DESCRIPTION OF A COMPUTER PROGRAM FOR THE DETERMINATION OF REGIONAL CEREBRAL BLOOD FLOW

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SUMMARY

The regional cerebral blood flow in man was measured, following a short injection of 133 *Xenon into the internal carotid, by processing the hemispheric clearance curves detected with an Anger gamma-camera.*

An automatic calculation program is described which permits the estimation of the two compartmental blood flows.

The merits of this procedure are discussed.

SOMMAIRE

Il est possible de mesurer chez l'homme le débit sanguin cérébral régional. Cette exploration peut se faire en injectant dans la carotide interne un embol de 133 *Xenon et en enregistrant la courbe de clearance hemispherique à l'aide d'une caméra de Anger.*

Cet article décrit un programme qui donne une estimation de deux débits compartimentaux.

Les avantages de cette méthode sont discutès.

INTRODUCTION

Measurement of the blood flow of organs with an elective arterial pedicle—and particularly of the brain—may be carried out by injecting a bolus of a radioactive inert gas into the artery which perfuses the organ. Detection of the gas desaturation

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in the tissue under study permits a multi-regional evaluation of the perfusion (Lassen and Ingvar, 1961).

The multiplicity of the curves to be analysed and the inaccuracy of the graphical analysis methods warrant the devising of a data acquisition and processing program. The latter, in a laboratory for medical applications of radio-elements, with as conventional an equipment as possible, should allow us to be free from graphical methods, and thus to achieve a double aim: more rapid and more accurate data processing.

MATERIAL

Figure 1 is a diagram of the unit used; it includes the acquisition, storage, processing and display equipment.

The data acquisition equipment is an Anger scintillation camera, with a 30·5 cm NaI crystal fitted with a 4500 hole collimator (Nuclear Enterprises, NB 8250) coupled to the Tridac-Multi 8 unit (Intertechnique).

The actual data processing is carried out with this Intertechnique unit, which includes a Tridac analyser with a 4096 channel memory and a Multi 8 minicomputer with a 12 K memory bank.

Storage is done on an 800 bpi, 24 ips Ampex magnetic tape, connected to the Tridac. It can record data supplied by the scintillation camera at a maximum frequency of four images a second.

Lastly, the input–output devices are a Teletype ASR33 printer (connected to the Multi 8), an oscilloscope display (linked to the Tridac memory) and a light pen (connected to the Tridac).

METHOD

An internal carotid of the patient, who is lying in dorsal decubitus, is catheterised by cervical transcutaneous approach, after a non-vasoconstrictive local anaesthesia. Five mCi of 133 Xenon, dissolved in 1 ml of physiological liquid, are injected as quickly as possible. A profile recording of the radioactivity of the corresponding cerebral hemisphere is made, second by second, during 16 min.

Owing to the speed of the injection, to the inert and diffusible nature of the gas and to its very low recirculation through pulmonary elimination, the global or regional curves of hemispheric activity have a decreasing aspect and their slope accounts for the desaturation of cerebral tissue following the rapid invasion.

Should the flow remain constant throughout the experiment, where the injection would be instantaneous, the tracer would not recirculate but remain inert and very speedily diffuse in all the tissue, and where, finally, the blood volume would be small

in relation to the tissular volume, the analysis of the curves could be made according to the compartment method (Lassen and Ingvar, 1961); the desaturation of each tissular compartment of this pattern has a decreasing mono-exponential aspect.

$$R_t = R_0 \exp(-Kt)$$

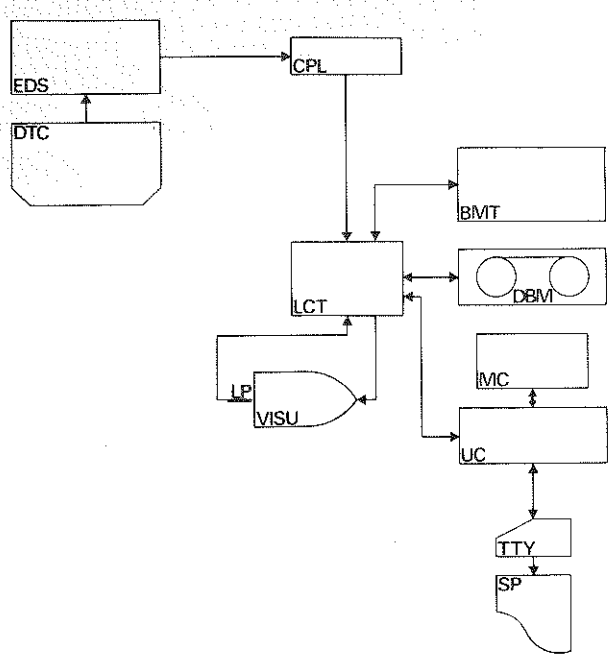

Fig. 1. General description of the device.

