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Analysis of thallium-201 myocardial SPECT images using fuzzy set theory

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Using the fuzzy set theory, a method was developed for analyzing the extent and severity of ischemia by comparing the exercise and delayed SPECT images with Thallium-201. For each short axial image (slice) for exercise and delayed study, a defect probability matrix (DPM) is created so that it shows the severity of ischemia of myocardium in that slice. Each slice is divided into 8 equi-angle sectors, and the left ventricle (LV) also is divided into 8 equi-angle vertical sectors from apex to base. Using DPMs, the defect probability is calculated for each slice, sectors of each slice and vertical sectors of the LV. The results are displayed on a CRT by means of images, curves and histograms. They show what percentage of the area of each slice and that of the lateral, anterior, septum and inferior portions have how much defect. They provide comprehensive and easily understood information about the condition of the LV in exercise and delayed stages. Persistent and transient ischemia can be diagnosed by visual comparison of patients' curves and histograms with their corresponding normal limits.

Key words: Fuzzy set theory, Defect probability, Thallium-201 myocardial SPECT images, Ischemic heart disease

INTRODUCTION

MYOCARDIAL TOMOGRAPHY with Thallium-201 is widely used in detecting ischemic myocardial lesions. The advantage of rotational myocardial tomography over planar imaging is that it can detect and localize the myocardial lesion and also estimate the extent of the lesion more accurately.[1,2]

There are different ways for interpreting the myocardial images. For example, quantitative analysis methods such as "circumferential profiles" and "washout ratio",[3] also quantitative display methods such as "Bull's eye"[4] and "Stereo-View"[5] are widely used. The subjective interpretation of myocardial images is strongly influenced by such factors as the experience of the observer, the quality of the images, the ratio of myocardial background activity, the characteristic of display system and many others.[3]

We have applied the fuzzy set theory to analyzing the Thallium-201 SPECT images. In 1965, L.A. Zadeh introduced the concept of a fuzzy set as a model of a vague fact, and the idea of modeling predicates via fuzzy subsets with values in the unit interval.[6,7] Since then it has found many applications in different fields of science including expert systems and computer aided diagnosis.

In the set theory, when a set is defined, one can definitely say that an element belongs to the set or does not belong to it. That is, the membership of an element in a set is either true or false. But in fuzzy sets, since the set itself is vague and not clearly defined, membership of an element in the fuzzy set is not simply true or false, but it is partly true or partly false.

Thus the degree of membership of an element in a fuzzy set is defined by a number in the interval [0, 1]. This number can be thought of as the probability with which an element belongs to the fuzzy set.

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For example "A patient with heart disease" can be a fuzzy set, because there are many cases in which we cannot definitely say that the patient has heart disease, but we could say that he might have it because of such and such evidence. On the other hand "A patient who lost one hand in an accident" is a set, because we can surely show that a patient belongs to this set or does not belong to it.

In our method, we defined a fuzzy set for myocardial images according to which the defect probability (severity of ischemia) for pixels in myocardium is calculated for exercise and delayed stages. These probabilities are the main source of information that we have used to analyze the extent and severity of ischemia.

METHOD

Using the fuzzy set theory, we have developed a new method for analyzing the extent and severity of ischemia by comparing the exercise and delayed SPECT images with Thallium-201 after the peak physical exercise. For each of the exercise and delayed stages, 10 short axial images (matrices $64\times 64\times 16$ bits in size) are extracted from the apex to the base of the LV. These short axial images are referred to as slices. For each of these slices the region of the myocardium is determined automatically as described in section 2, and a defect probability matrix (DPM) of the kind described in section 1 is created. The DPMs show the severity of ischemia in the slices. Using this information, a set of images, curves and histograms are calculated for a patient and displayed on the CRT, in such a way that along with the normal limits (section 6), they provide comprehensive and easily understood information about the condition of the LV in exercise and delayed stages. Our method is programmed in FORTRAN-5 on the SCINTIPAC-2400 system which uses a NOVA 4 computer.

