Design of an Expert System for Diagnosis of Coronary Artery Disease Using Myocardial Perfusion Imaging

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Abstract: *Single Photon Emission Computed Tomography (SPECT) allows us to visualize functional information about a patient's specific organ. A myocardial perfusion SPECT is a nuclear imaging based technique used to evaluate heart's blood supply and the damage that might have been caused by a heart attack. However, visual interpretation of nuclear images is subject to substantial variability even by experienced observers.*

The purpose of this study was to develop a computer-aided diagnostic system or expert system for automated interpretation of myocardial perfusion images using knowledge discovery and heuristic approaches. The system correctly diagnose obstructions in the three main arteries, namely Right Coronary Artery (RCA), Left Anterior Descending (LAD), Left Circumflex Artery(LCX), and patient being normal i.e., with no obstructed arteries.

Keywords : *Myocardial SPECT, Nuclear imaging, Computer Aided Diagonostic system. Medical imaging.*

1. INTRODUCTION

The heart is a muscular organ, which receives blood from the coronary arteries. Coronary artery disease generally refers to the buildup of cholesterol in the inside layers of these arteries causing the blood flow to slow or stop. If the myocardium i.e., the fibrous muscle of the heart does not receive enough blood due to narrowing or blockage of any of these coronary arteries, a myocardial infarction (heart attack) can occur.

There are two coronary arteries, Left and Right. The left starts as the 0.5 ~ 1 cm long Left Main (LM) and divides into the Left Anterior Descending (LAD) and Left Circumflex (LCX).

1.1 Nuclear Myocardial Perfusion Imaging

Nuclear medicine procedure is sometimes described as an "inside-out" x-ray because it records radiation emitting from the patient's body rather than radiation that is directed through the patient's body. Nuclear medicine procedures use small amounts of radioactive materials, called radio-pharmaceuticals, to create images of anatomy. Radio-pharmaceuticals are substances that are attracted to specific organs, bones or tissues. They are introduced into the patient's body by injection, swallowing or inhalation. As the radio-pharmaceutical travels through the body, it produces radioactive emissions.

Technetium-99^{m} sestamibi was approved for use as myocardial perfusion tracer [9]. The SPECT images were recorded with either a 180^{o} or 360^{o} collection. A step-and-shoot acquisition with 32 or 64 stops separated by 3° to 6° degrees were used. The duration of acquisition at each stop was 25 sec/image for high dose technetium 99^{m}-Sestamibi. SPECT images were acquired using a high-resolution collimator. To minimize artifacts due to attenuation, a scintillation camera with attenuation correction capabilities is usually used. Two sets of images showing blood flow are obtained: the first following a period of rest, and the second following a period of stress (i.e., exercise). This exercise makes your heart work harder, causing an increase in blood flow, which helps the doctor see if there are blockages.

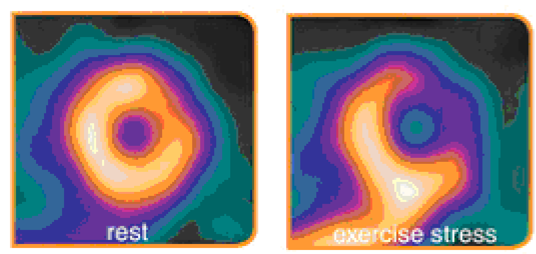


Figure 1: A nuclear image of a heart with CAD at rest and after exercise. The change in color shows that less blood is reaching a part of the heart muscle.

1.3 Bull's Eye Polar Maps

A polar map display, called a bull's-eye image, has been developed to characterize the three-dimensional images of the left ventricle of heart in two dimensions thus representing all the areas of the myocardium in a single image. The polar map is computed from cross-sectional slices of the Left Ventricle (LV). For each slice, the center and a radius of search that contains the LV are determined and the LV is divided into radial sectors [3]. The maximum count value of each sector is computed, generating a profile. Profiles are plotted as concentric circle onto the map. The most apical profiles are thus mapped to the central, the most basal profiles to the peripheral. The resulting map is a compression of 3D information (LV perfusion) onto a single 2D image.

