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Digital Image Processing Algorithm for Functional Analysis of Renal Perfusion.

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DIGITAL IMAGE PROCESSING ALGORITHM
FOR
FUNCTIONAL ANALYSIS OF RENAL PERFUSION

طريقه مستنبطه لمعالجة الصور الرقميه لتحليل وظائف الكلى

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ملخص البحث :

تقدم عملية التصوير الرقمي في المجال الطبي وسائل متنوعة لاستخدام تقنيات الحاسبات الخبيرة و الهندسة الحيوية في دراسة تلك الصور. فبعد حقن كمية من اوساط التباين في اوردة الساعد (الطرفية) يمكن الحصول علي سلسلة من الصور للعضو المراد فحصه. يتم تشفير تلك الصور رقميا و تخزينها كمصفوفة ٥١٢ x ٥١٢ من العناصر الثنائية. هكذا تعكس المعلومات الرقمية لكل عنصر في سلسلة الصور التغيرات الزمنية لتركيز الصبغة في النسيج الممثل بهذا العنصر طبقا لمعادلة لوغاريتمية خاصة باضعاف تاثير اشعة اكس اثناء مرورها بهذا النسيج.

من قبل كان يتم تحديد وظيفة كل كلية علي حدة بتدخل جراحي يحتاج الي خبرة خاصة كما انه يستغرق وقتا ليس هينا. لقد وجد ان المعلومات الرقمية الدالية التي تحتويها تلك الصور قد اهملت نسبيا بالمقارنة بالدلالات التشريحية . ان استخدام تلك المعلومات يمكننا من الحصول علي علاقة زمنية لتدفق الدم في الاعضاء المختلفة و من بينها الكلي.

ان الهدف من البحث هو استنباط الجوريثم هيكلي لتمثيل العلاقات الزمنية المحتواه في متوالية الصور علي شكل منحنيات و استخلاص ارقام دالة ذات اهمية خاصة في التطبيقات الاكلينيكية و حساب النسب بينها وهذا يمكننا من تحديد وظيفة كل كلية علي حدة و كذا وظيفتها النسبية لنفس الفرد. و قد تم كتابة البرنامج بلغة الميدكول المتخصصة في هذا المجال و كذلك تم اختبار اداء الطريقة المقترحة علي ٣٨ حالة لمتبرعين عاديين حيث امكن تحديد نطاقات محدودة للارقام الدالة للوظائف في حالة الكلي السليمة مما يعطي البرنامج قدرة تشخيصية ملحوظة في اكتشاف اي تباين غير طبيعي بين الكليتين. و كذا امكانية تحديد اي خلل (في بناء الاوعية الدموية الكلوية) غير ملحوظ و لايمكن اكتشافه بصور الاشعة التناظرية.

ABSTRACT:

A timed series of video images (dynamic study) may be taken for a human organ under examination, after i.v. injection of contrast material. The images are digitized and stored as matrices of 512 x 512 pixels. Numerical data for each pixel within the sequence reflects then the temporal changes of the dye concentration in the tissue represented by that pixel according to a well-known x-ray attenuation logarithmic relation. A structured algorithm is developed to perform mathematical analysis and manipulation for those "functional images" on a pixel-by-pixel basis with the aim of deriving out some useful time-density variables and curves. The algorithm is applied to 38 normal individuals to study their renal function and the results proved to be of a remarkable diagnostic value.

INTRODUCTION:

The digital imaging process [1] offers unique opportunities in the application of biomedical engineering techniques to improve health care delivery. Regional blood flow and organ perfusion [2] can be evaluated by different imaging modalities as digital subtraction angiography (DSA), dynamic CT and MR imaging and radionuclide scintigraphy.

The application of digital computers to the radiographic image processing has increased steadily during recent years [3]. Efficient handling of the large amounts of data obtained by digitizing dynamic imaging sequences [4] has been primarly derived from the rapid development of digital electronic technology.

Accurate determination of the individual renal function requires uretric catheterisation to assess clearance from each kidneys [5]. This technique is not only invasive but it is also time consuming and needs surgical expertise to perform.

Digital substraction angiography [6], a relatively new diagnostic imaging technique, has the best temporal and spatial resolution of any of the above imaging techniques [7]. Its potential to give informations not only about the kidney structure but also its function, can be realized by the application of parametric imaging which is able to assess quantitatively the two variables of iodine contrast: density and time, after an intravenous injection of the dye [6-8]. However, those temporal informations have been largely ignored [6].

Utilizing the functional contents of the DSA-timed sequence of images data, we aim in this work to develop and test an "Image-Processing" procedure for analyzing the time-density curves and relations in the case of normal kidney perfusion. The main object of its application is to investigate the behaviour of three proposed parameters : maximum density, T-maximum and T-half maximum values as well as ratios between the right and left kidney which may be useful for detecting abnormalities and for studying the relative renal function. In other words, we try to establish normal values for the renal blood flow and introduce a simple way to obtain some important facts about the time density parameters through non-invasive image processing techniques.

