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REVIEW

THE POSITRON EMISSION TOMOGRAPHY AND ITS APPLICATIONS

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Abstract

Emission reconstruction tomography is a branch of nuclear technology that advanced tremendously during the last five years. This progress is the result of the efforts for building more powerful detection machines in nuclear medicine, of the spreading of cyclotron research centers and of the increasing interest in the synthesis of radiopharmaceuticals.

The paper reviews the basic principles of positron emission reconstruction tomography. The detection requirements are detailed on the basis of applicability of the projection equation and the unique advantages of the positron emitters are emphasized. Among the mathematical methods that may be potentially used for the image reconstruction, the technique of linear superposition of filtered backprojections is specifically described. The design of the tomographs that are presently in biomedical use and the configuration of the prototypes under study are briefly outlined.

Some actual or desirable performances of the emission tomographs are discussed, such as spatial resolution, counting capabilities and time of examination.

An overlook on the applications of positron emission tomography illustrates the fact that this technique opens nuclear medicine to up-to-now inaccessible investigations of physiological processes, metabolic pathways and pharmacodynamical problems.

Key-words : Radionuclide imaging — Computerized axial tomography — Isotope labeling.

Introduction

The introduction of X-ray transmission reconstruction tomography (33, 1, 45, 47) yields considerable progress in diagnostic radiology. In a parallel way, radionuclide emission reconstruction tomography, more recently developed, makes possible an actual quantitative in vivo "autoradiography" and opens nuclear medicine to advances in the field of the non-invasive evaluation of many physiological and metabolic processes, on a high-precision quantitative and high-resolution regional basis.

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Although the idea of tomography in nuclear medicine is almost fifteen years old (37), the elaboration of quantitative methods and the implementation of their clinical applications is far more recent and is the result of the convergent progress of three branches of the radiation sciences :

1) the realization of *emission reconstruction tomographs,* depending especially on the availability of high-performance coincidence detection units, on the elaboration of appropriate reconstruction algorithms and on the development of minicomputers;

2) the spreading of research centers with *cyclotrons* designed for the production of short-lived positron emitting radionuclides (32);

3) the increased interest in the *synthesis of radiopharmaceuticals* suitable for the tracer study of physiological processes, metabolic pathways and pharmacodynamical problems (66).

The increasing availability of short-lived positron-emitting radionuclides, noteworthy of radioisotopes of the principal elements of the biosphere (^{15}O, ^{13}N and ^{11}C) offers new possibilities for the regional, in vivo, investigation, not only of many physiological functions (regional blood flow, blood volume, oxygen consumption, exchangeable water, blood brain barrier permeability, etc.), but also of metabolic pathways (glucose consumption, amino acids and fatty acids diffusion and incorporation, nucleic acid metabolism, etc.), hormone and transmitter dynamics (catecholamine distribution and metabolism etc.), and of pharmacodynamics. The possibilities to incorporate positron emitting radionuclides in a great variety of radiopharmaceuticals and metabolites widens the field of development of these studies.

The elaboration of new modalities for radiation detection and the design of high performance detectors, is an important factor of progress in this field. The purpose of the present paper is to review some basic principles of positron tomography and to facilitate the approach of this recent field of technological research in nuclear medicine.

Objectives and background of the emission tomography

The major goal of radionuclide detection in nuclear medicine is the 3-dimensional spatial and temporal quantitative description of the distribution of the isotope.

The conventional detection devices—rectilinear scanners, gammacameras and uni- or multiprobes systems—, based on single photon detection (SPD) and absorbing collimators, have permitted major progress in morphological and functional studies, but they have three drawbacks :

1) The SPD with absorbing collimators entails a low, depth-dependent spatial resolution, with unfavourable resolution/sensitivity ratios and with difficult-to-control attenuation factors and scatter contributes in the countings.
2) The SPD conventional imaging systems yield 2-dimensional images in which the 3-dimensional distribution of the radionuclide is telescoped. Even in the case of dynamic studies performed with uni- or multiprobes systems, the precise geometry of detection remains an open question.
3) The quantitative aspect of the radionuclide distribution is completely overlooked in the volume of the object and all possible quantitative treatment of the data is restricted to a parametric analysis, in terms of space, in the so-called quantitative scintigraphy, or as a function of time.

The objective of tomography is the quantitative, high-resolution and high-sensitivity evaluation of the 3-dimensional distribution of radionuclides in the body, on a microCi $\times$ cm^{-3} of tissue basis.

The concept of tomography was introduced in nuclear medicine as early as 1963 (66). Advances in the field of morphology followed the introduction of *focal-plane tomography* techniques, that are based on SPD and whose principle is to blur the visibility of the out-of-focus structures of the object by imparting a rotating movement to the patient, to the detector or to the collimator (66, 2, 27, 43).

The techniques of *reconstruction tomography* were developed in nuclear medicine on the basis of the mathematical theory of information transfer and of image reconstruction, applied in radioastronomy (4, 5), in electron microscopy (22) and, more recently, in diagnostic radiology (33). The reconstruction of the 3-dimensional distribution of a radionuclide in an organ derives from principles that are common with the reconstruction of X-ray tissue densities, but it offers

some special impediments, linked to different conditions of detection (51):

1) fewer events are available for the image reconstruction in emission than in transmission tomography;
2) the attenuation of the photons in the body is to be corrected and attenuation factors appear as an additional set of unknowns in the treatment of the data;
3) the expected spatial resolution is worse than in X-ray transmission tomography;
4) the larger object contrast in emission tomography partially balances these limitations.

The basic principles of the reconstruction tomography remain the same, whatever the spatial configuration of the detection system and the reconstruction algorithm: the problem of reconstituting the distribution of the radionuclide in the examined volume is partitioned in the reconstruction of a series of thin, 2-dimensional, transaxial sections, performed from multiple projections of the object in the corresponding transaxial plane.