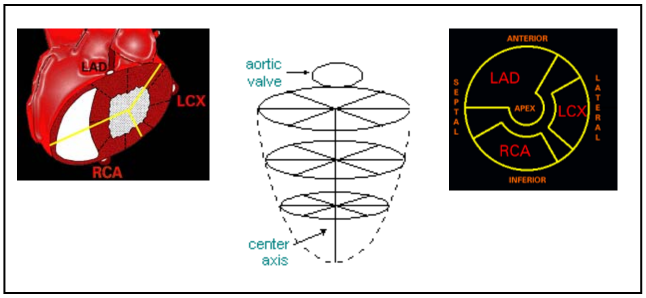


Figure 2. Polar map construction

2. DETECTING CORONARY ARTERY DISEASE

Georgia Tech., have developed a rule based expert system called PERFEX [2], for automatic interpretation of Cardiac SPECT data. This system infers the extent and severity of coronary artery disease (CAD) from perfusion distribution [10] and provides as output a patient report. D. Lindahl [1] uses artificial neural networks to detect CAD in two vascular territories, using coronary angiography as gold standard. A "leave one out" procedure was used for training and evaluation. The performance of the networks was compared to those of two human experts. Iliad [11] uses Bayesian reasoning to calculate the posterior probabilities of various diagnoses under consideration, given the findings present in a case. Iliad, which was developed primarily for diagnosis in Internal Medicine, now covers about 1500 diagnoses in this domain based on several thousand findings.

Our Expert systems contain sets of decision rules that are structured like tree branches with questions, conditions and hypotheses that must be answered or satisfied. Each answer directs the analysis down a different branch to another set of questions. The brief description of the different steps used to detect coronary artery disease in Perfusion SPECT images is given in Section 2.1 to 2.7.

2.1 Otsu's method for image thresholding

The goal of thresholding is to convert a greyscale image into a binary image. We select Otsu's method [7] for our dataset. Otsu's method is formulated as a discriminated analysis. Statistics are calculated for the two classes of intensity values (foreground and background) that are separated by an intensity threshold.

An image is a 2D grayscale intensity function and contains N pixels with gray levels from 1 to L. The number of pixels with gray level i is denoted by f_i , giving a probability p_i of gray level i in an image of

$$p_i = f_i \ / \ \mathbf{N} \qquad (1)$$

In the case of bi-level thresholding of an image, the pixels are divided into two classes [7], C1 with gray levels [1, …, t] and C2 with gray levels [t+1, …, L]. Then, the gray level probability distributions for the two classes are

$C1 : p_1 / \omega_1(t), \ldots . p_t / \omega_1(t)$ and

$C2 : p_{t+1} / \omega_2(t),\ p_{t+2} / \omega_2(t), \ldots, p_L / \omega_2(t),$

where

$$\omega_1(t) = \sum_{i=1}^{t} pi \qquad (2)$$

and

$$\omega_2(t) = \sum_{i=t+1}^{L} pi \qquad (3)$$

Also, the means for classes C1 and C2 are

$$\mu_1 = \sum_{i=1}^{t} i\ p_i \ / \ \omega_1(t) \qquad (4)$$

and

$$\mu_2 = \sum_{i=t+1}^{L} i\ p_i \ / \ \omega_2(t) \qquad (5)$$

Let μ_T be the mean intensity for the whole image. It is easy to show that

$$\omega_1 \mu_1 + \omega_2 \mu_2 = \mu_T \qquad (6)$$

$$\omega_1 + \omega_2 = 1 \qquad (7)$$

Using discriminate analysis [7], Otsu defined the inter-class variance of the thresholded image as

$$\delta_B^2 = \omega_1 (\mu_1 - \mu_T)^2 + \omega_2 (\mu_2 - \mu_T)^2 \qquad (8)$$

For bi-level threshold, Otsu verified that the optimal threshold t* is chosen so that the inter-class variance δ_B^2 is maximized; that is,

$$t^* = \text{Arg Max} \{ \delta_B^2 (t) \}. \quad 1 \leq t < L \qquad (9)$$

If the image has more than 5% black pixels (Blocked Area), the cardiac scan will be consider as abnormal and will have to be processed for further analysis.