MATERIALS AND METHODS:

A DVI (Digital vascular imaging) Philips system was used in the angiographic examination of all cases at the Urology and Nephrology Center, Mansoura University. The injection of the contrast medium urografin 76% was standardized (40 ml) using automatic injector at a rate of 10 ml/sec. The sequence of exposures is automatically adjusted according to the heart rate of the case examined (ECG-triggered). The DSA images obtained were then transferred to the Analytical Processing Unit (APU), a stand-alone computer system for image processing, where our developed program for renal perfusion study could be executed.

The APU enables fast, routine, off-line, qualitative as well as quantitative analysis of DVI runs by means of program-guided user/system dialogue. User-programing is available via the specially-developed MEDCOL language (Medical Computing Language) combined with rapid compile and edit functions. A support of RTL procedures (Real Time Language) together with a FORTRAN extended option and ASSEMPLY programming for the processor P854 are also available for reasons of flexibility and for applying advanced techniques. The storing capacity of the APU hard disk is 70 Mbytes of unformatted data with 34 Mbytes for image storage in 512 x 512 format.

PROPOSED ALGORITHM :

The algorithm proposed in this work can be summarized below:

a- Smoothing the reconstructed data.

b- Logarithmic subtraction of the images (DSA).

c- Applying the MEDCOL program for processing the subtracted images.

d- Modifying the final set using Hilbert space techniques .

Details of the different phases are explained as follows.

a. Smoothing and the sampling problem [9]:

A signal S(t) sampled ideally [10] at a frequency f = 1/T may be represented as a sequence of Dirac impluses as follows:

$$S_d(t) = S(t) \sum_{-\infty}^{\infty} \delta(t-nt) = \sum_{-\infty}^{\infty} S(nT).\,\delta(t-nT);\quad \delta(t) = \begin{cases} 1 & \text{for } t=0 \\ 0 & \text{elsewhere} \end{cases}$$

rewritten;

$$S_d(t) = S(t).\,\frac{1}{T}\,\text{Ш}(t/T);\quad \text{Ш}(t) = \sum_{-\infty}^{\infty} \delta(t-n)$$

Considering the Fourier transformation, the spectrum $S_d(f)$ will be given by :

$$S_d(f) = S(f) * \text{Ш}(Tf) = \frac{1}{T} \sum_{-\infty}^{\infty} S\left(f - \frac{n}{T}\right),$$

where * stands for convolution $\left((g(t) * h(t) = \int_{-\infty}^{\infty} g(\tau)\, h(t-\tau)\, d\tau\right)$

An errorfree reconstruction of such a signal requires an LP-Filter of the transfer function $H(f) = T.\,\text{rect}(f/2f_g);\ T \leqslant 1/2.f_g$ The errorfree reconstructed signal S(t) according to lüke [9] can be represented as a sequence of nT-shifted si-functions, Fig. (1):

$$S(t) = \sum_{-\infty}^{\infty} S(nT).\,\text{si}\left(\pi \frac{t-nT}{T}\right);\quad \text{si}(t) = \sin(t)/t.$$

The same equation may be applied for space sampling replacing T by D, t by d, where D distance between pixels.

In fact, we have a definite short scan time T_{sp} ($\simeq$ 80ms) and the signal would be better represented as a series of pulses.

$$S_p(t) = S(t).\,\sum_{0}^{M} \text{rect}(t-nT_e/T_{sp});\quad \text{rect}(t) = \begin{cases} 1 & \text{for } |t| \leqslant 1/2 \\ 0 & \text{elsewhere} \end{cases}$$

The sampling frequency does not fullfil the Nyquist rate and the reconstructed signal will be noisy because of overlapping, that is each pixel affecting its surroundings in time and space. Considering the shape of the si-function, and noting that an exact response function is not available, approximate smoothing schemes may be adopted

[11] to improve clarity of an image as well as continuity of the time density curves. The 9 points smoothing was found suitable where the value of each pixel is replaced by the average of the weighted values of the pixel itself and its 8 adjacent pixels according to the following weighting matrix, $\begin{bmatrix} 1 & 2 & 1 \\ 2 & 4 & 2 \\ 1 & 2 & 1 \end{bmatrix}$, which may be applied several times.

b. Logarithmic Subtraction (The main DSA procedure):

The images of the DSA sequence, made after the arrival of the contrast medium, have to be logarithmically subtracted from a pre-contrast image "the mask". This operation will vastly improve the conspiciuty of the blood vessels, where the background anatomy is removed.

