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A Novel Algorithm for Diagnosis of Thin Basement Membrane Nephropathy

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Abstract:

In this paper we have made an algorithm to diagnose the thin basement membrane nephropathy. The idea of our algorithm is based on content based image retrieval and Hough transform. The diagnosis of this disease is depending on calculating the membrane thickness to know whether it is normal or abnormal. The traditional way for calculating the thickness is by manually enlarging the pictures for more than 5 thousand times before calculating the thickness, so we suggest an automatic algorithm to detect the membrane in the pictures then calculates the thickness. Firstly, a database of the membrane shapes will be build by dividing the original image of size 512´512 pixel into sub images of size70´70 pixel, the sub image that contain membrane will be considered, other parts will be ignored. Then, the sub image that contain the membrane will be enhanced and converted into binary image to detect the edges, Hough transform and line detect method are used to detect the surface of the membrane by drawing lines on the surface of the membrane, by applying orthogonal line on two lines that lies on the corresponding membrane surface, we then calculated the distance between two lines by using Euclidian distance. Compared with the manual procedures, our algorithm proves easy to use and can work round the clock.

Keywords: ***Medical Diagnosis; thin basement membrane; Hough transform; Euclidian distance, content based image retrieval.***

خوارزمية تشخيص مرض الغشاء الكلوي الوراثي

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الخلاصة:

اقترحنا في هذا البحث خوارزمية لتشخيص مرض وراثي يصيب الكلية وهذا المرض يصيب الغشاء الخارجي المحيط بكل خلية في الكلية حيث يكون السمك للغشاء مقياس للإصابة بهذا المرض اولاً . فكرة الخوارزمية مستوحاة من استرجاع محتوى الصورة وتحويلات هوغ. تشخيص هذا المرض يعتمد على حساب سمك الغشاء لمعرفة ما إذا كان

السمك طبيعي ام غير طبيعي. حيث كانت الطريقة التقليدية لحساب سمك الخلية يدويا عن طريق تكبير الصور لأكثر من 5 الاف مرة ومن ثم استخدام القياس اليدوي لحساب السمك ، لذلك اقترحنا خوارزمية تقوم اولا بالكشف عن الغشاء فقط وترك باقي اجزاء الخلية ومن ثم يحسب سمك الغشاء. والخوارزمية تقوم بالتالي:أولاً : سيتم بناء قاعدة بيانات من الأشكال الخاصة للغشاء عن طريق تقسم حجم الصورة الأصلية من 512´ 512 بكسل إلى اجزاء من الصورة بحجم 70´70 بكسل ، الصور الفرعية التي تحتوي على الغشاء سوف تؤخذ بنظر الاعتبار ، اما باقي الصور او الاجزاء الاخرى سيتم تجاهلها. ثم، نقوم بتحسين الصور الفرعية التي تحتوي على الغشاء وتحويلها إلى صورة الثنائية للكشف عن الحواف، حيث يستخدم تحويلات هوغ وطريقة كشف الخط للكشف عن سطح الغشاء وذلك عن طريق رسم خطوط على سطح الغشاء، حيث يتم رسم خط متعامد على خطين يتم رسمهما افقيا والذين يقعان على سطح غشاء بصورة متقابلة (خط في اعلى الغشاء وخط اسفل الغشاء)، ومن ثم نقوم بحساب المسافة بين خطين باستخدام نظرية اقليدس حيث كانت النتائج ممتازة بالمقارنه مع الطريقة اليدوية، الخوارزمية اثبتت سهولة في الاستخدام ويمكن أن تعمل على مدار الساعة.

1. Introduction

Thin basement membrane disease (TBMD, also known as benign familial hematuria and thin basement membrane nephropathy) is the most common cause of asymptomatic hematuria. The only abnormal finding in this disease is a thinning of the basement membrane of the glomeruli in the kidneys; the defining ultrastructural feature is diffuse thinning of the glomerular basement membrane GBM, in the absence of other significant glomerular alterations. The GBM attenuation primarily affects the lamina densa with relative preservation of the lamina rara interna and externa. The World Health Organization (WHO) uses a mean GBM thickness of <250nm for adults and 180nm for children aged 2–11 years to define TBMN [1].