The different reconstruction algorithms that have been described are broadly classified (11) as direct methods (matrix inversion, backprojection, iterative least-squares technique, other iterative algebraic techniques) and Fourier techniques, whose basis will be treated in more detail.

Concept of projection

The figure 1 displays a system detecting the radioactivity of a transverse plane of an object, along a detection line with polar coordinates t and θ. The sample of activity, $m(t, \theta)$, that is collected along this line may be merely considered as the sum of the contributions of a series of spatial elements, with activities $a(r, \theta')$. The *projection equation* is

$$m(t,\theta) = \sum_{r,\theta' \in (t,\theta)} k(r,\theta')\, a(r,\theta') \qquad (1)$$

the $k(r, \theta')$ are the weighting factors resulting from the unevenly distributed conditions of detection along the line (t, θ).

The problem to be solved is clearly: how to recover all the values $a(r, \theta')$ of the section from the external measurements $m(t, \theta)$? The $a(r, \theta')$ cannot be observed directly and are computed indirectly from multiple views and through reconstruction algorithms. The weighting factors $k(r, \theta')$ to be considered are a difficulty particular to emission tomography, as compared to transmission techniques.

Basic conditions of emission tomography

The use of multiple external measurements for a correct reconstruction of the radionuclide distribution pattern in the object requires three conditions to be fulfilled: optimized *detection conditions* are required, measurements are to be *adequately sampled* along precise angular and linear increments, the *spatial treatment of the data* is to be implemented in an adapted algorithm.

The ideal system should moreover prove a high sensitivity/resolution score, thus permitting altogether a low radiation exposure of the patient, an accurate counting statistics and an optimized information/time of examination ratio.

Finally, the arguments of feasibility, flexibility and cost also come into consideration.

Detection requirements

The reconstruction tomography should be based on detection conditions compatible with the projection concept (equation 1): constant sensitivity and resolution along the detection lines, corrected attenuation of the photons in the object, minimum participation of scattered radiation in the measurements, spatial and temporal linearity of the detection.

The widespread availability of *single photon gamma emitters* encouraged the design and building of SPD emission tomographs, either with scanning systems (39, 41), or with cameras (2, 12, 35, 46). The major difficulties encountered in these approaches result from the difficulty to ensure depth-independant

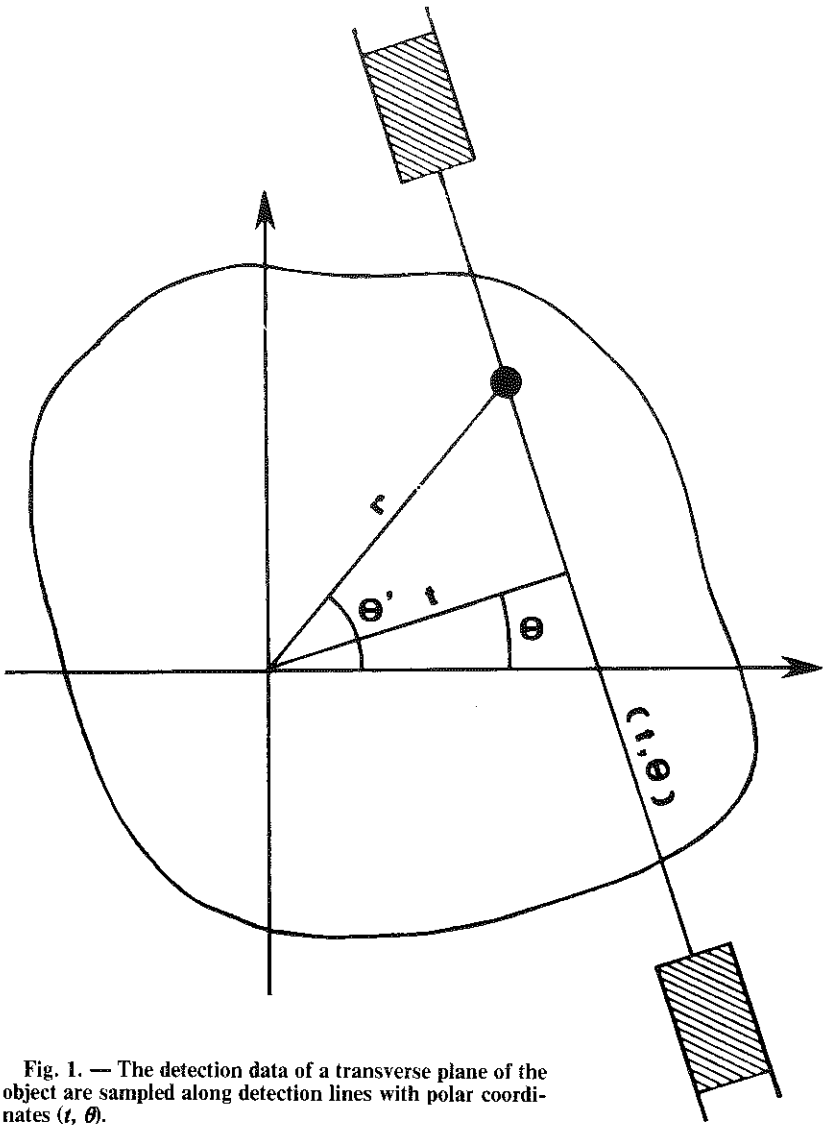

Fig. 1. — The detection data of a transverse plane of the object are sampled along detection lines with polar coordinates (t, θ).

resolution and sensitivity. Furthermore, in SPD, the attenuation factor is also a 3-dimensional unknown which should be introduced for each element of the section to be reconstructed (11, 13, 63). Encouraging results were obtained, but their quantitative value is limited and their application is restricted to rather symmetrical organs, such as the brain (38, 40).