2.2 Histogram Equalization

The histogram of the input image was mapped to a new maximally flat histogram [8]. The histogram is defined as *h(i)* , with 0 to P-1 gray levels in the image. The total number of pixels in the image, M*N, is also the sum of all the values in *h(i).* Thus, in order to distribute most uniformly the intensity profile of the image, each bin of the histogram should have a pixel count of *(M *N) / P.*

A simple and readily available procedure for redistribution of the pixels in the image is based on the normalized cumulative histogram, defined as

$$H(j) = \frac{1}{M.N}\sum h(i)$$

The normalized cumulative histogram can be used as a mapping between the original gray levels in the image and the new gray levels required for enhancement. The enhanced image g (m, n) will have a maximally uniform histogram if it is defined as

$$g(m,n) = (P-1).\, H(f(m,n))$$

2.3 Gaussian Smoothing

The Gaussian smoothing operator is a 2-D convolution operator that was used to `blur' images and remove detail and noise. The Gaussian function is

$$G(x,y) = \frac{1}{2\pi\sigma^2} e^{-\frac{x^2+y^2}{2\sigma^2}}$$

The variable σ is the standard deviation of the Gaussian, and determines the effective size of the smoothing function [8]. After applying different value of σ, it was observed that a value of 1.3 for σ produced a resultant image that was on a compromising situation regarding smoothing and fine edges detail.

2.4 Classification for Perfusion defect severity

Tracer uptake is currently evaluated visually for the four main vascular territories namely LAD, RCA, LCX, and Apex. Tracer uptake can be classified semi-quantitatively. The mapping of the gray scale image into percentage of the perfusion distribution was performed. The objective was to classify the blocked area of the artery/region of the left ventricle in percentage. As the gray scale image of polar map had maximum of 255 gray levels so the corresponding percentage can be calculated as under

e.g., for 10%: (10/100)*255 = 25.5
for 20%: (20/100)*255 = 51

In order to make the data continuous a little adjustment was made, round-up and round-down were used where the two percentages were equal.

We converted the 255 gray levels into 5 classes for the classification of perfusion defect severity. Thus the five classes according to percentage of perfusion or blood supply are

1 : Normal : 100% -70% perfusion
Definitely not CAD (255 to 179 gray levels)

2 : Mildly reduced : 69% - 50% Perfusion
Probably not CAD (178 to 128 gray levels)

3 : Moderately reduced : 49% - 30% Perfusion
May be CAD (127 to 77 gray levels)

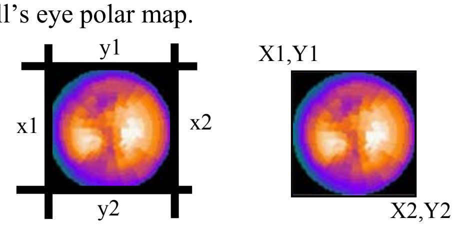
4 : Severely reduced : 29% -10% Perfusion
Probably CAD (76 to 26 gray levels)

5 : Absent : 9% - 0% Perfusion
Definitely CAD (25 to 0 gray levels)

2.5 Finding Coronary Artery territories in Polar Map using Bi-Level Mask convolution

To study the perfusion distribution in individual artery, the Bull's eye polar map was needed to be segmented into 3 main coronary arteries. Therefore 3 special Bi-level masks were carefully designed using the RJ-Clock algorithm. As the polar map is actually the three overlapped short-axis slices of the left ventricle, therefore the RJ- Clock algorithm works in the reverse order to segment it back in to three concentric circles representing the Apical third, the middle third and the Basal third region of the left ventricle. The step of the algorithm is as under:

1.
2. 1) Find the minimum enclosing rectangle of the
3. bull's eye polar map.



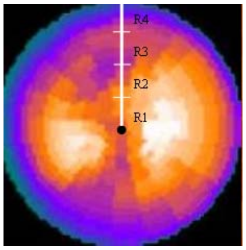
2) Find the centroid of the polar map by

$$x = (X1+X2)/2\ ,\ y = (Y1+Y2)/2$$

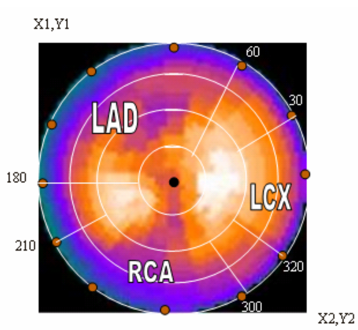
3) Find the radius of the circular polar map, which can be achieved by finding the difference of initial co-ordinates from the center, i.e.

$$r = x - X1 = y - Y1$$

4) Next the radius r is equally divided into 4 sub-radii R1, R2, R3, and R4.