Our paper attempts to reproduce the performance of one or more doctor's opinions, most commonly in a specific diagnosis, and try to find an accurate algorithm to diagnose the TBMD by detecting the membrane and calculating its thickness depending on doctors experties. In a manual way, the doctor enlarges the pictures to more than 5 times to make it easy to calculate the distance of the membrane thickness by using ruler to measure 20 random points and then divide the result onto the enlarge scale, and compare with 250nm for adults and 180nm for children to verify its normality. In the proposed algorithm, more than 100 random points will be taken on membrane surface to find out whether it is normal or not. In medical diagnosis, there are several specific requirements that the system must meet, in our paper we need to detect the membrane from the image and remove all the other image contents, many ways were tried, but it remains very difficult to remove all the contents with out removing some part of the membrane, this has made it very difficult to find an automatic method. Our algorithm is based on many image processing methods, the main idea is apply content based image retrieval (CBIR) to detect the membrane shape only and ignore the other contents by using database that consist of many samples of membrane in training stage. Also, an enhancement method is used to keep the pictures in the training and/or testing stages to have almost the same features, the proposed algorithm is successful in detecting and calculating the membrane distance without the need to achieve that manually.

2.Thin Basement Membrane Nephropathy

Thin basement membrane nephropathy (TBMN) is the most common cause of persistent glomerular bleeding in children and adults, and occurs in at least 1% of the population. Most affected individuals have, in addition to the hematuria, minimal proteinuria, normal renal function, a uniformly thinned glomerular basement membrane (GBM) and a family history of hematuria. Their clinical course is usually benign.[2].

TBMN disease is also sometimes referred to as 'benign familial hematuria'. This term is not exactly interchangeable; not all cases of TBMN are familial hematuria, and not all cases of familial hematuria are benign or caused by TBMN. Notwithstanding, cases of TBMN have been shown to have type IV collagen mutations, providing a link between this disease and Alport syndrome [3].

2.1 Content-Based Image Retrieval (CBIR)

Content-based image retrieval (CBIR) is a technique which has been an advancing research area since the 1990s. The aim of this technique is to search for images from large multimedia DB and digital libraries by granting the autonomous adaptation to the user's preferences and conceptions regarding the relevance and similarity of images. This can be achieved by examining the user's reactions on the retrieval results in the form of relevance feedback. The CBIR relies on the characterization of primitive features such as color, shape, and texture that can be automatically extracted from the images themselves. These primitive features are incorporated in IR in order to remedy the problems that occur when text-based image retrieval is used [4].

Content -based image retrieval (CBIR) has been largely explored in the last decade. In the CBIR context, an image is represented by a set of low-level visual features, which have no direct correlation with high-level semantic concepts, and the gap between high-level concepts and low-level features is the major difficulty that hinders further development of CBIR systems [5].

Obviously, annotating images manually is a cumbersome and expensive task for large image databases, and is often subjective, context-sensitive and incomplete. As a result, it is difficult for the traditional text-based methods to support a variety of task-dependent queries [6]. This has failed to meet the diverse requirements arising in a generic image (or multimedia) DB system for retrieval of content specific data. Thus, other research found that the systems of CBIR are one of the kind of systems that let users retrieve desired images automatically from a collection on the basis of primitive features representing color, texture or shape either singly or in combination [6]. The aim of such systems is to enable the users to pose queries such as, retrieve images similar to a given image, to retrieve images similar to one chosen by the user (query-by-example), from a large image database. This has brought together the image processing, IR and database communities together, as the problems involved are diverse. In

fact, based on fundamentals of CBIR and its components, these systems need to extract image features, index those using appropriate structures and efficiently process user queries providing the required answers [7].
There are two approaches to image retrieval: Text-Based approach and Content-Based approach. The former solution is a more traditional approach, which indexes images by using keywords. The keyword indexing of digital images is useful, but it requires a considerable level of effort and is often limited to describe image content [8].

3. Algorithm

The aim of our algorithm is to find automatic way for calculating and detecting the membrane previously done manually, the advantages of any expert algorithms or systems are: it provides consistent answers for repetitive decisions, processes and tasks, holds and maintains significant levels of information, encourages organizations to clarify the logic of their decision-making and never "forgets" to ask a question, as a human might. The algorithm has the following steps:

3.1. Image acquisition

Images are acquired using an electronic microscope with 6,000X magnification; all the images are captured in the JPEG format, with maximum resolution size544×655 pixels which were later resized to512×512 pixels.