The availability of cyclotron-produced *positron-emitting radionuclides* offers promising conditions of detection in nuclear medicine (68, 6), particularly in the field of tomography (15, 20).

The β^+ particle, emitted in the positron decay of a proton-rich nucleus, interacts with a negative electron after a very short distance, whose range depends on the maximum kinetic energy of the positron. The annihilation of the two electrons yields two geometrically opposed, 511 KeV photons that may be selectively detected by two opposed

NaI(Tl) detectors, coupled with a coincidence counting circuit (fig. 2).

The spatial resolution of an annihilation coincidence detection (ACD) system is typically depth-independant (7, 59, 49). The iso-counting profiles have the shape of coaxial cylinders between the two detectors. The need for collimators is eliminated. The full width at half maximum (FWHM) of the linespread function (LSF) of ACD is about 40% of the exposed frontal diameter of the two NaI(Tl) crystals. The spatial resolution remains depth-independant in an absorbing material (49).

The loss of detection efficiency due to the *attenuation* of the pair of photons in the object is also depth-independant, even within an heterogeneous volume; the two 511 KeV photons must indeed traverse the entire length of material between the two detectors, independant of their depth of origin along the line of detection.

If one considers the value of k to be introduced in the projection equation (1) as the weighting factor resulting from the attenuation, this equation may be simplified, in the case of ACD :

$$p(t,\theta) = \frac{m(t,\theta)}{k(t,\theta)} = \sum_{r,\theta' \in (t,\theta)} a(r,\theta') \qquad (2)$$

$k(t, \theta)$ is constant along (t, θ); $p(t, \theta)$ is the corrected value of $m(t, \theta)$ for attenuation.

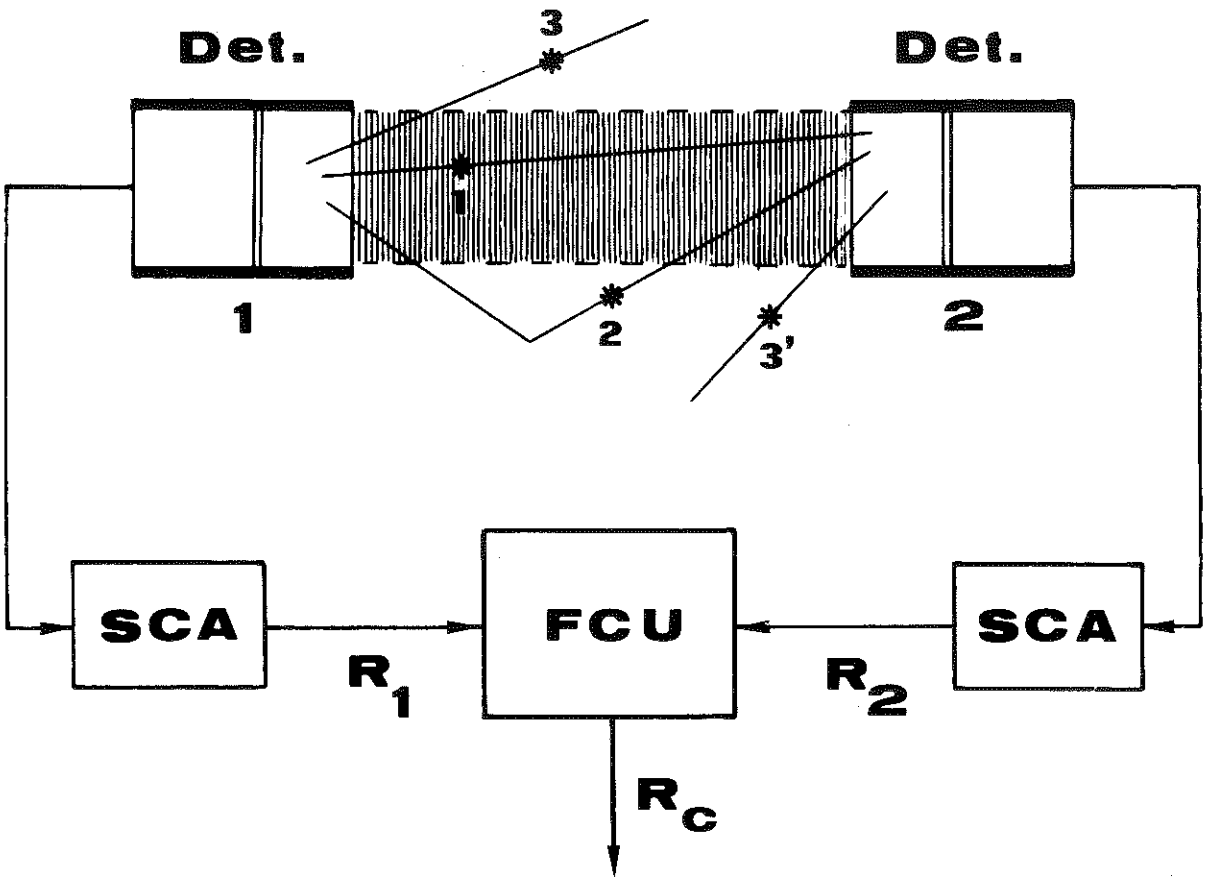

Fig. 2. — A coincidence detection unit. Det. NaI(Tl) crystal, with preamplifier and amplifier; SCA single scale analyzer; FCU fast coincidence unit; hatched area detected volume; asterisks some positron annihilations: 1, a true coincidence, 2, a coincidence due to scattering, 3 and 3', random coincidence; R_1 and R_2, single channel counting rate; R_c, coincidence counting rate.