The attenuation of X-ray in a given medium can be described by the equation:

$$I = I_0 \exp. (- \mu ET)$$

Where I_0 is the initial intensity T the thickness, E the radiation energy, μ the attenuation coefficient and I the resulting intensity (Note: $E \propto \rho$ the iodine concentration).

At a given location (x, y), the construction of the DSA images may be illustrated mathematically in the following steps.

1. Determine the "mask" image:

$$M (x,y) = I_0 (x,y). \exp. (-\mu \rho_1 T_1)$$

2. For each image after arrival of contrast medium :

$$I (x,y) = M (x,y) \exp. (- \mu \rho_2 T_2)$$

3. Taking the logarithmic difference:

$$D\,(x,y) \doteq K\,[\ln \mathcal{M}(x,y) - \ln \mathcal{I}\,(x,y)]$$

$$= K \mu\, \rho_2\, T_2\,(x,y)$$

This indicates that D(x,y), referred to as the logarithmic difference image, is directly proportional to the iodine concentration ρ_2 and the thickness T_2 of the tissue at location (x,y). The above procedure is performed utilizing a bluit-in program [11].

C. The MEDCOL Language and the program "Renal perfusion":

The timed series of subtracted images may be then processed by our program "Renal Perfusion" on a pixel-by-pixel basis. Taking an individual pixel position, a time-concentration curve is constructed that reflects the temporal passage of contrast material through the tissue represented by that pixel. A region of interest (ROI) consists then of a defined number of pixels.

The program "Renal Perfusion" is written in MEDCOL language, a powerful high level language which is essentially a control language used for the specification of the so-called clinical procedures. The language offers also facilities normally found only in algorithmic languages such as flow control and subroutine statements, variables and records. FORTRAN subroutines can be used for example to define regions of interest where the ROI attribute RA(X,Y) will be assigned the value "1" if the pixel belongs to the ROI, otherwise "0". The program utilizes also the facility of color-coding, that is a look-up table mapping the entire grey scale into a spectrum scale of 16 color degrees. Other procedures such as smoothing and contrast enhancement are utilized to reduce the noise, hence offering better image quality for further processing.

The steps of the program are illustrated in the flow chart of fig(2). The actions of the program are summarized below:

1- Declare and initiate the variables : (real, integer, time or key).

2- Choose an image for processing: (Resolution: 256 x 256, color-coding, smoothing and contrast enhancement).

3- Draw the ROI'S on the image : (Two similar anatomic regions are defined on both left and right kidneys-also an appropriate background ROI is chosen inbetween).

4- Generate the bolus curves : (After subtracting the background, the time-density curves for both kidneys are constructed and smoothed)

5- Calculate the descriptive parameters: (From each curve, 3 parameters are obtained : the peak density and the times taken to reach the peak value and the 1st half peak value. Ratios of the values for both kidneys are done).

6- Approximate the curves and calculate modified results : (A 6th degree polynomiol was used to fit the curves. It can be actually derived out of the known gamma-fit for the bolus curves : Density = K. $(t-t_0)^A \exp [B\ (t-t_0)\ ]$)

D. A note to step 6 : The approximation problem in Hilbert space [12] :

Let V be a Hilbert space with the scalar product (f, g) and the norm $p(f)\ \underline{\mathrm{def}}\ \| f \| = \sqrt{f,f}$, whose lements f(x), g(x),... are functions, defined on the common interval I. Further, let $f(x) \in V$ be a fixed element and $G_n \subseteq V$ be an n-dimensional subspace (same norm).

The general approximation problem AP $(f, G_n, \| \|)$ will be : Search a function $\hat{g}(x) \in G_n$, such that :

$$D\ (f;g,p\ (f))\ \underline{\mathrm{def}}\ \inf_{g \in G} [p(f-g)] = p(f-\hat{g})$$

$\hat{g}(x)$ will be called a best approximation and the number D called defect. In Hilbert spaces [12]. There exists a unique solution $\hat{g}$, for which $(\hat{g}-f, h_i) = 0$ for all $= h_i \in G_n$ where

$$\hat{g}(x) = \sum_{K=1}^{n} C_k^{(n)} \quad h_k\ (x)$$

A special case is when $V=L_2(a,b)$, the lattice of all possible combinations of the functions $y=f(x)$, defined in the interval $[a,b]$ and $G_{n+1} = P_n$, the set of all nth degree polynomials.