3.2. Pre-processing

Many of the pictures collected to build database by colouring the membrane red depends on the doctor diagnosis, because we need to detect the membrane only and ignore the other picture contents as shown in **Figure. (1)**. These coloured pictures will be compared with the original ones to build database, by dividing the coloured image with its original into many sub images (70×70 pixel) and keeping all sub images of the original image that corresponds to sub images containing the red colour (membrane) to save into the database, other parts that do not contain the red colour will be ignored as they are not part of the membrane, many shapes of membrane will be saved in the database which will then be used to detect the membrane and then to calculate the distance, as shown in Figure 2. All pictures are collected from the (Xiang Ya hospital in Changsha-china).

After getting database for membrane shapes we have to convert the sub images (membrane) into gray level pictures as the pictures are collected at different years and they have to be enhanced to have same properties by using one of image enhancement methods, we tried many enhancement methods, finally the experiment explores that, the adjustment image is the best one because we need high contrast as shown in Figure 3-b. Image adjustment which removes the unwanted part of the image that came from some noises (converted from negative to normal ones) is the first step. High contrast for the image is needed in our work [9,12].

$$y = \begin{cases} ax, 0 \le x < x_1 \\ b(x - x_1) + y_{x1}, x_1 \le x < x_2 \\ c(x + x_2) + y_{x2}, x_2 \le x < B \end{cases} \quad (1)$$

where a, b, and c are appropriate constants, which are the slopes in the respective regions, and B is the maximum intensity value. The intent here is to enlarge low values and reduce high values of the pixel intensities while keeping the intermediate values approximately intact.

We need to apply 5×5 average filter to delete the noise and small objects from the sub images to keep the membrane only as shown in Figure 3-c [10].

