\
    \tanh \left[ \alpha_k^T x + \theta \right] & \text{For MLP SVM}
\end{cases}
\]

(9)
where $\sigma$, $\kappa$ and $\theta$ constants.

For the case of two classes, one assumes

$$
\begin{cases}
  w^T \varphi(x_k) + b \geq +1, & \text{if } y_k = +1 \\
  w^T \varphi(x_k) + b \leq -1, & \text{if } y_k = -1
\end{cases}
$$

which is equivalent to

$$
y_k [w^T \varphi(x_k) + b] \geq 1, \quad k = 1, \ldots, N
$$

where $\varphi(\cdot)$ is a nonlinear function which maps the input space into a higher dimensional space. (Suykens & Vandewalle, 1999).

$$
\min_{w, b, \epsilon} C_{LS}(w, b, \epsilon) = \frac{1}{2} w^T w + \gamma \frac{1}{2} \sum_{k=1}^{N} e_k^2
$$

subject to the inequality constraints

$$
y_k [w^T \varphi(x_k) + b] = 1 - e_k
$$

One defines the Lagrangian

$$
L(w, b, \epsilon; \alpha) = C_{LS} - \sum_{k=1}^{N} \alpha_k \left\{ y_k [w^T \varphi(x_k) + b] - 1 + e_k \right\}
$$

where $\alpha_k$ are Lagrange multipliers. These values can be either positive or negative due to the equality constraints as follows from the Kuhn & Tucker conditions (Fletcher, 1987).

The condition for optimality can be written as
for $k=1,\ldots,N$ can be written as the linear system

\[
\begin{bmatrix}
I & 0 & 0 & -Z^T \\
0 & 0 & 0 & -\gamma^T \\
0 & 0 & \gamma & -I \\
Z & Y & I & 0
\end{bmatrix}
\begin{bmatrix}
w \\
b \\
e \\
\beta
\end{bmatrix}
= 
\begin{bmatrix}
0 \\
0 \\
0 \\
1
\end{bmatrix}
\] (16)

where $Z = [\varphi(x_1)^T y_1; \ldots; \varphi(x_N)^T y_N]$, $Y = [y_1; \ldots; y_N]$, $\mathbf{1} = [1; \ldots; 1]$, $e = [e_1; \ldots; e_N]$, $\alpha = [\alpha_1; \ldots; \alpha_N]$. Elimination of $w$ and $e$ gives

\[
\begin{bmatrix}
0 & Y^T \\
Y & ZZ^T + \gamma^{-1} I
\end{bmatrix}
\begin{bmatrix}
b \\
\alpha
\end{bmatrix}
= 
\begin{bmatrix}
0 \\
1
\end{bmatrix}
\] (17)

Mercer’s condition is applied to the matrix $\Omega = ZZ^T$ with $\Omega_{kl} = y_k y_l \varphi(x_k, x_l)$.

See (Suykens, 2002) for more information.

The Mahalanobis Distance

The Mahalanobis distance can be defined as dissimilarity measure between two random vectors $x$ and $y$, where $x = (x_1, x_2, \ldots, x_N)^T$ and $y = (y_1, y_2, \ldots, y_N)^T$. $S$ is the covariance matrix of the distribution. The Mahalanobis distance is defined as

\[
d_M(x, y) = \sqrt{(x - y)^T S^{-1} (x - y)}
\] (18)

The Euclidean Distance
The Euclidean distance between two vectors, \( x = (x_1, x_2, \ldots, x_N) \) and \( y = (y_1, y_2, \ldots, y_N) \), can be defined as
\[
d_E(x, y) = \sqrt{(x - y)^T(x - y)} = \sqrt{(x_1 - y_1)^2 + (x_2 - y_2)^2 + \cdots + (x_N - y_N)^2}
\] (19)

**EXPERIMENTS**

Detection of acute renal rejection after **kidney transplantation** has become an ongoing collaboration between the CVIP Lab at the University of Louisville and the University of Mansoura where Dynamic Contrast-Enhanced Magnetic Resonance Imaging (DCE-MRI) is applied prior to biopsy for its superior functional and anatomical information. Ninety-three sequences of DCE-MRI subjects were obtained at the Urology and Nephrology Department at University of Mansoura in Egypt. Thirty-eight and fifty-five kidney subjects are used in the training and testing steps, respectively. For each subject, 72 temporal sequences of coronal scans are taken with 4 seconds intervals.