In our case, however, using the diskrete Tschebyscheff-norm $\|f\|_T^N = \max_{x_i} |f(x_i)|$ and choosing N points on the curve such that $N=n+1$, the AP $(f, G_{n+1}, \| \|_T^N)$ will turn into an Interpolation problem. We have adopted the Newtonion interpolation form for all calculations [12], according to the following iteration :

$$I_n(x) = \sum_{j=0}^{5} C_j \, N_j(x),$$

$$N_0(x) = 1; \; N_j(x) = (x-x_0)(x-x_1)\dots(x-x_{j-1}); \; j=1,2,\dots 5,$$

$$C_j = [x_0 \, x_1 \dots x_5].$$

RESULTS:

The program was applied for 38 individuals, 28 females and 10 males. aged from 18 to 50 years with mean age 29 years, who underwent DSA as part of their work up, having normal renal function as assessed by clinical and biochemical criteria. 5 cases were excluded because of insufficient no. of images and bad motion artefacts.

The time density curves obtained proved to possess a consistent pattern and the 6th degree polynomial-fit was justified with a correlation coefficient $r > 0.955$ for all cases, that is :

$$\text{Density} = \sum_{i=0}^{6} K_i (t-t_0)^i .$$

Although in most cases K_1, K_2 and K_3 were the most effective constants, a 5th degree polynomoil-fit resulted in correlation coefficients $r<0.9$ for some cases.

Figure 3 represents an illustrative example for the main DSA procedure, i.e. logarithmic subtraction, together with ROI definition.

Figures 4 and 5 illustrate representative cases for the screen display of the final results before and after approximations. Table 1,2 and 3 show the distribution of the values of maximum density, T-maximum and T-half-maximum in the different kidneys for the 33 cases which underwent the study. Table 4 illustrates the distribution according to the right to left kidney ratios of maximum perfusion.

Table (1) : Distribution of the maximum density in 33 individuals

Maximum density value	No. of cases before fitting Rt. Kid	Lt.Kid	No. of cases after fitting Rt.Kid	Lt.Kid
15-25	2	1	1	1
26-35	5	4	5	4
36-45	3	6	4	5
46-55	10	7	9	8
56-65	7	10	8	10
66-75	2	3	3	3
76-85	4	2	3	2
Total	33	33	33	33

Table 2 : Distribution of the T-Maximum values in the 33 cases

T-maximum value (seconds)	No of cases before fitting Rt.kid	Lt. kid	No of cases after fitting Rt. kid	Lt.kid
3.5-5.5	6	10	5	8
5.6-7.5	16	14	19	17
7.6-9.5	11	9	9	8

Table (3) : The T-half-maximum values in the 33 cases

T-half maximum (seconds)	No. of cases (before fitting)		No. of cases (after fitting)	
	Rt. kid	Lt. kid	Rt. kid	Lt. kid
2.0-3.0	4	5	3	4
3.0-4.0	18	21	18	20
4.0-5.0	11	7	12	9

Table (4) : The disribution of the ratio for maximum density (R/L)

Rt/ Lt. kidney ratio	No of cases (before fitting)	No. of cases (after fitting)
1.3	1	0
1.2	6	5
1.1	5	6
1.0	13	15
0.9	6	6
0.8	2	1

Statistical analysis

The Kruskal-Wallis test, a non-parameteric test for comparing two groups, was applied to measure the significance of the difference between the values obtained before and after fitting for each measurable parameter. No significant difference was detected for all variables ($P > .1$) . The χ^2-test was more appropriate for ratios. Again, there was no siginificant difference ($p > .2$). The Microstat program was used on an IBM 386-AT compatible machine. Fig. 6 represents a Bar diagram for table 4 using the harvard graphs (HG3) for the same computer.

DISCUSSION:

Digital radiography may be regarded as an imaging procedure with the potential of providing both useful function information and good anatomical resolution in the same time [13]. To utilize those data diagnostically; normal ranges may be first established.

Image processing techniques provide us with the ability to select regions of interest for the generation of iodine time-density curves, Fig(3-5). These curves form the basic part of the study, from which the different variables and parameters could be obtained to evaluate the renal perfusion. Pavlick et al. [14] concluded that these techniques are sufficiently accurate for the use of time-density curves as a relative mearsure for organ function. Hunter et al. [6] and Kuni [15] presented a simple method using modest computer facilities, for obtaining certain parameters out of the DSA series of images .

In this work we try to simplify the techniques of functional angiographic imaging of the kidneys, construct the time-density curves, extract relevent parameters from them and display all as a set of readily interpretable data, Figs (4,5).

Among many variables, we found that the three parameters: Maximum density, (Table 1) time-to-maximum (Table 2) and the half-life-time (Table 3) are easily and widely clinically applicable. In our work, the three parameters appear to fall within well defined and reproducible limits. The maximum density value was found to be 30 to 65 in 76% of normal individuals, while the T-maximum value was from 5 to 8 secs in 82% and the T-half maximum values lie between 2.5 to 4.5 secs in 85% of the cases. These normal values were partly in agreement with the figures obtained by Hunter [7], whereas we suggested a new parameter which is the ratio between both kidneys for each measurable parameter and it was found to be from 0.8 to 1.2.