$$y(i, j) = \frac{1}{MN} (\sum_{i}^{M} \sum_{j}^{N} x(i, j)) \quad (2)$$

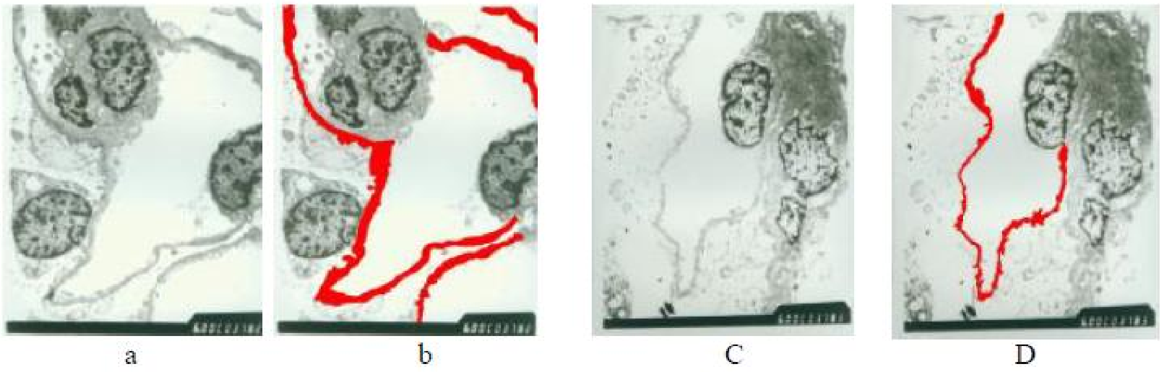

Fig. (1) {a and c original images (b and d) colouring images}

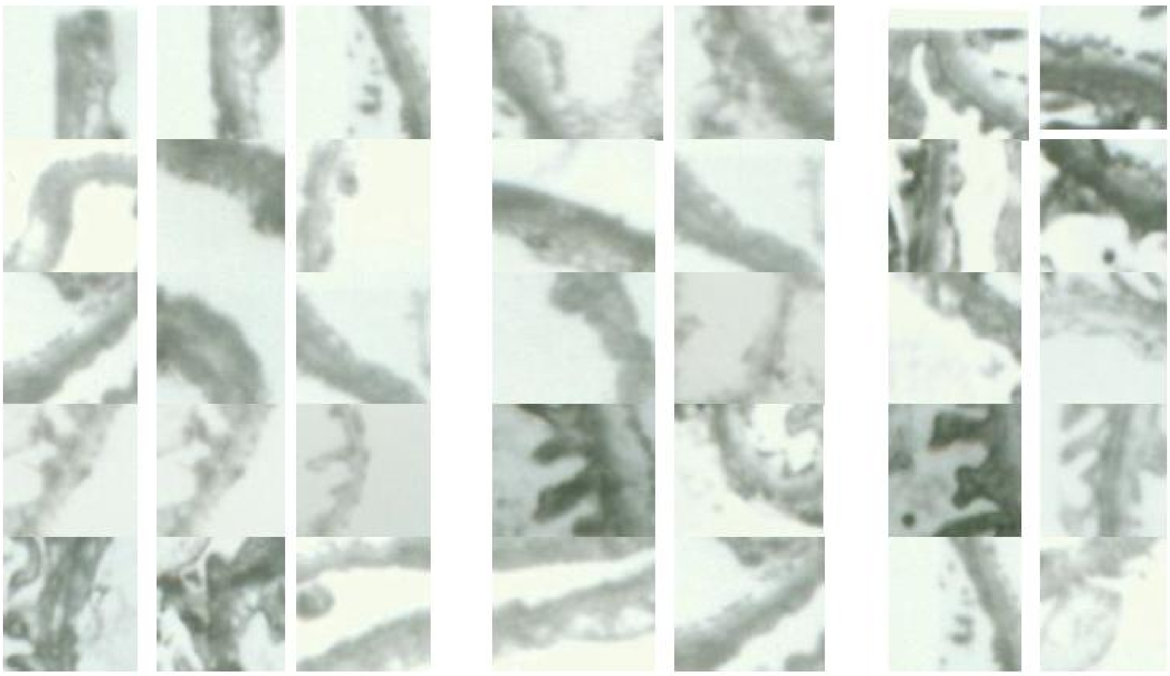

Fig. (2) sample of sub images that detected and stored in data base to use later

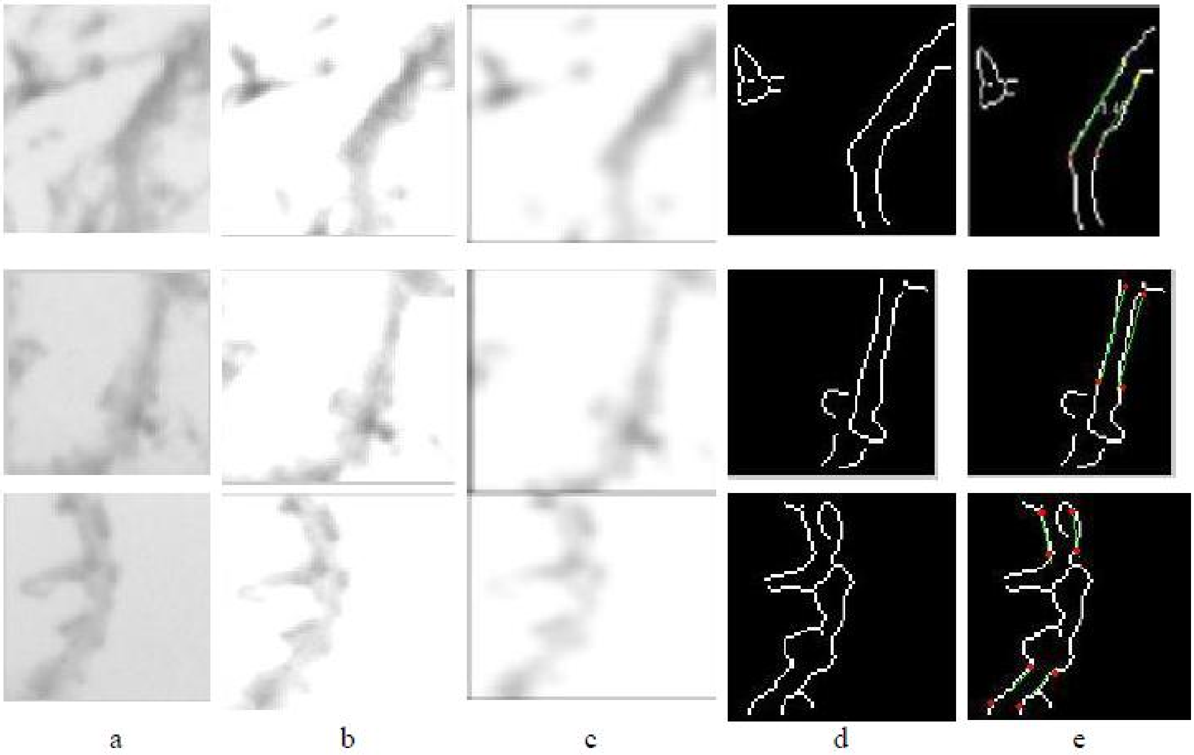

Fig. (3) (a) original sub image (b) after enhanced by using image adjustment (c) applying 5×5 average filler (d) converted to binary image using Canay filter (e) line detection