Our aim is to successfully construct a **renogram** (mean or maximum intensity signal curves) from the DCE-MRI sequences, showing the behavior of the kidney as the contrast agent perfuse into the transplant.

**Training Step**

They used 38 kidney data sets in this step. First, they classify normal and rejected kidney data sets. Our aim is to obtain reference vectors for each class. The data sets are segmented using the level sets method. After the segmentation process, they obtain the medulla and the cortex regions as show in Figure 2. Then, renograms of each data set are obtained based on the mean (average) and maximum gray level value of the cortex and medulla regions. At this point they obtain 38 vectors for each class. The mean of these vectors are obtained to be used as a normal and rejected reference. These renograms are shown in Figs. 4-7.

In Figs. 4 and 5, the y-axis shows the mean (average) and the maximum intensity of the medulla region, respectively. In Figs. 6 and 7, the y-axis shows the mean (average) and the maximum intensity of the cortex region, respectively. In all figures, the x-axis shows the slice number (frame/scan).
Figure 4: The reference vectors of normal and rejected kidneys based on the mean (average) intensity values of the medullar region. These vectors are obtained by averaging all feature vectors of 38 training kidneys' medulla region.

Figure 5: The reference vectors of normal and rejected kidneys based on the maximum intensity values of the medullar region. These vectors are obtained by averaging all feature vectors of 38 training kidneys' medulla region.
Figure 6: The reference vectors of normal and rejected kidneys based on the mean (average) intensity values of the cortex region. These vectors are obtained by averaging all feature vectors of 38 training kidneys' cortex region. (The experiments based on these reference vectors do not provide satisfactory results. They show these figures to show that the medulla region does not provide enough information between two classes.)

Figure 7: The reference vectors of normal and rejected kidneys based on the maximum intensity values of the cortex region. These vectors are obtained by averaging all feature vectors of 38 training kidneys' cortex region. (The experiments based on these reference vectors do not provide satisfactory results. They show these figures to show that the medulla region does not provide enough information between two classes.)
Testing Step

Our aim is to distinguish normal and rejected kidneys after the transplantation. In our testing procedure, they have used 55 data sets. For each testing data set, they find its renograms as described in the training step. Hence, they have 55 testing renograms to be compared with two reference vectors that are obtained in training part as shown in Figs.4-7.

In our experiments, the cortex regions did not provide enough information to distinguish rejected and normal kidneys. Figs. 6 and 7 show the response of the cortex regions for both rejected and normal kidneys. Our classification success is around 50% based on the cortex region. Therefore, they do not include the results based on the cortex region in this chapter.

The following descriptions are based on the medulla region. They use five classification methods (M1-M5), where M1, M2, M4, and M5 represent the classification methods based on the mean (average) intensity as described in the Table 1. In these methods, they use the Euclidean distance, threshold value, the Mahalanobis distance, and the least square support vector machines (LS-SVM), respectively. In these methods, the reference vectors shown in Figure 4 are used to be compared with renogram of each testing kidney data set.

M3 represents the classification method based on the maximum intensity of the medulla region. In this method, they use only a threshold to classify normal and rejected kidneys. The feature vectors shown in Figure 5 are used in this method. Also, the LS-SVM, Mahalanobis distance, and the Euclidean distance methods are applied based on this feature. Since the classification accuracy is about 50%, they do not include them in our methods in Table 1.