Our results can be of good diagnostic value in detecting abnormalities of the renovascular structure. The T-half-maximum values and the T-maximum values are indications for the blood flow in the faster and slower pathways, respectively. The ratios can help in easy detection of any abnormal imairment of renal perfusion and at which side, however the assessment of its value needs further study.

The curves seem to follow a certain relation (probably exponential) but this has to be examined in view of other variables [16] such as the cardiac output and the central blood volume, which is beyond the scope of this study. The effect of parameters like weight, age and heart rate of the patients can be investigated following restricted medical protocols, which are now in preparation.

Finally, we have to notice that our results like most of the medical figures are in fact a trial to describe some vague process, e.g. the kidney function, whereas a lot of factors and implications may affect our aims. A relatively new approach developed by Zedeh [17] for modeling human-centered system and linguistic descriptions under the radical name " Fuzzy Set Theoy" may be suitable to deal with medical data and medical diagnosis (decision making) in general [18]. In brief, We can describe a kidney according to our results as being excellent, very good and good. These linguistic descriptions, which are usually summary descriptions of complex situations, are fuzzy in essence and can be dealt using a multivalent logic, "the Fuzzy Logic" [17, 18].

CONCLUSIONS :

A structured algorithm for analysing and manipulating functional images on a pixel-by-pixel basis is developed.

1- This algorithm offers numerous advantages in the area of studying the urinary tract, where it has the potential to assess the renal function and anatomy as well as the vascular integrity and flow in a single study with minimal invasive nature.

2- The results for the relevant parameters obtained from the proposed algorithm were found to lie within well-defined ranges, and hence may be of remarkable diagnostic value in detecting abnormalities of the renovascular structure as well as impairements in renal function.

3- The procedures may be modified through more restricted protocols to investigate the influence of certain variables on the proposed parameters.

4- Medical data suffer, in general from vague inferences and complex implications. A fuzzy approach to deal with the data, evaluate them and even introduce them into medical knowledge, may be more appropriate and can be a proposal for a future work.

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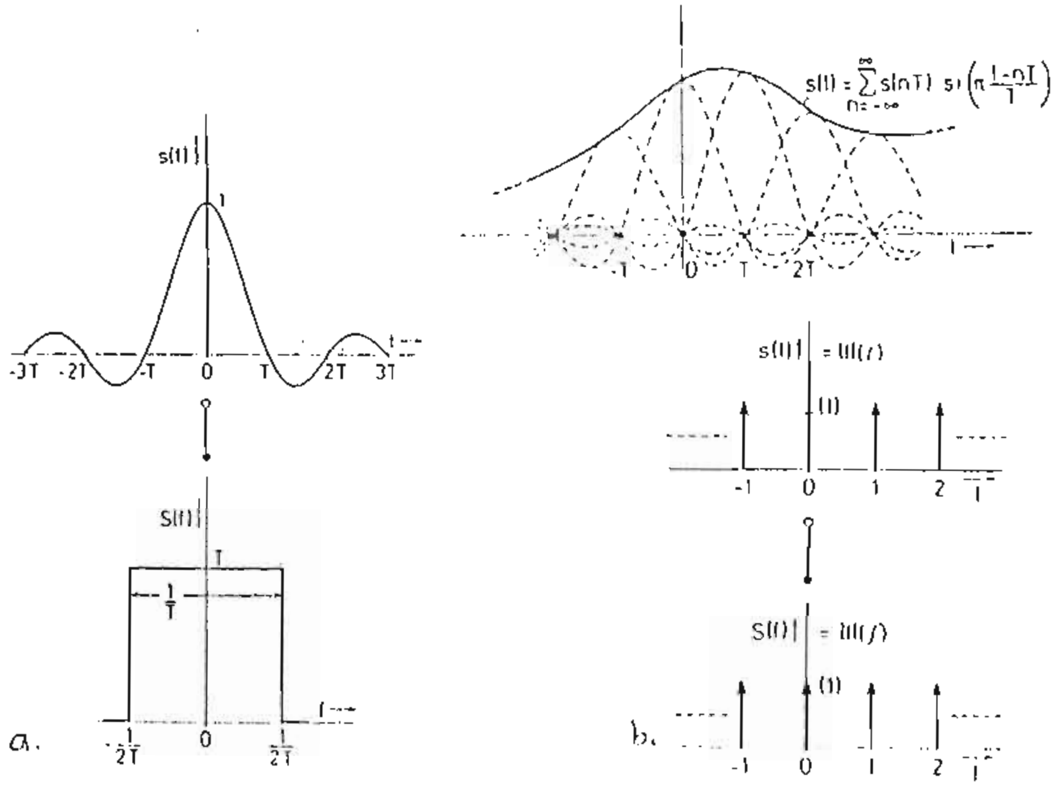


Fig 1.: The signal s(t) as the sum of nT-shifted si-functions.
a. The si-function and its transform b. the ꟺ function and its transform.