3.3. Hough transform for line detection

Hough transform is a powerful global method for detecting edges. It transforms between the Cartesian space and a parameter space in which a straight line (or other boundary formulation) can be defined, it is used in a variety of related methods for shape detection.

Hough transform for line detection yields an equation of a line for line l shown in Figure 4, [11].

$$r = x\cos q + y\sin q \tag{3}$$

where ρ is the normal distance of the line l from the origin O passing through a feature point P(x,y) shown in Figure 4 (or equivalently, the distance of the line OA that is normal to the line l). The angle θ represents between the x-axis and the line OA, with 0≤θ<2π and $-r_{\max} \le r \le r_{\max}$. Since ρ is reversed whenever θ=2π, 0≤θ<π and $-r_{\max} \le r \le r_{\max}$ are assumed, $r_{\max} = K/\sqrt{2}$ is measured from the center O of the image K×K. Note that, the point A is the most nearest point from the origin, among all the points on the line l.

There are an infinite number of lines which pass through a fixed pixel in an image plane, with each line represented by two parameters θ and ρ. Thus a single pixel in the image plane is mapped into an infinite number of points in the θ-ρ line parameter space. Detection of the dominant line in the image plane is achieved by finding a peak in the accumulators of parameter arrays.

Each of the straight lines passing through a fixed point in an image plane is mapped into a large number of discrete points (θ_n, ρ_{mn}), $0 \le n \le N$, $-M \le m \le M$, on a periodic sinusoidal curve in the θ-ρ parameter space, where N and (2M+1) represent the total numbers of quantized angle and distance cells, respectively. Note that θ_n is the *n*th uniformly quantized angle of θ in the bounded parameter space, for reduction of the computational complexity, and that ρmn denotes the quantized distance of ρn that corresponds to θn in Eq. (3).

To detect the boundary of the membrane in the sub image, there is need to first detect the edge of the membrane, by using Canny filter the sub image will be converted into binary image, after trying many edge detection filters we found that Canny filter gives the best results compare with others filters as shown in Figure 3-d. To find the membrane surface we can easily calculate the distance of the membrane. We need to know the distance between two lines which lies on two corresponding sides of the surface on membrane. So that we need to use the line detection method to draw some lines that lied on the surface of membrane, we may draw more than four lines as shown in Figure 3-e. from these lines we can easy calculate the distance of membrane.

3.4. Calculating the distance on the membrane

Calculate the thickness of membrane by using the Euclidean distance between two points that lie on two corresponding lines (the two lines lie on two corresponding side of membrane surface) to know the two points, we need to know the slope of each of two lines, assuming that, the first line have two points (x_1, y_1), (x_2, y_2), then the slope will be:

$$slope_1 = \frac{y2 - y1}{x2 - x1} \tag{4}$$

And the slope for second line is $slope_2$, by using equation 4 it is easy to calculate the value of slope for each of the two lines. Let's consider the case where we have straight lines in an image. We first note that, for every point (xi ,yi) in that image, all the straight lines passing through that point satisfy Equation 6 for varying values of line slope and intercept (k,b).

$$\mathrm{k} = {-1}/{\mathrm{slope}_1} \tag{5}$$

$$y_i = kx_i + b \tag{6}$$

Now if we reverse our variables and look instead at the values of (k,b) as a function of the image point coordinates (xi ,yi), then Equation 5 becomes:

$$b = y_i - kx_i \tag{7}$$

Equation 6 describes a straight line on a graph of k against b. At this point, it is easy to see that each different line through the point (xi,yi) corresponds to one of the points on the line in the (k,b) space. Now, consider two points P1 and P2, which lie on the line in the (x,y) space. For each pixel, we can represent all the possible lines through it by a single line in the (k,b) space. Thus, a line in the (x,y) space that passes through both pixels must lie on the intersection of the two lines in the (k,b) space, which represent the two pixels. This means that all pixels which lie on the same line in the (x,y) space are represented by lines which all pass through a single point in the (k,b) space.