For classification methods M1, M4, and M5, they obtain a distance classifier. \(d_{n1}\) represents the distance between the renogram of the test subject and the reference vector of normal kidneys. \(d_{r2}\) represents the distance between the renogram of the test subject and the reference vector of rejected kidneys shown in Figure 4.

They compare them as follows:

If \(d_{n1} \leq d_{r2}\), then \(a_i\) is classified as the normal kidney. If \(d_{n1} > d_{r2}\), then \(a_i\) is classified as the rejected kidney.

Table 1 summarizes our classification methods. The information (input) and the classification methods are shown in the table 1. The results of our experiment are shown in Table 2. In this table, total accuracy, diagnostic specificity, and diagnostic sensitivity of classification methods are shown.
Table 1: CLASSIFICATION METHODS ARE SUMMARIZED BASED ON THE INFORMATION OR INPUT AND THE FORMULATION METHOD.

<table>
<thead>
<tr>
<th>Methods</th>
<th>M1</th>
<th>M2</th>
<th>M3</th>
<th>M4</th>
<th>M5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information/Input</td>
<td>Average Intensity</td>
<td>Average Intensity</td>
<td>Maximum Intensity</td>
<td>Average Intensity</td>
<td>Average Intensity</td>
</tr>
<tr>
<td>Formulation</td>
<td>Euclidean Distance</td>
<td>Threshold</td>
<td>Threshold</td>
<td>LS-SVM</td>
<td>Mahalanobis Distance</td>
</tr>
</tbody>
</table>

Table 2: THE EXPERIMENTAL RESULTS; TOTAL ACCURACY, DIAGNOSTIC SPECIFICITY, AND DIAGNOSTIC SENSITIVITY ARE SHOWN FOR EACH METHOD.

<table>
<thead>
<tr>
<th>Method</th>
<th>M1</th>
<th>M2</th>
<th>M3</th>
<th>M4</th>
<th>M5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of subjects identified correctly</td>
<td>46</td>
<td>37</td>
<td>30</td>
<td>45</td>
<td>46</td>
</tr>
<tr>
<td>Total number of subjects tested</td>
<td>55</td>
<td>55</td>
<td>55</td>
<td>55</td>
<td>55</td>
</tr>
<tr>
<td>Total accuracy</td>
<td>84%</td>
<td>67%</td>
<td>55%</td>
<td>82%</td>
<td>84%</td>
</tr>
<tr>
<td>Number of normal subjects identified correctly</td>
<td>22</td>
<td>15</td>
<td>15</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>Number of normal subjects tested</td>
<td>23</td>
<td>23</td>
<td>23</td>
<td>23</td>
<td>23</td>
</tr>
<tr>
<td>Diagnostic specificity</td>
<td>96%</td>
<td>65%</td>
<td>65%</td>
<td>92%</td>
<td>96%</td>
</tr>
<tr>
<td>Number of rejected subjects identified correctly</td>
<td>24</td>
<td>22</td>
<td>16</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Number of rejected subjects tested</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
<td>32</td>
</tr>
<tr>
<td>Diagnostic sensitivity</td>
<td>75%</td>
<td>69%</td>
<td>50%</td>
<td>75%</td>
<td>75%</td>
</tr>
</tbody>
</table>

DISCUSSION

In our experiment, they use five different methods to validate our proposed algorithm. M1, M4, and M5 have the maximum accuracy of our experiment. The accuracy of M2 and M3 are not satisfactory. During M1 and M5, 46 subjects are classified correctly out of 55 kidneys. The classification accuracy, diagnostic specificity, and diagnostic sensitivity are 84%, 96% and 75% for both methods. For the method M4, the classification accuracy, diagnostic specificity, and diagnostic sensitivity are 82%, 92% and 75%, respectively. Classification results of M1, M4, and M5 show much more accurate results than the classification results of M2 and M3 which are based on the threshold value.