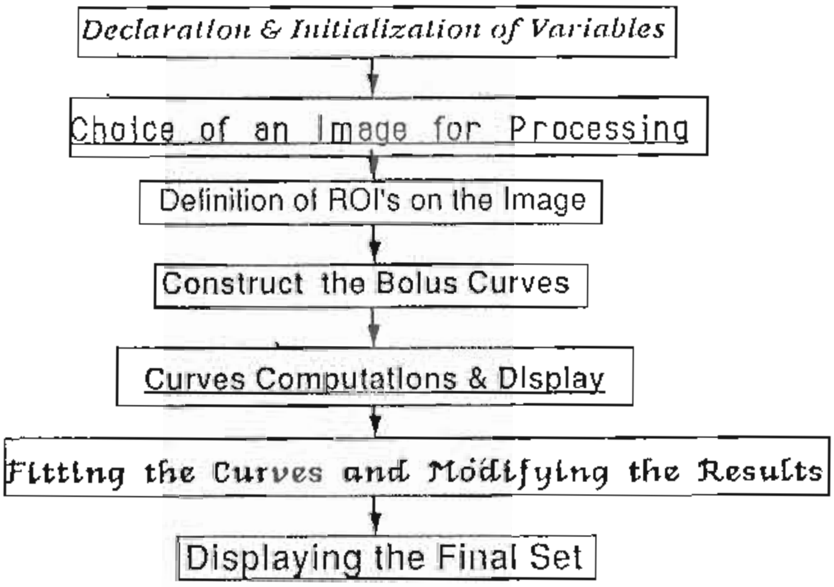
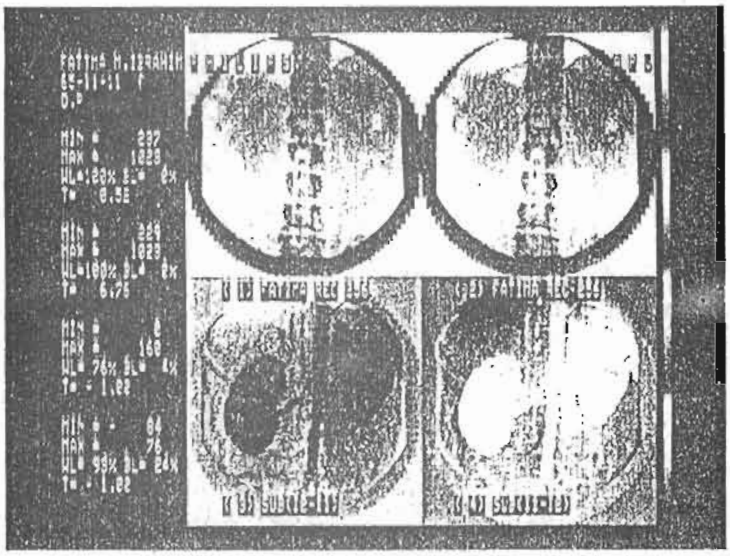
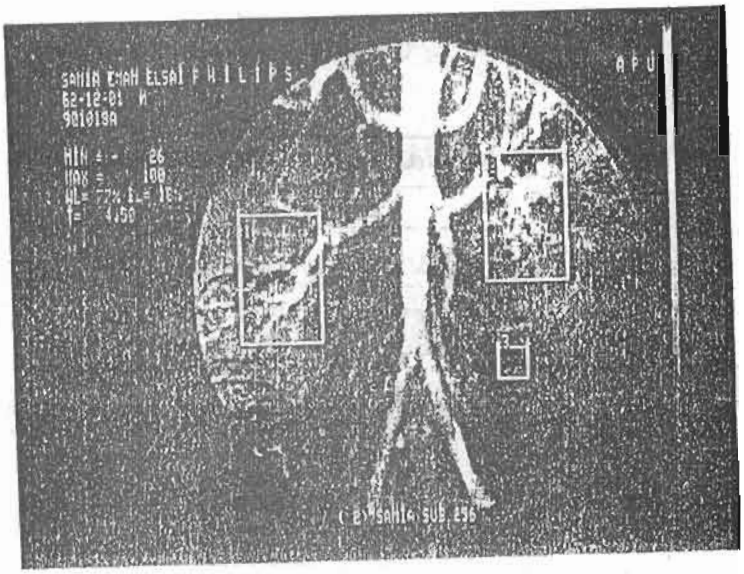


Fig. 2.: Flow chart for the main procedures of the "Renal Perfusion" program.