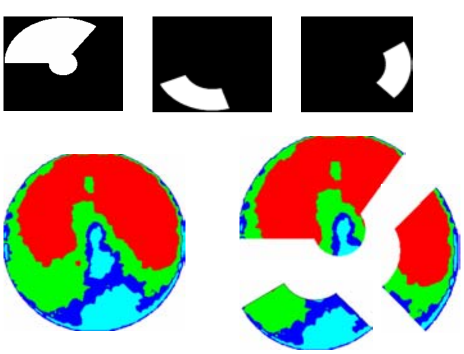
5) The Pixels were classified according to the polar coordinates (radius & theta). e.g., for Right Coronary Artery (RCA), All the pixel which are in between R2 & R4, and whose angle is greater than or equal to 210^o and less than equal to 300^o (Anticlockwise).



The pixels satisfying the above two condition in term radius and theta were given a value of 1 (white) while the other entire are assigned the value zero (Black).

2.6 Polar Map Extractor

The three masks produced in section 2.5 are convoluted with the labeled polar map. These labeled polar maps have all the pixels classified in one of the five classes. The five different gray-shades show the different classes



Segments of polar map based on RJ-clock algorithm

2.7 Rules for Predicting Coronary Artery Disease

Number of pixels in each class was counted and compared with that of the whole region to get a percentage value. Based on these Percentages, the wining class of the coronary Artery can be deduced which ultimately explain the condition of the blockage and extent of the disease.

Winner class is the class having maximum percentage.

e.g. in Patient Stress Data, **S**tress **W**inner **L**eft **A**nterior **D**escending **(SWLAD):**

```
if ((70 <= LAD) && (LAD <= 100 )) SWLAD = 1 ;
if ((50 <= LAD) && (LAD <=  70 )) SWLAD = 2 ;
if ((30 <= LAD) && (LAD <=  50 )) SWLAD = 3 ;
if ((10 <= LAD) && (LAD <=  30 )) SWLAD = 4 ;
if (( 0 <= LAD) && (LAD <=  10 )) SWLAD = 5 ;

if (SWLAD == 1)
 {
   Finding[j] = "LAD has Normal Perfusion" ;
    j++   ;
 }

if (SWLAD == 2)
 {
 Finding[j] = "LAD has mildly reduced Perfusion" ;
  j++    ;
 }
```

The regional ejection fraction is also a very important factor in the study of heart pumping function and volume of the blood that it pumps.

The Normal limits for the Ejection Fraction (EF) are 52% to 76%.

```
If (  ((EF < 52) || (EF>76)) && (perfusion=1) )
{
 Suggestion[k] = "Evaluate for Cardio-myopathy" ;
 k++ ;
}
```

Similarly we have rules for diagnosing Ischemia in the knowledge base. The Severity of Reversible Ischemia is identified by the jump of the artery from one class to another. e.g., if there is a jump of one class then there is minor evidence of Ischemia and if there is a jump of two classes then moderate evidence of Ischemia. Finally, a jump of more than two classes is representing a major evidence of Ischemia.

e.g., for Stress-Rest Analysis of coronary arteries.
Stress **W**inner **L**eft **A**nterior **D**escending **(SWLAD)**
Rest **W**inner **L**eft **A**nterior **D**escending **(RWLAD)**

```
if ( (SWLAD == 1) && (RWLAD == 3) )
Findings[j] = "Major evidence of Ischemia" ;

if ( (SWLAD ==4) && (RWLAD == 5) )
Findings [j] = "Minor evidence of Ischemia" ;
```

For Example a Patient-A's Perfusion Data under Stress is as given in table 1

Table 1 . Perfusion Data under Stress

	Class1	Class2	Class3	Class4	Class5
LAD	**68%**	21%	6%	5%	0%
RCA	30%	**45%**	15%	7%	3%
LCX	20%	18%	15%	**40%**	7%
Apex	18%	23%	20%	**30%**	9%

And the Patient-A's Perfusion Data at Rest is as in table 2

Table 2. Patient-A's Perfusion Data at Rest

	Class1	Class2	Class3	Class4	Class5
LAD	**54%**	22%	9%	15%	0%
RCA	22%	25%	**35%**	17%	1%
LCX	18%	15%	18%	**42%**	7%
Apex	15%	23%	20%	**33%**	9%

Transition from Class-2 to Class-3 in RCA, Evidence of Minor Ischemia.