They apply different methods to classify normal and rejected kidneys after the transplantation. They test our classification methods to the medulla and the cortex regions. As mentioned, the cortex region does not help us in the classification. The test results based on the cortex region are around 50%. Hence, they focus on the medulla region. The mean (average) and...
maximum intensity vectors (renograms) of the medulla region are tested using the LS-SVM, threshold, Mahalanobis distance, and Euclidean distance. Based on the results, they determine that the mean (average) intensity vector of the medulla region is very helpful to classify normal and rejected kidneys.

In Table 3, the experimental results of each testing subject are shown. In this table, 'false -ve' and 'false +ve' represent the failure of diagnosis sensitivity, and the failure of diagnosis specificity, respectively.

FUTURE RESEARCH DIRECTIONS

As stated above, detection of acute renal rejection after kidney transplantations has become an ongoing collaboration between the CVIP Lab at the University of Louisville and the University of Mansoura. The collaboration will continue to search for more hidden details in DCE-MRI technology.

Early detection of the kidney rejection is important for the treatment of renal diseases. The most common diagnosis method to detect kidney rejection is biopsy although it has the negative effects of subjecting the patients to risks like bleeding and infections. Also, the relatively small needle biopsies may lead to over or underestimation of the extent of inflammation in the entire graft. Hence, researchers have been trying to find a method which has not negative effects.

They introduced a new automatic approach to classify normal kidney function from kidney rejection using Dynamic Contrast Enhanced Magnetic Resonance Imaging (DCE-MRI). The data sets which are used in our experiments were acquired prior to biopsy. They realized that the medulla region has specific responses to DCE-MRI that are helpful to identify kidney rejection. Our experimental result shows that the response of medulla regions to DCE-MRI helps to identify rejected kidneys from normal kidneys. To validate our algorithm, they employed several classification methods such as the Euclidean distance, Mahalanobis distance, and least square support vector machines (LS-SVM).

Our preliminary results are very encouraging. Nevertheless, they do not claim that the biopsy should be suspended before doctors and researchers approve our proposed method which can be applied to any kidney DCE-MR Image. The doctors and researchers who are interested to find any method to identify rejected from normal kidneys without biopsy can test the proposed framework. This chapter is a single step to prove that the medulla region in the DCE-MRI has specific features. In DCE-MRI technique, the features of the medulla region can be deeply investigated. If the proposed method or its derivations would be tested by other clinics and doctors, biopsy would not be needed in the near future.

Another perspective is to assess the renal glomerular filtration rate (GFR) using the dynamic MRI. This is not our issue in this study but they are hoping in the future to develop new software to calculate the GFR that can replace of isotope study.
CONCLUSION

In this paper, they have proposed a novel method to classify normal and rejected kidneys after transplantation. This experiment suggests that normal and rejected kidneys can be distinguished without the risk of biopsy. The high accuracy of M1, M4, and M5 shows that the segmentation, feature vector, and classification methods work satisfactorily. Hence, they propose that the mean (average) intensity of the medulla region has important features. This information helps us to classify normal and rejected kidneys. In the near future, this algorithm can be used to classify normal and rejected kidneys without the disadvantages of the biopsy. Preliminary results are very encouraging and a reproducibility of the results was achieved for 55 clinical data sets. The classification accuracy, diagnostic sensitivity, and diagnostic specificity are 84%, 75%, and 96%, respectively.

ACKNOWLEDGEMENT

This research has been supported by US National Science Foundation (Grant IIS-0610528). Special thanks go to Dr. Dongqing Chen, Mike Miller, Nick Blumenthal, and Ham Rara who spent their valuable time for technical discussion in this experiment and correction of this chapter.
Table 3: 'FALSE -VE' AND 'FALSE +VE' REPRESENT THE FAILURE OF DIAGNOSIS SENSITIVITY, AND THE FAILURE OF DIAGNOSIS SPECIFICITY, RESPECTIVELY.

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