As the attenuation factor affecting each measurement is independant of the depth, it is possible to measure the autoattenuation factor $k(t, \theta)$ of each line (t, θ), by introducing an external positron emitting source (for ex. a source of ^{64}Cu) and by performing the measurements in the presence and in the absence of the object (59). If the external source is calibrated, it is possible to convert the data into absolute units of radioactivity (23). Simplified and more approximative techniques compute the attenuation factor from the physical dimension of the object and its mean attenuation coefficient.

The elimination of the need for absorbing collimators in ACD permits to achieve a *higher overall sensitivity* than in SPD. Indeed, the solid angle of detection is not occluded by any collimator and, when several detectors are opposed, the use of many coincidence combinations between them is possible (fig. 3).

Spatial treatment of the data

Several mathematical methods may be potentially used for the reconstruction of the distribution of a radionuclide in an object from multiple external measurements performed in a transaxial plane (11). The principal techniques on use in ACD systems are based on the linear backprojection on the image of each of the measurements, along the lines (t, θ). When several data, obtained at different values of (t, θ), are backprojected

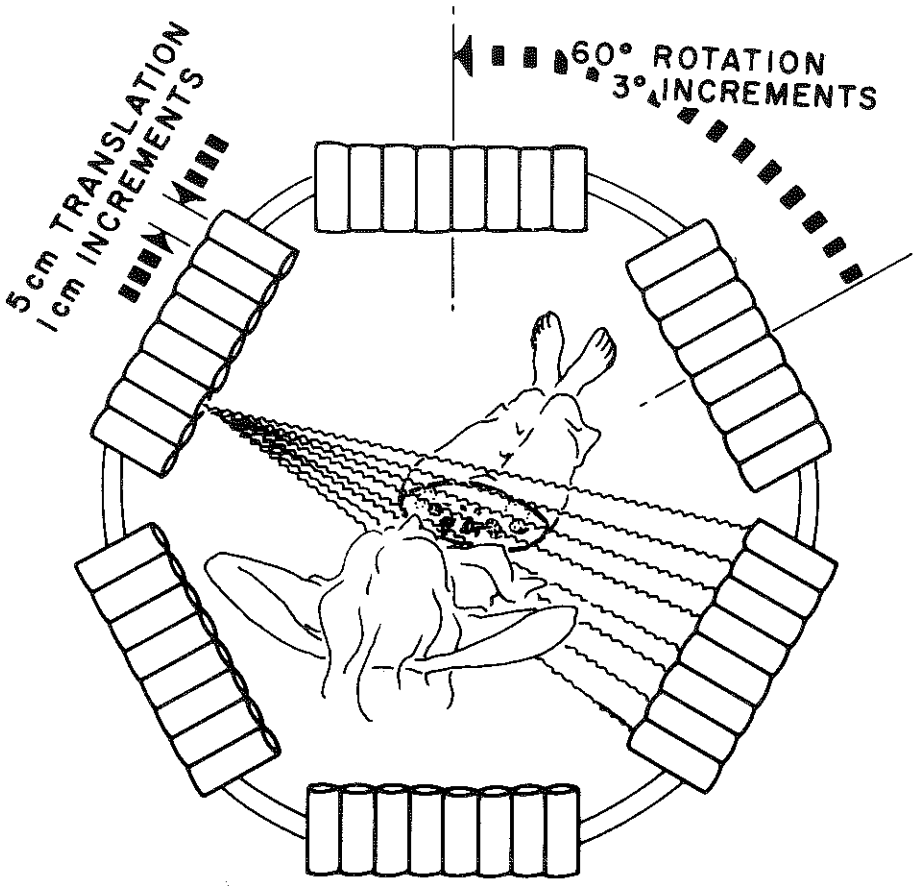

Fig. 3. — Diagram of PETT III (positron emission transaxial tomograph) (courtesy of M.M. Ter-Pogossian, 61).

and superimposed, each element of the resulting image, $b(r, \theta')$, is equal to the sum of the measurements converging on the corresponding point of the object. This sum may be written, from equation (2),

$$b(r, \theta') = \sum_{(t,\theta) \cap (r,\theta')} p(t, \theta) \qquad (3)$$

A tomographic effect is obtained, but the reconstructed values $b(r, \theta')$ do not reproduce the true values $a(r, \theta')$. The activities from all the other parts of the section act indeed as a blur on each of the elementary activities to be reconstructed, and have the effect of suppressing the high spatial frequency components of the source distribution.

Theoretical considerations permit to consider that the true values $a(r, \theta')$ may be reconstructed by the back-projection, not of $p(t, \theta)$, but of a derived function of space $g(t, \theta)$:

$$a(r, \theta') = \sum_{(t,\theta) \cap (r,\theta')} g(t, \theta) \qquad (4)$$

The apparent values $b(r, \theta')$ of equation (3) are the result of the convolution of the true image function $a(r, \theta')$ with a filter function, as a consequence of the apparent rotation of the object during the sampling procedure. The problem of deconvolution is solved through the use of spatial Fourier transforms: bidimensional Fourier transform on the regional values after linear backprojection (3), or one-dimentional Fourier transform before backprojection (15). In the latter case, the values to be backprojected are the result of the inverse Fourier transform of the product of the filtering function $H(\varrho)$ with the Fourier transform of the data $p(t, \theta)$: $a(r, \theta')$ is reconstructed by backprojection of

$$g(t, \theta) = \mathcal{F}^{-1}\{H(\rho)\, \mathcal{F}[p(t, \theta)]\} \qquad (5)$$

The procedure concretely results in a compensatory enhancement of the high frequency components of the image, that are amplified more than the low frequencies. The treatment of the data acts as a spatial filter and so the method is called *linear superposition of filtered backprojections.*

This method restores the true image of distribution only under ideal conditions (56), especially noise-free measurements and infinite number of angular projections through π radians, collimated near 0 width. The practical impossibility to literally respect these conditions implies a deleterious effect on the image and needs some methodological adjustments: especially, the finite number of data to be backprojected and the occurrence of statistical noise necessitate to fix a cutoff spacial frequency limit in the filtering procedure, to avoid artifact or parasite frequencies to be amplified.