1. Definition of defect probability

In this application of the fuzzy set theory, we define the fuzzy set to be the "defective pixel inside the myocardium". The degree of membership of pixels in this set is defined by a number in the interval [0, 1]. For a pixel inside the myocardium, the degree of membership in the above set, the defect probability (DP) and the severity of ischemia have the same meaning. The degree of membership for a pixel with the gray level value of zero, is defined as 1. This means that the pixel is 100% defective or its DP is equal to 1. The degree of membership for a pixel which has a maximum gray level value in all 10 slices, is defined as 0. This means that this pixel is defective with 0% of probability. For each slice, the DP of all pixels in the myocardium region are calculated and stored in a matrix called the defect probability matrix (DPM) which is the same size as the image matrix. For exercise slices the DPM is created as follows:

Let EXMAX10 be the maximum gray level for all pixels over all 10 slices of exercise, and C(i,j) be the gray level for an exercise pixel (i, j) belonging to the myocardium. Then, the DP of this pixel is defined as:

$$0\leqslant \mathrm{DPM}\ (i, j)=1-(C\ (i, j)/\mathrm{EXMAX10})\leqslant 1.$$

For delayed slices, the DPM is calculated in a similar way. A closer value for DPM (i, j) to 1 shows that it is more probable that the pixel (i, j) is defective.

2. Automatic extraction of region of myocardium

The center of each myocardial slice is determined as follows: The global region of interest (ROI) of a slice is extracted according to a cut off level equal to 20% of the maximum gray level of that slice[8].

Assume a rectangle the sides of which pass through the pixels positioned at the minimum and maximum row numbers and the column numbers of the ROI.

Consider a circle the center of which is positioned at the center of this rectangular and its radius is equal to 1/4 of the smaller side of the rectangular. Then all pixels inside this circle are tested, if none of them has a gray level less than the cut off level, then the cut off level is increased by a constant (for example, 5% of the maximum gray level for that slice), and the above routine is repeated. Otherwise, among those pixels which have a gray level lower than the cut off level, the one which is located at the center of this cluster of pixels is selected as the center point of the LV cavity of that slice.

The approximate shape of the inner and outer edges of the myocardium are determined as follows:

Let C be the center of the LV cavity as described in above, and M be a pixel of that slice which has the maximum gray level value. Assume two points D and B located on the inner and outer edges of that myocardial slice (Fig. 1). Then two circles centered

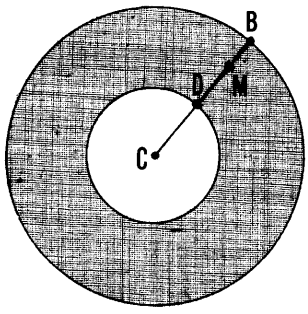

Fig. 1 C is the center of the LV cavity of a slice, D and B are points on the inner and outer edges of the myocardium. M is the point with the maximum gray level value.

at C, with radiuses CB and CD are drawn to determine the approximate shape of that myocardial slice (the shaded ring in Fig. 1). The points D and B are determined as follows:

D is a pixel the gray level of which is equal to or greater than 65% of the maximum gray level and CD<CM, and also it has the minimum distance from C.

B is a pixel the gray level of which is equal to or greater than 65% of the maximum gray level and CB>CM, and also it has the maximum distance from C.

In our method only those pixels which lie inside the myocardium are considered in defect probability calculation and the rest are taken as background.

3. Description of defect probability curve for one slice

The pixels inside a myocardial slice are defective at 0% to 100% of probability. The interval 0 to 100 is divided into 20 intervals, i.e., 0–4, 5–9, ... and 96–100. The total number of pixels the DP of which lie in each of these intervals are calculated and displayed on a graph (see Fig. 4). The total number of pixels in a myocardial slice is normalized with the length of the X axis. The Y axis shows the DP.

The DP curve for one slice is displayed by means of a set of horizontal bars, like a step function. Comparing the length of these bars with the length of the X axis, we understand that what percentage of the area of that slice has how much defect. The shape of this curve contains valuable information about the condition of the myocardium. The gap between these DP curves and the normal limit curves (described in section 6) is a measure of the severity of the ischemia of the slice. The larger the gap the greater the severity. In our method two curves are created for each slice, one for exercise and the other for the delayed stage. If there is an overlay between the exercise and delay curves, the overlay part is shown in white.

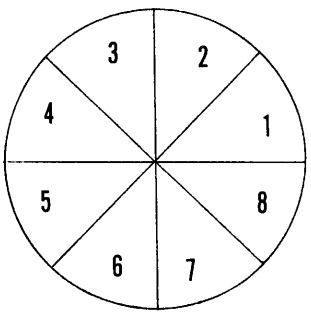

Fig. 2 Dividing a myocardial slice into 8 equi-angle sectors.

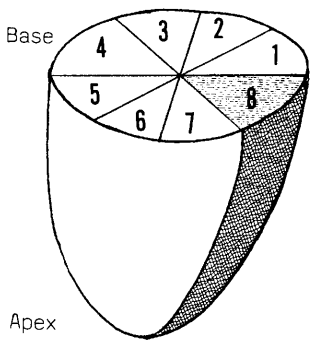

Fig. 3 Dividing the LV into 8 equi-angle vertical sectors from apex to base.