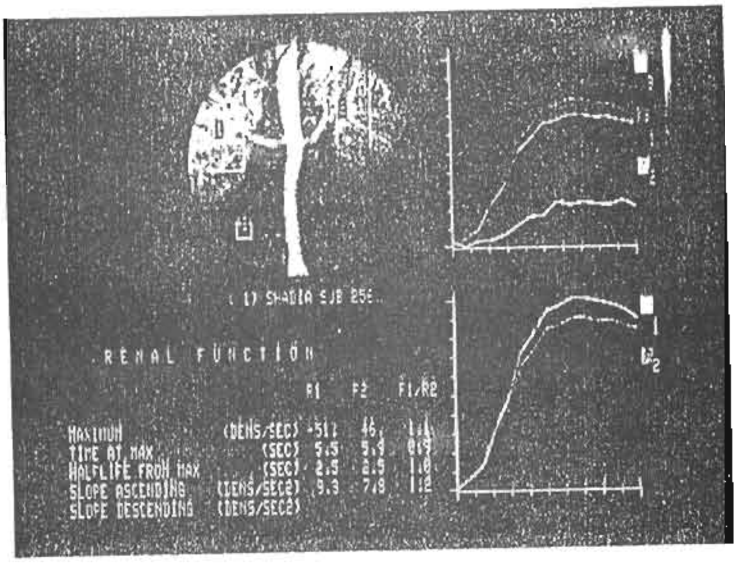


a) vascular imaging 3,4 are the subtracted and negative subtracted images of 1,2



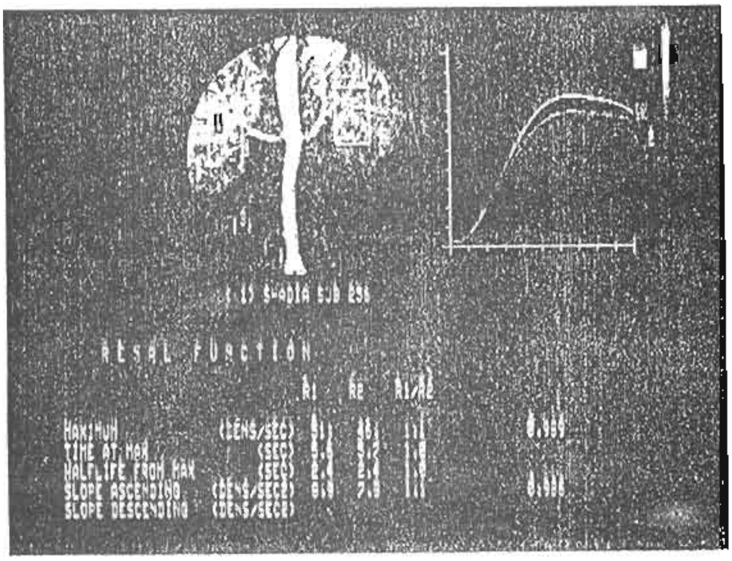
b) Defining regions of interest.

Fig. 3: Logarithmic subtraction (the main procedure of DSA)



		R1	F2	F1/R2
MAXIMUM	(DENS/SEC)	51	46	1.1
TIME AT MAX	(SEC)	5.5	5.9	0.9
HALFLIFE FROM MAX	(SEC)	2.5	2.5	1.0
SLOPE ASCENDING	(DENS/SEC2)	9.3	7.8	1.2
SLOPE DESCENDING	(DENS/SEC2)			