Sampling of the data

The image of the distribution of the radionuclide is reconstructed from a finite number of views. Several sampling modes of the information are realized in the many geometrical configurations of the tomographs that are presently in biomedical use and of the prototypes under study. The reader is referred to the abundant literature for details about each system (60), but some general remarks will be usefull as a guideline.

The major arguments that are taken into account in the design of the detection units may be summarized as follows:

1) maximum feasibility and flexibility, standard and modular elements, optimal cost;
2) optimized sensitivity, compatible with a high and homogeneous spatial resolution through the field of interest;
3) field of view sufficiently large for clinical applications;
4) not too sophisticated corresponding algorithms and a minimum reconstruction time;
5) easiness and accuracy of the correction for attenuation, with the possibility of calibration of the reconstructed values;
6) depth-independance of the statistical accuracy of the reconstructed values.

These objectives are unequally attained in the systems that have been proposed. The detection units include different numbers of NaI(Tl) cystals, symmetrically arranged, with the purpose to benefit from as great as possible solid angles for ACD, by the use of many coincidence combinations between opposed arrays of detectors (fig. 3). The difficulty of closely packing crystals, shields and photomultiplier tubes of a rather large diameter and the imperatives of sampling impose in most cases to import angular and linear movements to the detectors in the transaxial plane. The series of sections is obtained through a longitudinal incremental movement of the patient couch. Multislice systems avoid this translation movement.

The Massachusetts General Hospital positron camera PC-1 (14, 8) is formed by two heads rotating about a central axis, each having 127 NaI(Tl) crystals and 72 PMT. The sampling capabilities of PC-I have been increased in a more recent version, the PC-II (9).

The hexagonal configuration was tested in the positron emission transaxial tomograph (PETT) prototypes at the Washington University in Saint-Louis (59). The PETT III (fig. 3) (59, 49, 30), of clinical use, is designed as an hexagonal array, with 6 banks of 8 shielded NaI(Tl) crystals, to which combined rotatory and linear incremental movements are imparted. The ECAT (emission computerized axial tomograph) (52) is built on a similar plan, with 6×11 detectors. The PETT IV (62) is another development of PETT (fig. 6), with multislice capabilities and a transverse and longitudinal display of the sections. The hexagonal configuration has the advantage of insuring a constant geometrical resolution in all the field of each section. Moreover, the use of all the coincidence combinations between opposed banks of detectors results not only in an increased overall sensitivity of the system, but also in a redundant collection of information in the central regions of the object, thus permitting to obtain a depth-independant statistical accuracy of the reconstructed image (51).

The ring geometry was already developed in 1973, with a 32 NaI(Tl) detectors system (54). The University of California CRTAPC (circular ring transaxial positron camera) (fig. 4) (17, 18), includes 64 NaI(Tl) detectors packed in a ring. A prototype with 280 closely packed NaI crystals of low diameter, optically coupled with several PMT via light-pipes is being developed at Berkeley (21).

The circular geometry has the advantage of yielding a maximum overall sensitivity of the system by permitting the greatest number of ACD combinations between opposed detectors. This configuration reduces the need for a movement of the system during the sampling procedure; it is reduced to an oscillation (18) or suppressed (21). These advantages are balanced by some drawbacks : this configuration needs a high number of detectors; the spatial resolution deteriorates with increasing distance from the ring axis, because of the increase and of the asymmetry of the apparent size of the crystals at oblique angles, especially if the shield is light (in the Berkeley system, the point spread function is circular at the center—FWHM = 7.5 mm—and elliptical at 10 cm the center in a Lucite phantom—FWHM = 8×12.5 mm) (21); the statistical accuracy is worse in the central than in the peripheral regions of the image and is not compensated by a redundant sampling, as it is in the hexagonal configuration.

Other authors develop ACD tomographs based on *Anger gamma cameras* (36, 44).

Some performances

Spatial resolution

The spatial resolution of each detector pair is dependant on the exposed diameter of the crystals. Resolution may be enhanced by placing shadow shields in front of the detectors, as in PETT III and in ECAT.