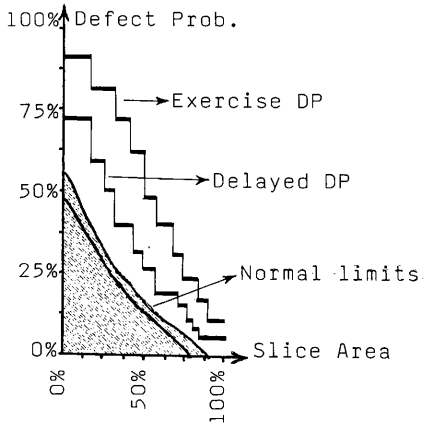

Fig. 4 Profile of DP curve for exercise and delayed study for one myocardial slice. The shaded area shows the normal limit area. In the actual display on the CRT, the DP curves for exercise and delayed study and their corresponding normal limit curves are shown in yellow and blue, respectively.

4. Description of DP curves for vertical sectors of LV

To visualize the amount of blood flow in three coronary arteries, the LV is divided into 8 equi-angle vertical sectors from apex to base (Fig. 3). Using the DPM of slices, for each of these 8 vertical sectors which is a three dimensional volume, a DP curve is created by a similar method to that described in section 3. These curves show what percentage of each of these vertical sectors is defective with how much probability. The gap between these DP curves and their coresponding normal limits (described in section 6) is a measure of the occlusion of the coronaries. Fig. 5 is an example of these curves and the corresponding normal limits.

5. Description of DP histograms

In order to understand the DP of lateral, anterior, septum and inferior, we have divided each slice into 8 equi-angle sectors, as shown in Fig. 2. For each exercise and delay slice, the mean defect probability for each of these 8 sectors is calculated and displayed in histograms on the CRT. The length of the histogram

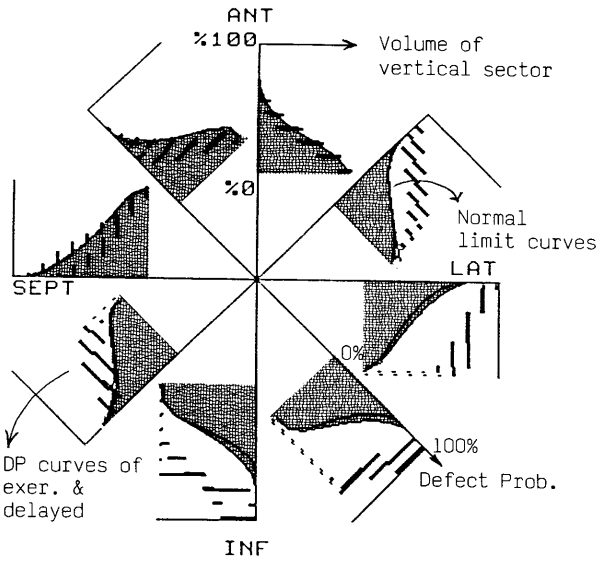

Fig. 5 Profile of the DP curves for exercise and delayed study of 8 vertical sectors of the LV. The shaded area shows the normal limit area. In actual display, the DP curves corresponding to exercise and delayed stages and their normal limits are shown in yellow and blue, respectively.

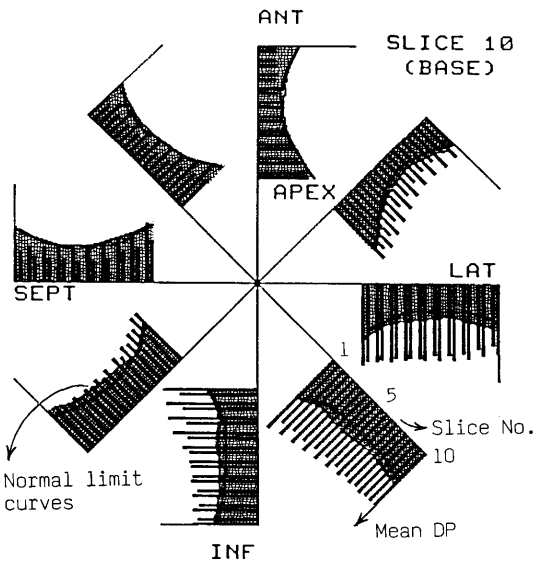

Fig. 6 Profile of a histogram of the mean DP for 8 sectors of each of 10 slices for exercise and delayed study. The shaded area show the normal limit area. In actual display, the histogram bars and the normal limit curves for exercise and delayed study are shown in yellow and blue, respectively.

bar shows the severity of ischemia in the corresponding sector. If the length of a histogram bar is equal to its maximum size (the length of the X axis), this means that its corresponding sector is 100% defective. Fig. 6 shows an example for these histograms and the normal limits.