Legend: DTC Detector.
EDS Spectrometer.
CPL Converter.
LCT Tridac Control Logic.
LP Light Pen.
BMT Tridac Memory Module.
DBM Magnetic Tape Handler.
MC Multi 8 Central Memory
UC Multi 8 Central Unit.
TTY As R 33 Teletype.
SP Punched Tape.
VISU Visualisation (4096 channels—matrix).

R_t being the activity recorded as a function of time t, R_0 the initial activity; K enables us to calculate the blood flow d per unit of tissue weight according to the equation:

$$d = \lambda K$$

λ being the partition coefficient of the gas between the blood and the tissue under study.

It can be accepted that, with regard to the xenon gas, the cerebral tissue is similar to the above-described pattern. Indeed, the experimental desaturation curves obtained by gamma-ray counting on the scalp, after a rapid injection of 133 Xenon in the internal carotid artery, may generally be analysed in two mono-exponential components to which two slope coefficients K_1 (rapid) and K_2 (slow) correspond.

$$R_t = R_{0_1} \exp(-K_1 t) + R_{0_2} \exp(-K_2 t) \tag{1}$$

It is possible to calculate two corresponding flow values, expressed in millilitre per minute and per 100 g tissue weight:

$$d_1 = 100\lambda_1 K_1 \qquad d_2 = 100\lambda_2 K_2 \tag{2}$$

Several arguments induce one to think that cerebral compartment 1, rapidly desaturated, is the cerebral cortex, and that compartment 2, where desaturation is slower, is the white substance (Lazorthes, 1967).

The partition coefficients corresponding to both tissues have been evaluated for xenon (Veall and Mallett, 1965); for a normal value of blood hematocrit, the values generally utilised are $\lambda_1 = 0{\cdot}8$ and $\lambda_2 = 1{\cdot}5$.

The apparent mean flow of the system can also be calculated with the following weighted average:

$$d = 100 \frac{R_{1_0} + R_{2_0}}{\dfrac{R_{1_0}}{\lambda_1 K_1} + \dfrac{R_{2_0}}{\lambda_2 K_2}} \tag{3}$$

A mean flow value can also be calculated by the following equation, evolved from the stochastic analysis of the same desaturation curve:

$$d_s = \frac{100\lambda R_0}{\displaystyle\int_0^{\infty} R_t \, \mathrm{d}t} \tag{4}$$

d_s being the so-called stochastic flow, in millilitres per minute and per 100 g of tissue, R_0 the amplitude of the curve peak, and λ the mean distribution coefficient of xenon between the blood and the cerebral tissue.

The classical formulae (eqns. (1), (2), (3) and (4)) are the basis of the algorithm described below.

DATA PROCESSING PROGRAM

Data processing for determination of the regional cerebral blood flow is carried out off-line from the impulses recorded on the magnetic tape. An immediate data analysis, which would prove ideal for eventually controlling the measurements during the experiment, would not enable one to calculate the compartmental flows, since recording of an adequate segment of the slow exponential must, in this case,

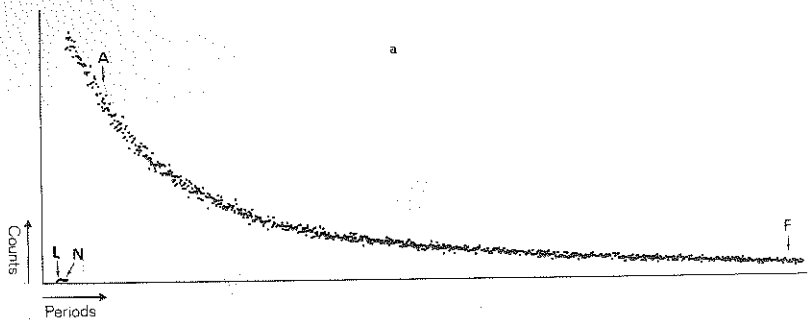

Fig. 2(a)

Fig. 2. Visual interactive data processing of results. (a) Raw data (selection of points A, F, L, N). (b) Smooth data (selection of points B, C, D, E). (c) Final adjustment.

precede any data processing. In our experimental records, the analysis of the initial flow index, for the study of rapid variations in cerebral flow, always remains possible.

The distribution of the global carotid flow in the various hemispheric zones is visualised by the cumulative image of the first ten seconds. Xenon scintigraphy enables one to visualise a possible disturbance in regional distribution and to outline the cerebral topometry. The zones of interest are selected on this image by a light pen or by indexes.