There a need to know the two points lie on two lines in the same membrane but in corresponding position, so we assume that an orthogonal line intersection the two lines in points (x1,y1), (x2,y2) as shown in Figure 5. We need to know how to calculate the intersection points between the two lines and orthogonal line, by using the Cramer's rule for the first and second line with the orthogonal as following [11]:

$$\begin{aligned} b_{line1} &= -k_{line1} x_{line1} + y_{line1} \\ b_{orgline} &= -k_{orgline} x_{orgline} + y_{orgline} \end{aligned} \tag{8}$$

$$\begin{gathered} A_1 = \begin{bmatrix} -k_{line1} & 1 \\ -k_{orgline} & 1 \end{bmatrix}, \quad D_{x1} = \begin{bmatrix} b_{line1} & 1 \\ b_{orgline} & 1 \end{bmatrix}, \\ D_{y1} = \begin{bmatrix} -k_{line1} & b_{line1} \\ -k_{orgline} & b_{orgline} \end{bmatrix} \end{gathered} \tag{9}$$

$$x_1 = \frac{D_{x1}}{A}, \quad y_1 = \frac{D_{y1}}{A} \tag{10}$$

where x1, y1 are the intersection point between the first and the orthogonal line, and we can also calculate the intersection point between second line and orthogonal line by using the same equations (8-10). Then, it is easy to calculate the distance between two line dependence on the two intersection points between the two lines and orthogonal line. By using Euclidean method we can calculate the distance between two points in two lines, assume the orthogonal line intersect the first line at point (x1, y1) and cross the second line at point (x2, y2), the Euclidean distance between them is [12]:

$$dis = \sqrt{(x_1 - x_2)^2 + (y_1 - y_2)^2} \tag{11}$$

In each sub image there are many lines, and we only need the lines in corresponding sides of the membrane. This distance means the thickness of the membrane in these two points. The

proposed method calculates many points in each sub image, and summations with others sub images to find the average value which represent the thickness value of membrane.
The final value is computed in pixels, so we have to convert the measurement unit from pixel unit to nm (nanometre) since the standard unit for comparing with normal with abnormal is nm(nanometre), since all pictures are acquired with 6,000X magnification, with the scale of pictures is 300dpi in both horizontal and vertical, and centimetres $=10^7$ nanometre so that

$$pixel = \frac{inch}{dpi} = \frac{2.54\times10^7}{300\times6000} = 14.1nm \quad (12)$$

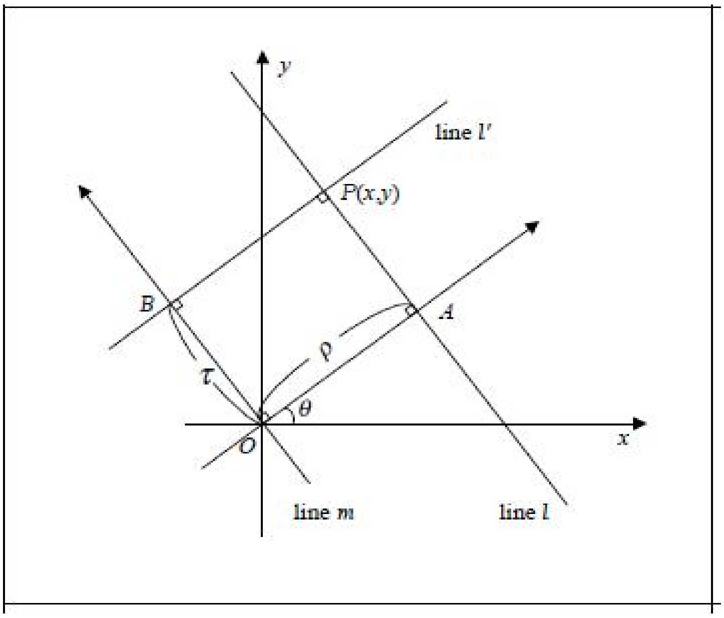

Fig. (4): HT for line detection.