6. Definition of normal limits

We have used ten normal volunteers, whose average age were 51 years, for which the DPMs were calculated as described in the previous sections. For every volunteer, from his DPMs the exercise and delay DP curves are calculated for each slice, each of 8 sectors in a slice and each of 8 vertical sectors of the LV. The normal limit curve for slice k (k=1 to 10) is calculated as the mean plus 2 standard deviations of DP curves for slice k of all 10 normal volunteers. The normal limit curve for each of 8 sectors in a slice and each of 8 vertical sectors of the LV are calculated in a similar way.

Figures 4, 5 & 6 are profiles showing the normal limit curves for exercise and delayed study for one slice, 8 vertical sectors of the LV and 8 sectors of each of 10 slices, respectively. The DP curves and histograms which are displayed inside the normal limit area indicate no defect. But those displayed outside the normal limit area show the existence of ischemia in that area of the LV which they represent. The distance of the DP curves and histograms from the corresponding normal limit curves show the severity of ischemia.

EXPERIMENTAL RESULTS

We have tested our method on several patients with infarction (persistent ischemia) and effort angina (transient ischemia), for which we could easily understand the extent and severity of ischemia in their exact location on the LV. These results are shown in Fig. 7, 8 & 9. In which the curves and histograms are seen in yellow and blue representing the exercise and delayed stages, respectively.

Figure 7, shows the result for a normal volunteer, where all curves and histograms are displayed within the normal limit area.

The results for a patient with transient ischemia are shown in Fig. 8. In the lower part (part A) of Fig. 8a, the exercise DP curves are seen far over their normal limits, but the delayed ones are within their normal limits. For slices closer to the apex (slice 1) and the middle of the LV (slices 4 to 6), the gaps between the exercise DP curves and their normal limits are larger than those near the base (slice 10).

In the upper part (part B) of Fig. 8a, ten images are displayed for exercise and delay, respectively. Each represents the DP for region of myocardium in one slice. In these images, the black represents a very high DP and the red stands for a very low DP. The colors in between show the severity of the defect depending on their closeness to black or red. These images show the exact location of the defects and their severity.

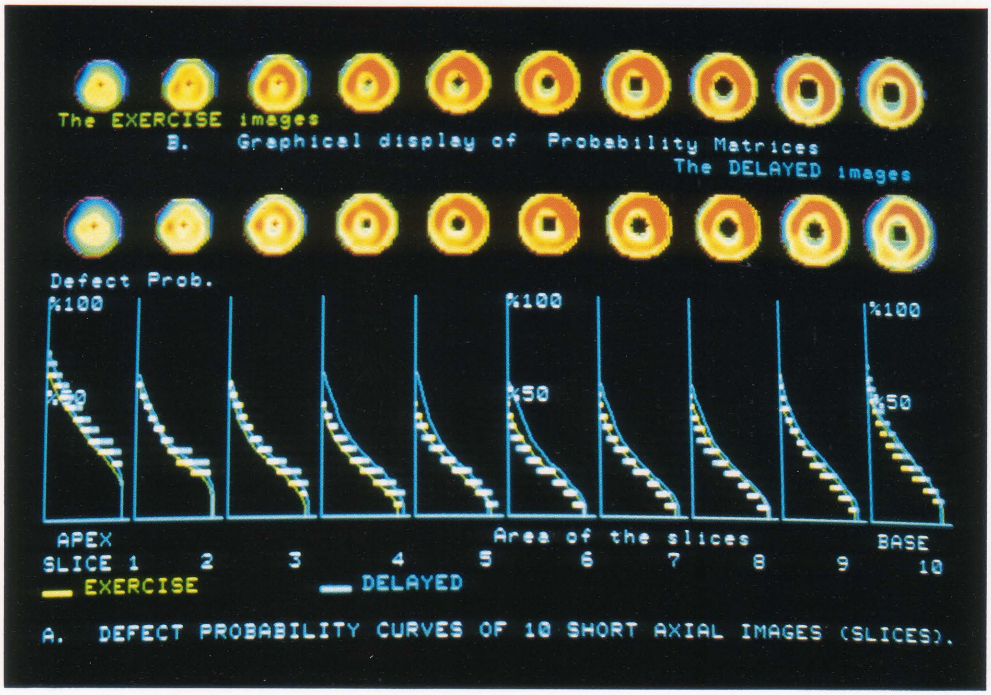

Fig. 7a A normal volunteer. The DP curves for 10 slices (part A) and the graphical display of the DPM (part B) for exercise and delayed study. All curves are displayed within their corresponding normal limit area. The color of most parts of the DPM is close to red, which means there is almost no defect in any slice.