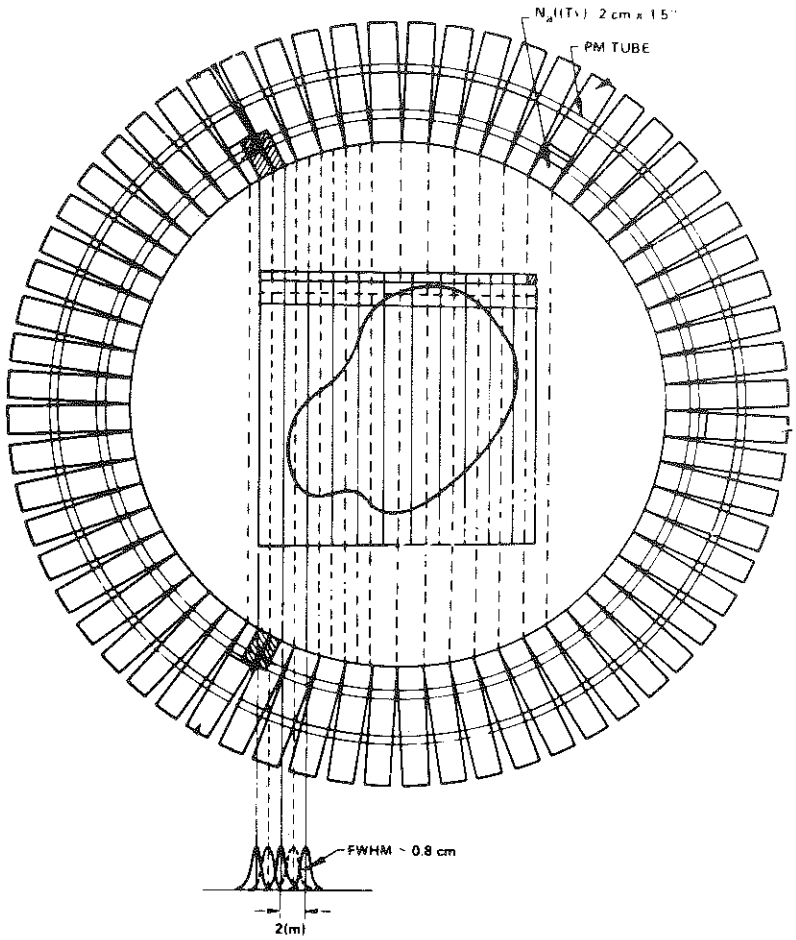

Fig. 4. — Diagram of CRTAPC (circular ring transaxial positron camera) (courtesy of Z.H. Cho, 18).

The resolution depends not only on the spatial impulse response of the detectors but, in the case of ACD, the positron spatial range and the annihilation angle spread are to be taken into account. Notably, the spatial range of the positron from its site of origin limits the expected spatial resolution of the imaging device, to an extend depending on the E_{max} of the positron and on the density of the absorbing material (29, 16, 48, 50) : this effect has been shown significant only if positron emitting radionuclides of $E_{max} \geqslant 1.5$ MeV (for ex. : ^{15}O, $E_{max} = 1.72$ MeV) are employed with detectors with a resolution of a few millimeters, especially in tissues of low density, such as the lungs.

The overall spatial resolution of the reconstructed image results from the spatial resolution of the coincidence detection pairs, from the sampling conditions and from the reconstruction method.

For example, the spatial resolution of PETT III, evaluated in a 18 cm diameter cylindrical phantom filled with water, with 2 mm diameter linear sources of ^{64}Cu and with photopeak detection, is characterized by a linear spread function on the reconstructed image of FWHM = 12 mm, while the same

value for the individual pairs of detectors is 11 mm (51). Performances of the same order of magnitude are attained by most actual systems. It must be emphasized that these levels of spatial resolution can only be reached if a sufficient statistical level of information quantity is obtained.

Effects of random coincidences

The ACD system accepts all pairs of photons reaching the coincidence unit within the resolving time 2τ (fig. 2). When two photons, not originating from the same positron annihilation are detected within this time, they are accepted as random coincidence and incorrectly assumed to have originated in the true coincidence region. The random coincidence counting rate C_R of an ACD system is

$$C_R = 2\tau N_1 N_2$$

where N_1 and N_2 are the singles counting rates of the individual detectors of the system. The random coincidences appear as an undesirable background to the measurements. If one considers that the mean value of N is proportionate to the detected radioactivity, it appears that the true coincidence counting rate is a linear function of N, whereas the random counting rate grows with the square of N. This is a general limit to the counting capability of the ACD systems, which imposes some compromises.

1) The resolving time should be made as short as possible, without loosing true coincidence events; the present performance of the coincidence units on use is of the order of τ = 8-15 nsec. It must be kept in mind that the time-of-flight of photons through the object is of the order of 1 nsec for 30 cm.
2) The single photons from regions out of the section of interest are to be rejected by a suitable shielding.
3) The setting of an energy threshold should keep the scatter contribution in the randoms as low as possible. A compromise is to be accepted as the photopeak contribution in the absorption of 511KeV photons in the Na(Tl) crystals is rather low, especially when small crystals are used. When an energy threshold of 100 KeV is used with PETT III, in the conditions described hereabove, the spatial resolution is characterized by a FWHM of the LSF of 12 mm for the individual coincidence units and of 14 mm on the reconstructed image (51). The use of graded absorbers to reduce scattered radiation from the patient permits also to overcome a too large effect on the randoms of lowering the energy threshold (44).
4) As the random coincidences contribute a low spatial frequency background to the image, it is possible to substract them from the reconstructed values; it is still better to keep randoms as low as possible, to minimize the non-zero components of spatial fraquency resulting from the randoms and the statistical error due to the substraction itself (51).
5) Positron emitting radionuclide levels used for this test should not be too high : for example, in the working conditions with PETT III, it is considered that an overall single detector counting rate of 12000 cps entails a random coincidence rate less than 5% of the true coincidence counting rate (49); the performance of ECAT is of the same order of magnitude (52).

Time of examination

The time of examination is usually the sum of the times required for the performance of the emission scan and of the transmission scans with and without the patient, for the imput of information by the operator and, finally, for the treatment of the data and the reconstruction of the image. The time that is necessary to perform a 5-slice emission scan, with measured attenuation correction, is of the order of 25 min. with the ECAT. This is a maximum estimate and it is actually dependent on activity of injected

radiopharmaceutical, shadow shields and type of scan.

The time of examination should be as short as possible, for two main reasons :

1) several tomographic slices are necessary for the complete visualization of the organ of interest;
2) the physical decay of short-lived radionuclides may be easily corrected from slice to slice, but the regional effective half-life of the imaging radiopharmaceutical is also to be considered (62).

As the activity to be employed is limited to keep radiation exposure of the patient and random coincidence counting rate as low as possible, multislice tomographs have been designed and builded. They have the additional advantage of being able to suppress the slice-to-slice movement of the patient couch and to insure a strict parallelism between sections. The MGH camera (14, 8), the positron Anger camera (44), and the Humongotron (36) have multislice possibilities. The PETT IV (62) performs seven simultaneous slices and displays the information in transversal and longitudinal planes (fig. 6).