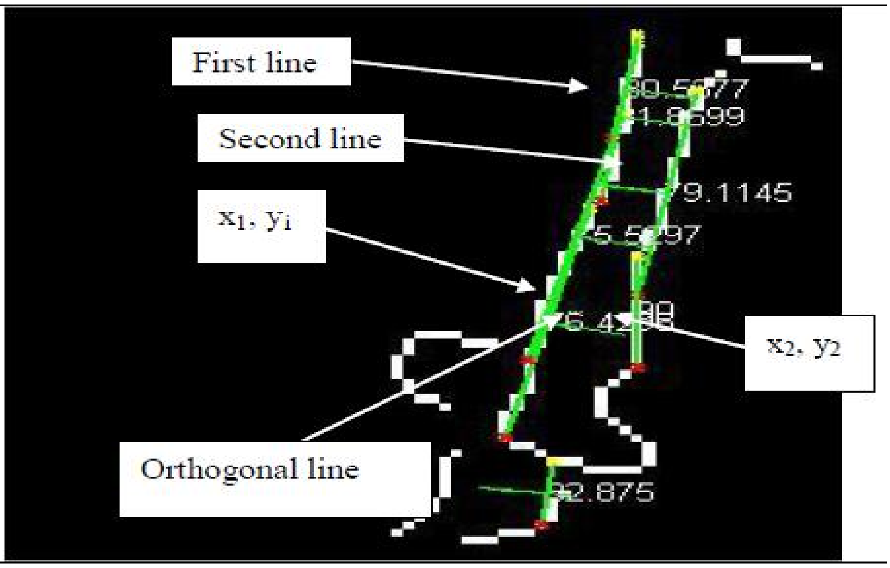

Fig. (5): illustrated the two lines on membrane; the orthogonal line and two cross points.

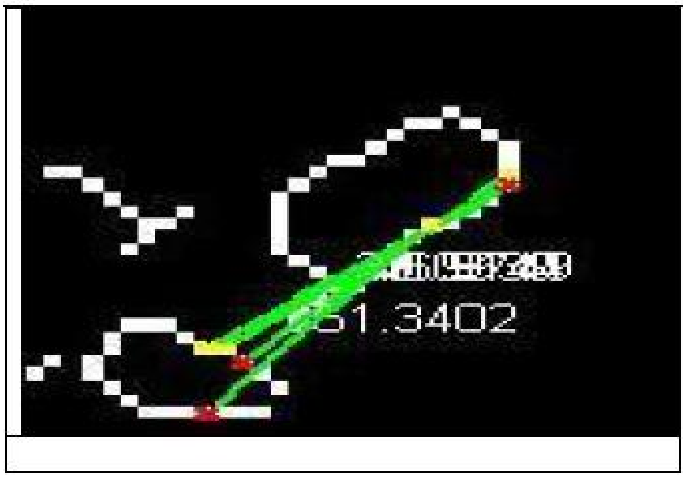

Fig. (6) :many lines lied on the same side of the membrane

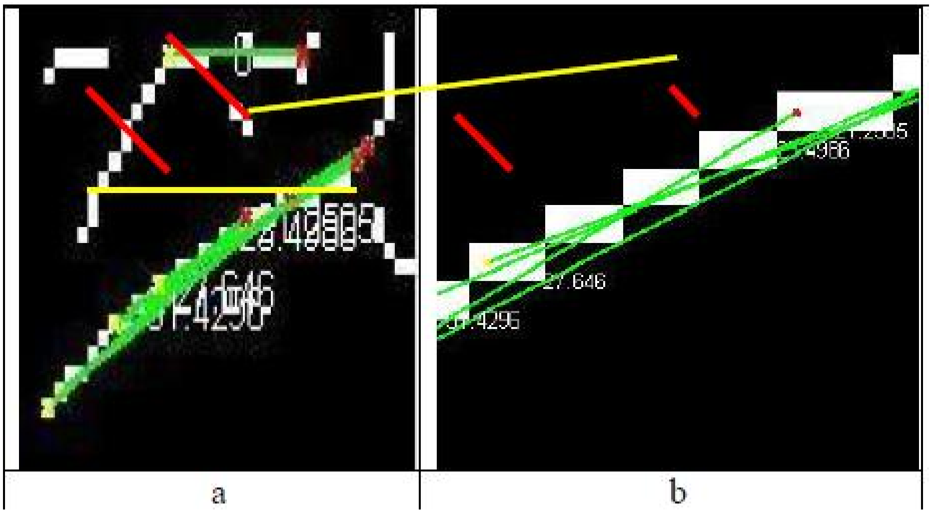

Fig. (7): a) many lines lied on the same side of the membrane b) enlarge the (a) to see the small distances