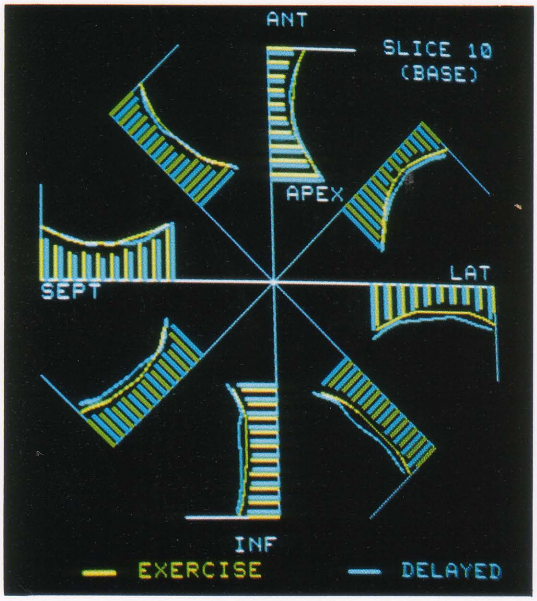

Fig. 7b The histogram for the mean DP for 8 sectors of all 10 slices at exercise and delayed study. All histogram bars are within the normal limits, showing no sign of ischemia.

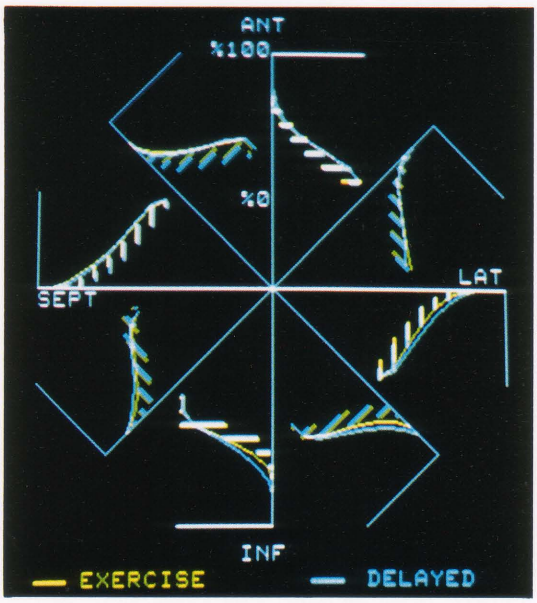

Fig. 7c The DP curves for 8 vertical sectors of the LV for exercise and delayed study. All curves are within the normal limits.