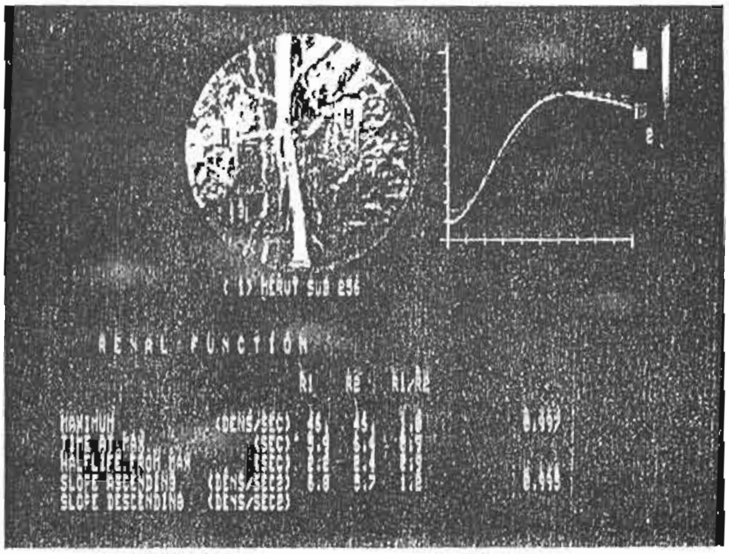
a) before,



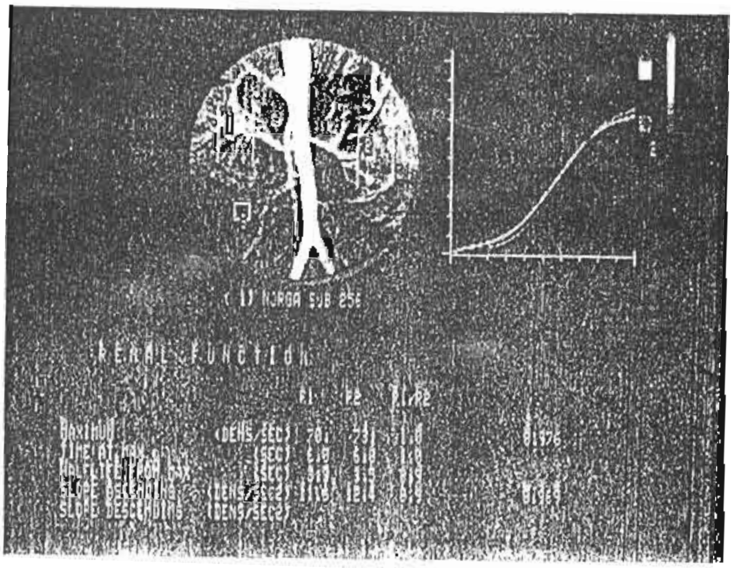
		R1	R2	R1/R2	
MAXIMUM	(DENS/SEC)	51	46	1.1	0.999
TIME AT MAX	(SEC)	[illegible]	[illegible]	[illegible]	
HALFLIFE FROM MAX	(SEC)	2.4	2.4	[illegible]	
SLOPE ASCENDING	(DENS/SEC2)	[illegible]	7.8	[illegible]	[illegible]
SLOPE DESCENDING	(DENS/SEC2)				

b) after modifying.

Fig. 4: The time-density relations for a 32 years old female

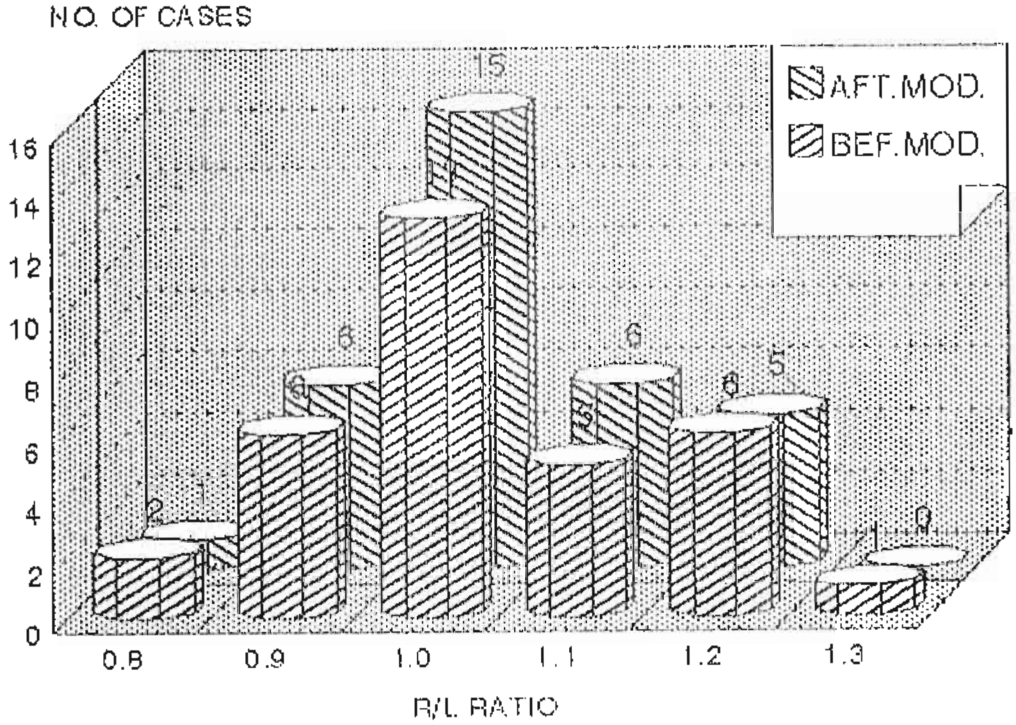


a) 22 years old,



b) 30 years old.

Fig. 5: Normal kidney perfusion for two females(after modifying)



DISTRIBUTION FOR THE RATIO OF MAXIMUM DENSITY (R/L)
BEFORE AND AFTER MODIFICATION

CHI-SQ=1.656, D.F.=5, P=.8 > .2(NON SIG)

Fig. 6: A Harvard graph-Bar diagram representation for table (4).