Radiation exposure

Ter-Pogossian has recently reviewed the radiation exposure resulting from the use of the most employed positron emitters (61). When an external source of radionuclide is used for the generation of the attenuation factors, 50 to 150 mrad are to be added (table 1).

Table 1. — *Absorbed doses of radiation from some positron emitting radiopharmaceuticals. (Ter-Pogossian)* (61).

Radiopharmaceutical	*Route of administration*	*Absorbed dose (mrad/mCi)*	
		whole body	*critical organ*
^{11}CO	inhalation	10	80 (blood)
^{11}C-glucose	IV	10	50 (liver)
^{11}C-bicarbonate	IV	8	10 (liver)
$^{13}NH_3$	IV	6	250 (kidney)
^{68}Ga-EDTA	IV	35	540 (kidney)

Applications of the positron emission tomography

The positron emission transaxial tomography is still a method that is in tremendous technological progress; it has reached a level of routine application in some cyclotron research centers.

The trends in this field result from convergent progress, not only in the development of tomographs, but also in the production of positron-emitting, short-lived, radionuclides and in the preparation of radiopharmaceuticals of physiological and metabolic interest (64, 67, 55, 66).

The positron-emitting radionuclides have some prominent properties :

1) The annihilation coincidence detection systems offer high resolution and high sensitivity capabilities in the detection of positron emitting radionuclides, with an easy and precise correction for attenuation and a possibility of calibration of the measurement in radioactivity units.
2) These properties are the basis of the development of emission reconstruction transaxial tomographs of high performance.
3) Around 50% of all radionuclides are positron emitters and the only short-lived radio-isotopes of the biologically important elements C, N and O fall into this category.
4) These biologically interesting radionuclides permit the organic synthesis or the biosynthesis of radiopharmaceuticals and metabolites without disrupting their physiological or metabolic properties. The potential for preparing ^{11}C labeled metabolites is very large : ^{11}CO red blood cells (64), ^{11}C-glucose and fructose (42), ^{11}C-palmitate (57), ^{11}C-catecholamines (26), ^{11}C-amino acids (19), ^{11}C-pyrimidines, ...

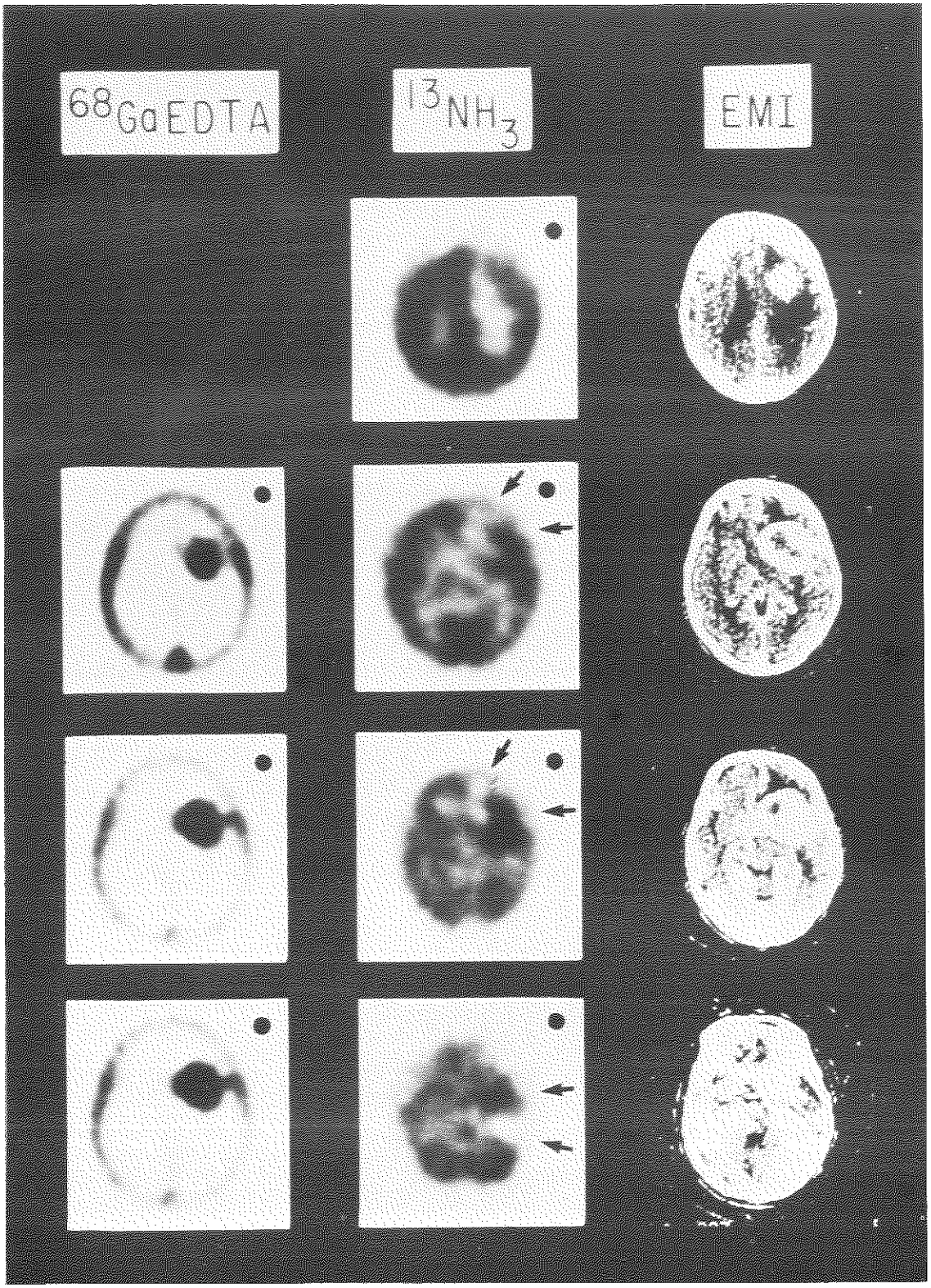

Fig. 5. — Tomographic scan of a brain by the ECAT, showing the comparative study of the regional brain perfusion ($^{13}NH_3$) and of the blood brain barrier permeability (^{68}Ga EDTA), in a case of right frontal glioblastoma. Reduced perfusion coincides with an edema-like image of EMI scan. Arrows show reduced perfusion at site of tumor and increased perfusion at the periphery of the tumor (from M.E. Phelps et al., 52).