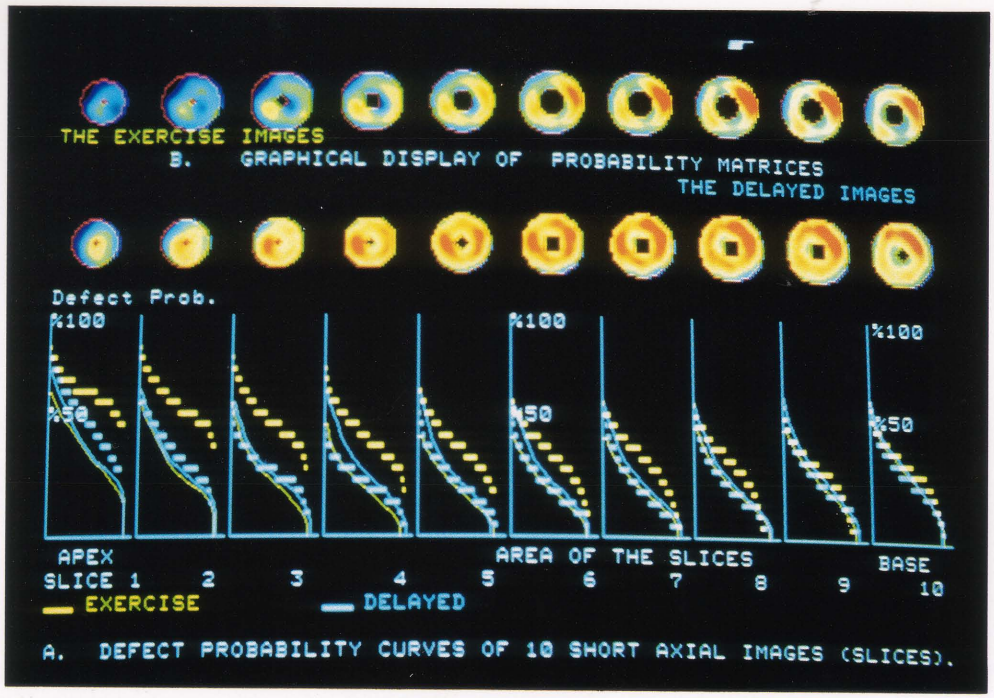

Fig. 8a A patient (50 Y, Male) with effort angina. CAG: RCA (1) 90%, LDA (6) 100%. The DP curves for exercise are far from normal limits in slices close to the apex and the middle of the LV. The delayed DP curves are mostly within their corresponding normal limits. This shows the existence of effort angina in these areas. Part B shows the location of ischemia in the anterior and septal walls.

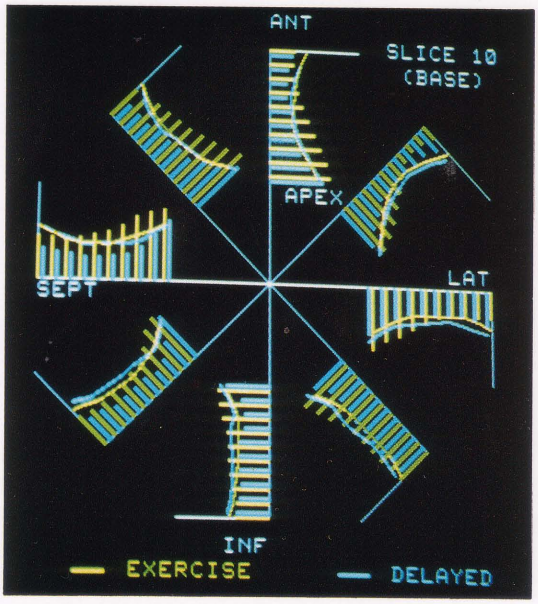

Fig. 8b The histogram bars for the mean DP for sectors of slices. In the anterior and septal areas, some of exercise histogram bars pass through the normal limits, but the delayed ones are within the normal limits. This shows the existence of effort angina in these areas.

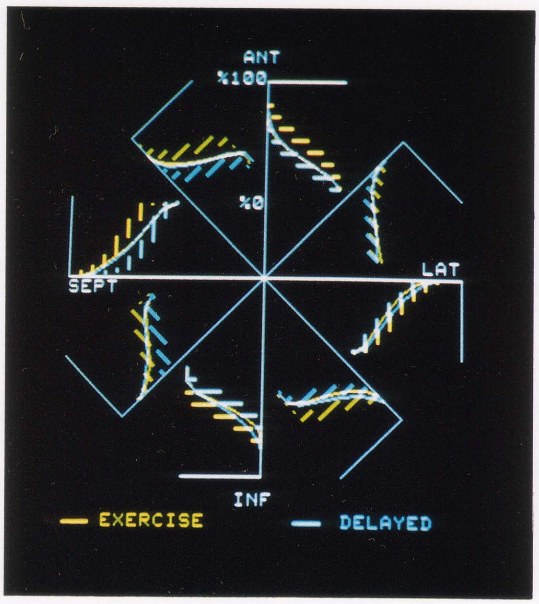

Fig. 8c The DP curves for 8 vertical sectors of the LV. The exercise curves show abnormality in the anterior and septal walls, but the delayed curves are within the normal limits.