The regional activity curves are displayed on the oscilloscope by magnetic tape reading (Fig. 2). They include three main sections:

1. the noise, recorded prior to injection;
2. the injection peak, the profile of which is a function of the shape of the radioactive bolus at the input of the detection area (input function) and of its dynamics through this field (transfer function).
3. the actual bi-exponential decrementation which is linked to the transfer function only.

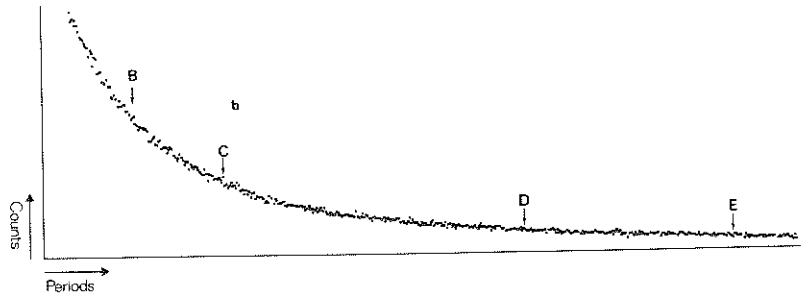

Fig. 2(b)

The Teletype keyboard then allows the initiation of the program and the inscription of administrative and clinical comments.

Each curve is analysed (Fig. 2) through the selection by the light pen of four points outlining the noise (points L and N) and the bi-exponential (points A and F), the noise thus being determined separately before each injection, if the latter is to be repeated. This manual selection enables the operator to control the duration of the analysis and the choice of the initial point, A. The possibility of several choices is a great advantage for the visual observation of anomalies in the initial peak. The influence of a non-instantaneous input function of the radioactive tracer in the detection field can thus be obviated by discarding in the analysis the very first points of the injection peak (Depresseux, 1972).

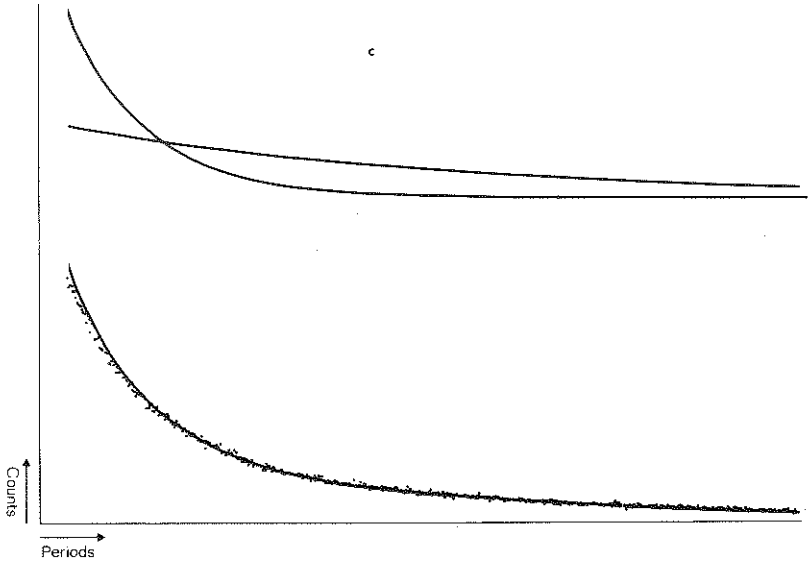

Fig. 2(c)

The device then calculates the mean noise and, after subtracting it, smooths the useful curve, according to a five weighted point formula.

The physical and biological measurement parameters are then fed to the keyboard: integration time of each point and partition coefficients of the gas utilised in the two cerebral compartments.

A manual selection is made of the two zones of the curve: segment BC, in which the fast exponential is preponderant, and the DE segment, where the slow exponential is

almost pure. This division can be facilitated by the optional display of the curve in semi-logarithmic co-ordinates. We thought that the manual selection of both exponentials would be more simple and more reliable. The application of automatic methods of exponential recognition, of a more sophisticated concept, may prove hazardous in view of the dispersion of the experimental points on either side of the perfect theoretical curve. On the other hand, the operator can detect the existence of physiological artefacts likely to distort a segment of the experimental curve and to involve errors due to a too automated processing.

The following stage is entirely automatic: the exponential decremental curves of the two selected segments are calculated by approximation according to the least squares analysis. The iterative algorithm described hereafter analyses the two compartments of eqn. (1), which can be written as:

$$R_1 = f_1 + f_2$$

with a function f_1 preponderant over the $\overline{BC}$ segment of the curve and an f_2 function almost pure in the $\overline{DE}$ segment.