4. Experiment

Experiments for 10 new pictures have been carried out and the obtained result greatly approximates the manually calculated ones with simple errors percentage as shown in Table 1, and Figure 8. These pictures are collected from (Xiang Ya first hospital- Changsha- China) four pictures for abnormal children, four pictures for abnormal adult and tow pictures for normal adults. In the proposed method, we tried many different shapes of membrane and the algorithm met some challenges for example in the Figure 6 where there are only two lines lying on the same side of the membrane but we need to calculate the distance between two lines that lies on two corresponding side. Another problem in **Figure 7** is that, the two lines are not exactly in the same side but when the orthogonal line intersects them, the algorithm calculated the distance, this distance is not the actual one and it may reduce the value of the membrane thickness because it is very small.

Thus, we suggest two conditions; the first is not allow calculating the distance between two lines that lie in the same side of membrane or not parallel by ignoring the smallest distance, and the second condition is to consider that at least there are 20° angle between two corresponding lines.

Then we can ignore the small distance and let the algorithm to calculate the smallest distance that may give wrong result.

Our algorithm has more accuracy than the manual ways by section the random points number ,where the manual way select 20 random points and then calculate the average of the thickness, while our algorithm select at least 150 random points as shown in **Table 2** and **Figure 9.**

Table 1. Illustrate the result from our algorithm and manually way.

No. of cases	Manual	Our algorithm	Error	Error %
1	104	108	4	3.8 %
2	141	130	11	7.8 %
3	95	91	4	4.2 %
4	208	204	4	1.9 %
5	213	218	5	2.3%
6	301	309	8	2.6%
7	184	185	1	5.3%
8	222	213	9	4%
9	324	344	20	6.17%
10	176	186	10	5.6%

Table 2. Illustrate the number of points selection to calculate the thickness from our algorithm and manually way.

No. of cases	Manual	Our algorithm	Difference
1	20	301	281
2	20	259	239
3	20	366	346
4	20	324	304
5	20	251	231
6	20	253	233
7	20	287	267
8	20	222	202
9	20	385	365
10	20	313	293

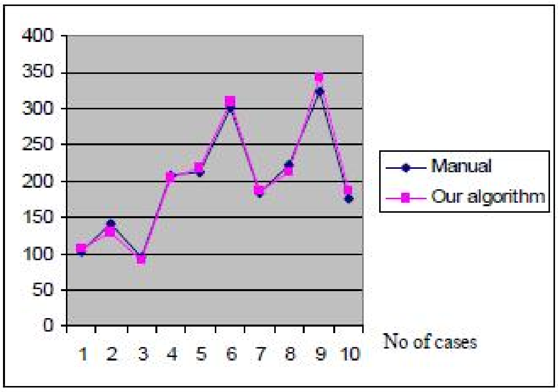

Fig. (8) errors percentage

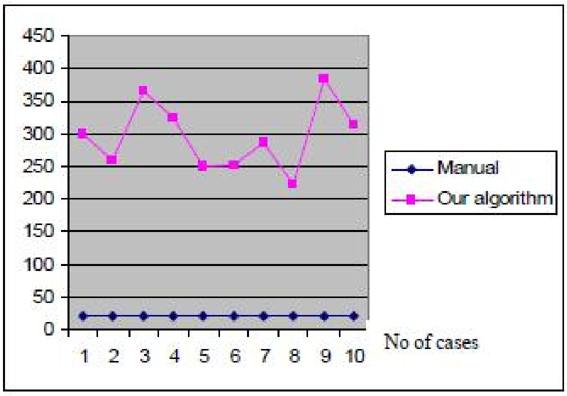

Fig. (9) show the difference between the our algorithm and manual way by points number that used to calculate the thickness

5.Conclusion

The proposed method is designed to principally replace the manual one, and it has the advantage that, any doctor can easily use it. Also, the method requires no expert doctor to diagnose whether the diagnosis is normal or abnormal. Moreover, the method can be used at any time and in any place without the need for spatial devices necessary for manual method.

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