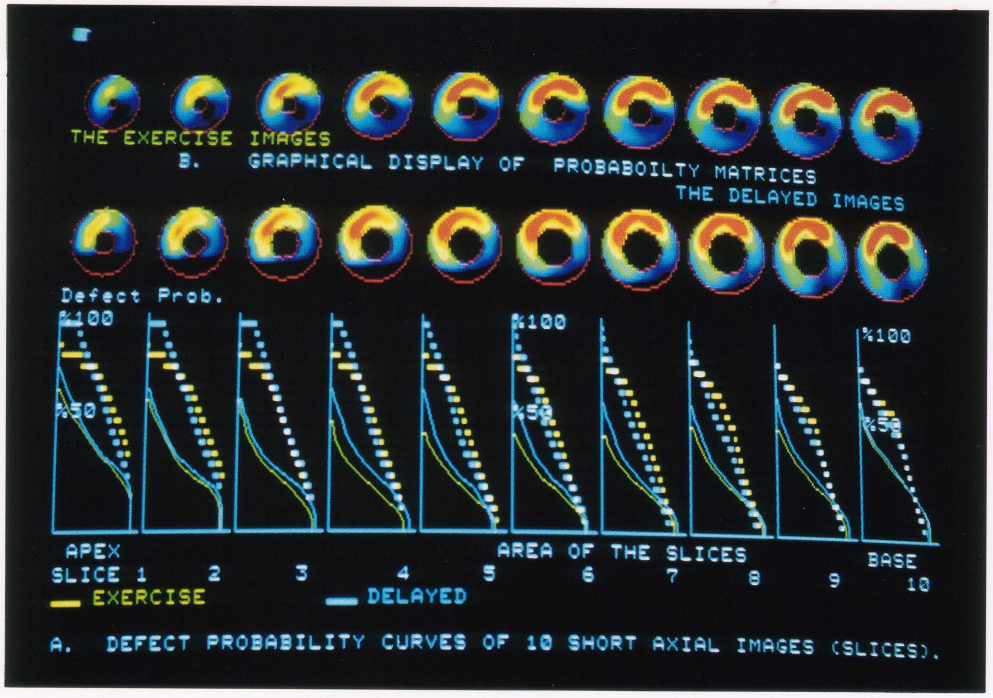

Fig. 9a A patient (62 Y, Male) with infero-lateral infarction, CAG: RCA (3) 95%. In part A, the DP curves for exercise and delayed study have similar patterns and are close to each other, but far from the normal limits. This shows the existence of infarction in all slices. In part B, the low activity in infero-lateral walls is seen during exercise and delayed study.

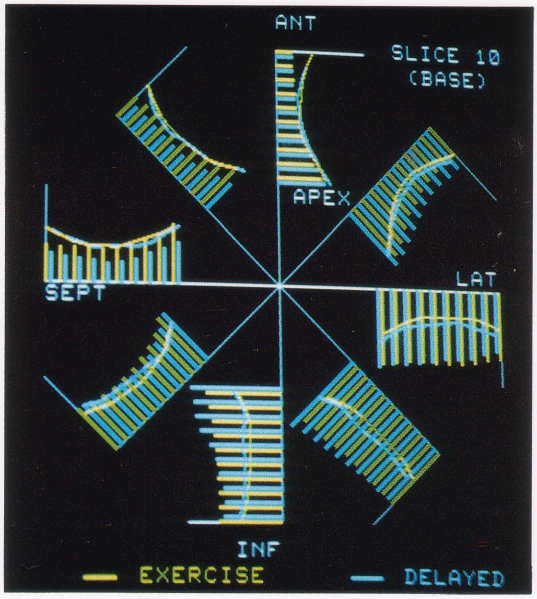

Fig. 9b The histogram bars for exercise and delayed study in the infero-lateral area go far beyond the normal limits and most of them are very close to their maximum length. This shows a severe defect in these areas.

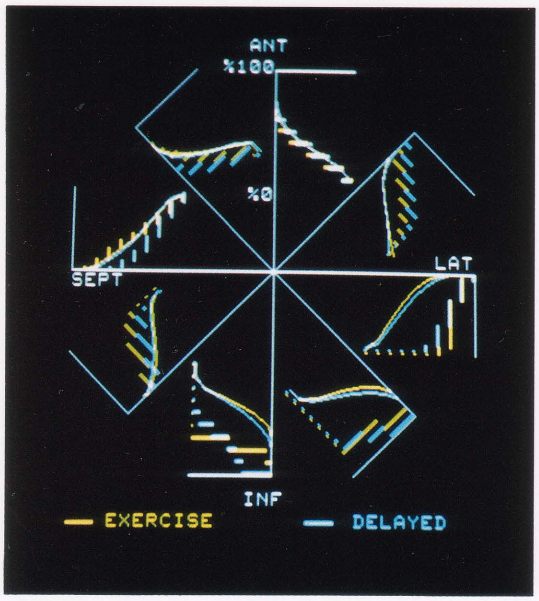

Fig. 9c The DP curves for 8 vertical sectors of the LV in exercise and delayed study. The big gap between the DP curves for the patient and the normal limits in the infero-lateral area shows the existence of severe infarction.