Clinical information, such as Heredity, Gender, Age, Smoking, High Blood Pressure, Blood Cholesterol Levels, Stress, Obesity, Lack of Exercise, and Diabetes has been included in the overall analysis.

In the Risk factor analysis the patient history and clinical information is compared with the normal limits using production rule.

```
e.g.  if (Cholesterol  > 200)
      {
      Impression [i] = "Cholesterol Level is high" ;
      i++ ;
      }

if ( (Systolic_BP  > 140) || (Diastolic_BP<90) )
{
   Impression [i] = "Blood Pressure Problem" ;
   i++ ;
}
```

3 RESULTS AND DISCUSSION

The purpose of the present study was to develop a computer-based method for automatic detection and localization of coronary artery disease in myocardial bull's eye scintigrams. A population of 84 patients who had undergone myocardial technetium99m-sestamibi rest-stress scintigraphy within 8 months was studied. There were 72 abnormal scans while 12 normal scans. The recognition performance of our preposed system was compared with the two year experienced physician (Human Expert). The report produced by the expert system after making quantitative analysis of the rest and stress polar maps comprised of three sections.

1. Impression. 2. Findings. 3. Suggestion.

The bull's-eye images were presented to the experts in random order. The experts had to rely on four bull's-eye images per patient study i.e., rest's perfusion image, stress's perfusion image, Regional Ejection Fraction image (stress) and Regional Ejection Fraction image (rest). The experts classified each patient study and each vascular territory for the presence of CAD using a 4-grade scale; 'definitely not CAD', 'probably not CAD', 'probably CAD' and 'definitely CAD'.

3.1 Evaluation Measure for Diagnostic Procedure

These measures relate the binary results of a test with the presence or absence of disease as established by the RJ-Clock Algorithm. The sensitivity and specificity of a test express the accuracies with which positive cases and negative cases are respectively recognized.

	Disease	
Test	+ (present)	- (absent)
+	True Positives	False positives
-	False negatives	True negatives

Table 3. Evaluation measure for diagnostic procedure.

Sensitivity : The fraction of those with the disease correctly identified as positive by the test.

$$Sensitivity = \frac{\text{True Positives x 100}}{\text{True Positives + False Negative}}$$

Specificity : The fraction of those without the disease correctly identified as negative by the test.

$$Specificity = \frac{\text{True Negatives x 100}}{\text{True Negatives + False Positives}}$$

Positive predictive value : The fraction of people with positive tests who actually have the condition.

$$\text{Positive predictive value} = \frac{\text{True positives x 100}}{\text{True positives + False Positives}}$$

Negative predictive value : The fraction of people with negative tests who actually don't have the condition.

$$\text{Negative predictive value} = \frac{\text{True Negatives x 100}}{\text{True Negatives + False Negatives}}$$

$$\text{Predictive accuracy} = \frac{\text{(True positives + True Negatives) x 100}}{\text{Total Cases}}$$

Performance of our proposed System

		True		False				
Vessel	Cases	Pos.	Neg.	Pos.	Neg.	Sens.	Spec.	Acc.
RCA	72	51	12	7	2	0.96	0.63	0.87
LAD	72	42	23	6	1	0.97	0.79	0.90
LCX	72	47	17	6	2	0.95	0.73	0.88
Apex	72	53	14	5	0	1.00	0.73	0.93

4 CONCLUSION

Our proposed system is essentially a production rule system (i.e., composed of IF-THEN rules) used in conjunction with temporal and uncertainty reasoning. The system reports the defect(s) in the stress tomograms and then state how each defect changes in the rest tomograms. The report comments on the presence (if any) of inducible perfusion abnormality, infarction and significant artifact. If there is an abnormality, its location (in terms of segments affected), extent (in terms of number of segments affected) and severity stated. We found it possible to develop a computer-based method to classify myocardial perfusion bull's-eye images with performance as good or better than a human expert. Our proposed system is capable of predicting both ischemia and infarction.

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