The functional organigramme evolves according to the following scales:

1. Calculation of the parameters of f_1, according to the values of segment $\overline{BC}$ reduced to the corresponding values of f_2, presumed to be null on first iteration, and memorised for future iterations.
2. Display of the evaluated f_1 exponential.
3. Calculation of the parameters of f_2, according to the values of segment $\overline{DE}$, less the corresponding values of f_1, calculated from scale 1.
4. Display of f_2.
5. Display of the function $R_t = f_1 + f_2$ calculated in this way.
6. Calculation of the mean standard deviation between the calculated and the experimental curves.
7. Editing of the parameters of f_1 and of f_2.
8. Return to 1, unless ordered otherwise by operator.

The fast and slow exponentials are thus displayed on the oscilloscope in cartesian co-ordinates, with their sum which may be visually compared with the experimental curve (Fig. 2). The printer simultaneously edits the values of the slope coefficients, the corresponding compartmental flows and the mean standard deviation which best characterises the degree of approximation of the calculation.

The device affords two criteria for evaluating the degree of approximation of the analysis at the end of each iteration: the printing of the mean standard deviation and the display of the calculated curve. When the adjustment is adequate, the operator interrupts the processing and the system edits the following results: the coefficients of exponential slope (K_1, K_2) in sec^{-1}, the respective initial activities for the two compartments (R_{0_1}, R_{0_2}) in impulsions/sec, the values of the compartmental flows (d_1, d_2), of the apparent mean flow (d) and of the approximative global flow by the stochastic method (d_s) in ml/100 g/min (Fig. 3).

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* ETUDE ISOTOPIQUE DU DEPIT SANGUIN CEREBRAL *
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DATE : 25.01.73

NOM : DUPONT                    NE  LE : 10.08.25

PRENOM : JEAN

NUM. DOSSIER : 73 - 02

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INDIC. : 133XE              MCI : 2          CAROT. INT. : GAUCHE

POINTS L,N,A,F.               DT.(SEC.) : 1

INCIDENCE : PROFIL GAUCHE

REGION : S7.28/14.14

A1 : 0,8          A2 : 1,5          A : 1              ML./G.

ACTIV. INIT. : 1554,0          IMP./SEC.       SUR 360,00    CANAUX.

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ITERATION  1


POINTS B,C,D,E.=>  B: 10,00   C: 120,0   D: 340,0   E: 910,0  SEC.


K1  : 0,0067    K2  : 0,0009     /SEC.

RO1 : 1541,0    RO2 : 187,20     IMP./SEC.

D1  : 32,330    D2  : 8,4960     D   : 24,800    ML./100G.MIN.

S : 427100    IMPULSIONS        DS  : 24,280    ML./100G.MIN.


R.M.S. : 75,150    IMP./SEC.

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ITERATION  2                                    ML./100G.MIN.

                                 DS  : 27,670    ML./100G.MIN.

K1  : 0,00

                    IMP./SEC.

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ITERATION  6


K1  : 0,0098    K2  : 0,0019     /SEC.

RO1 : 1134,0    RO2 : 446,70     IMP./SEC.

D1  : 47,370    D2  : 17,650     D   : 32,100    ML./100G.MIN.

S : 342600    IMPULSIONS        DS  : 27,680    ML./100G.MIN.


R.M.S. : 13,130    IMP./SEC.
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Fig. 3. Teletype edition of the results of successive iterations.

CONCLUSION

The automated processing of the hemispheric clearance curves of 133 Xenon for the determination of regional cerebral blood flow affords many advantages for the medical utiliser.

This processing method proves to be superior to the semi-logarithmic transcription and linear extrapolation techniques. In point of fact, at the data display stage, these techniques require a tedious and approximative retranscription of the curves in semi-logarithmic co-ordinates. Although the automatic semi-logarithmic transcription is very useful for estimating the general morphology of the curves, it is very aleatory as a step in the quantitative processing; semi-logarithmic amplifiers entail a certain degree of error, especially if the transformation takes place over several decades.

In the computing stage, the processing program we have described avoids an error which may have a double origin: the inaccuracy of the operator's judgement with regard to the asymptotic adjusting of the slow exponential and the postulate of all the graphic methods, which consider as negligible the interference of the fast exponential in the terminal part of the curve.

Finally, automation in no way hinders the operator's freedom, and he can either modify the processing in each stage or modify the parameters. A particularly attractive feature of the method we have described lies in the fact that it can operate with the devices usually found in the equipment of a hospital unit of nuclear medicine.

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