Figure 8b, shows the histogram bars which represent the mean DPs for the sectors of the myocardial slices. In the anterior and septal areas, some exercise histogram bars pass their normal limits, but those for delayed study are within their corresponding normal limits. The DPs for 8 vertical sectors of the LV are shown in Fig. 8c. The exercise curves show abnormalities in the anterior and septal walls, but the delayed curves are within their normal limits. The information in Fig. 8a, b & c shows that the infero-lateral walls are normal, but the anterior and septal walls have transient ischemia and their severity is greater in the area closer to the apex and the middle of the LV.

Figure 9 shows the results for a patient with persistent ischemia. In part A of Fig. 9a, the DP curves for exercise and delayed study almost completely overlap in most slices and exceed the normal limits. Fig. 9b gives detailed information about 8 sectors of all 10 slices. It shows that the anterior and septum are normal, (their histogram bars are within the normal limits). But the infero-lateral walls are very defective in the exercise and delayed stages. The DP curves for 8 vertical sectors of the LV are shown in Fig. 9c. The DP curves for exercise and delayed study almost completely overlap in most sectors. The big gap between these curves and normal limits in the infero-lateral walls indicates almost no activity in them soon after physical exercise and at the time of the delayed study. The information in the above three figures shows the existence of persistent ischemia in the infero-lateral walls.

DISCUSSION

In clinical medicine, the evidence of disease has always been the most important factor in diagnosis. But evidence is not always very clear and vagueness might give a degree of uncertainty to the diagnosis. In the case of computer aided diagnosis it will be very difficult to express the degree of uncertainty in natural language. Because natural language by itself can be vague in explaning the scientific meanings. The idea of vagueness in the fuzzy set theory shows us a method which can express the degree of certainty by a number in the interval of [0, 1].

In fuzzy set application, although the degree of membership in a defined fuzzy set is shown as a probability, but definition of the formula with which this probability is calculated is the key point. The accuracy of the results depends on the exactness of this formula.

Applying the fuzzy set theory to analyze the Thallium-201 myocardial SPECT images, we defined a term called "Defect Probability (DP)" as a number in the interval of [0, 1] showing the severity of ischemia for pixels inside the myocardium. Using the DP of the pixels, we created a set of images, curves and histograms which, along with some normal limits, gave us comprehensive information about the condition of the LV in exercise and delayed stages.

In automatic extraction of the myocardial slice, for slices near the apex which contain a highly defective portion, it might be difficult to determine their center with our method. In this case, slices 4, 5 and 6 which are in the middle of the LV are tested. If only very low activity (gray level greater than zero) is seen in the defective portion of these slices, our method can determine their center. Since the vertical axis of the LV is almost perpendicular to each slice, therefore the center of a middle slice can be used for all 10 slices.

The inner and outer edges of the myocardium are assumed to be well defined circles because it is very difficult to extract their exact shapes automatically. The problem with this assumption is that, some of the background pixels might be considered as pixels inside the myocardium region. This will result in some inaccuracy in the shape of the DP curves. However, this is not a serious problem, because the number of pixels which do not belong to the myocardium and are considered in DP calculation is not so great compared with those really belonging to the myocardium.

Our method provides us with two sets DP curves, and one set of DP histograms. One set of DP curves show the amount of blood flow in the myocardial slice. This clearly shows the existence of ischemia and its severity in each slice. The other set of curves show the amount of blood flow in each of 8 vertical sectors of the LV. The importance of these curves is that, they show the amount of occlusion in each of three coronary arteries. The DP histograms show the location, extent and severity of ischemic lesion. This information is available for exercise and delayed stages. The comparison of these curves and histograms before and after the operation is a good measure of the patient's recovery.

Persistent and transient ischemia can be simply distinguished, because in transient ischemia the exercise DP curves and histograms exceed exercise normal limits, but those for delayed study are within the delayed study normal limits. In persistent ischemia, the exercise and delayed study DP curves and histograms exceed their corresponding normal limits. The extent of ischemia is indicated by the number of curves and histogram bars which exceed the normal limits. Its severity is shown by the gap between the

patient's curves and normal limits and the length of the histogram bars.

The only input parameter required for our method is the file name for the myocardium images. The rest of the calculations and the CRT display are carried out automatically.

CONCLUSION

In conclusion, we would like to mention the following advantages offered by this analytical method:

1. Ischemic heart disease can be diagnosed on the basis of the fuzzy set theory.
2. The region of the myocardium can be extracted automatically with a relatively high degree of accuracy.
3. The ischemic myocardial lesion, its extent and severity can be identified.
4. It is very easy to distinguish between persistent and transient ischemia.
5. This method is very easy to use, reproducible and independent of observer bias. It provides us with the tools necessary for automatic diagnosis of ischemic heart disease.

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