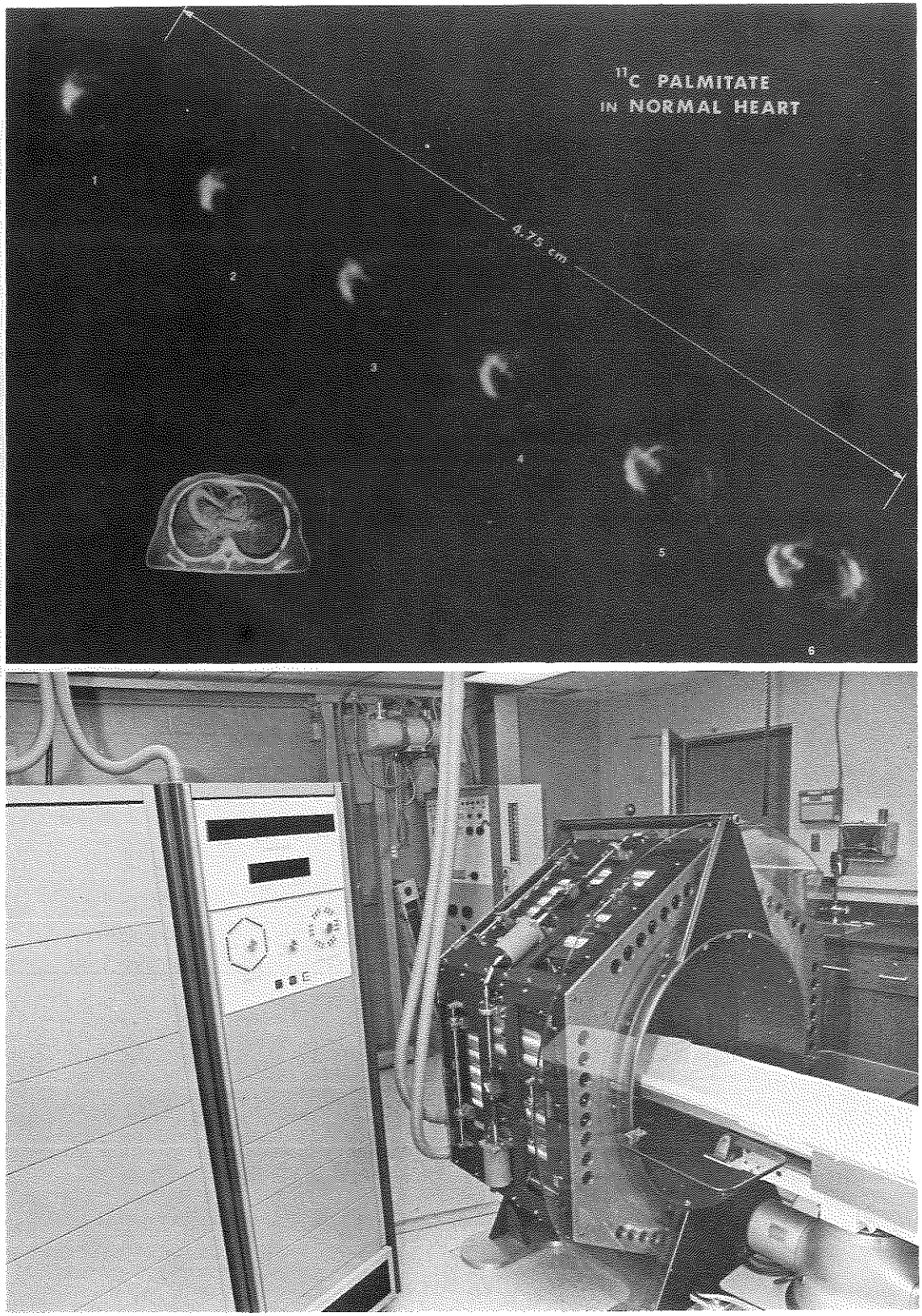

Fig. 6. — Upper part: simultaneous cross section images of the ^{11}C palmitate distribution in the myocardium, obtained with the PETT IV.
Lower part: the PETT IV system (courtesy of M.M. Ter-Pogossian).

In a parallel way, ^{18}F opens possibilities, among others, for the synthesis of very interesting pseudometabolites, such as ^{18}F-5-Fluorodopa (24) and ^{18}F-5-fluorouracil (25).

5) All the positron emitters are detected in the same ACD conditions; by making profit of the short half-life of the majority of these radionuclides, it is possible to compare the regional concentration of tracers in the same geometrical conditions of detection.

Among other fields, the investigation of cerebral physiology and physiopathology is possible with $^{13}NH_3$ for brain regional perfusion, with ^{11}CO red blood cells (64) for brain regional blood volume (fig. 7), with ^{11}C-glucose (53) for brain regional glucose metabolism and with $^{15}O_2$ for oxygen cerebral extraction (34). All these biological parameters may be measured with a high precision regional localization and their local relationship may be studied (fig. 5). The deep regions of the brain, particularly the central grey nuclei, are presently accessible to the in vivo metabolic investigations. Other prospects are open for the study of more specific metabolic pathways in the brain, for instance of the amino acids (19, 58) and of the neurotransmitters (24).

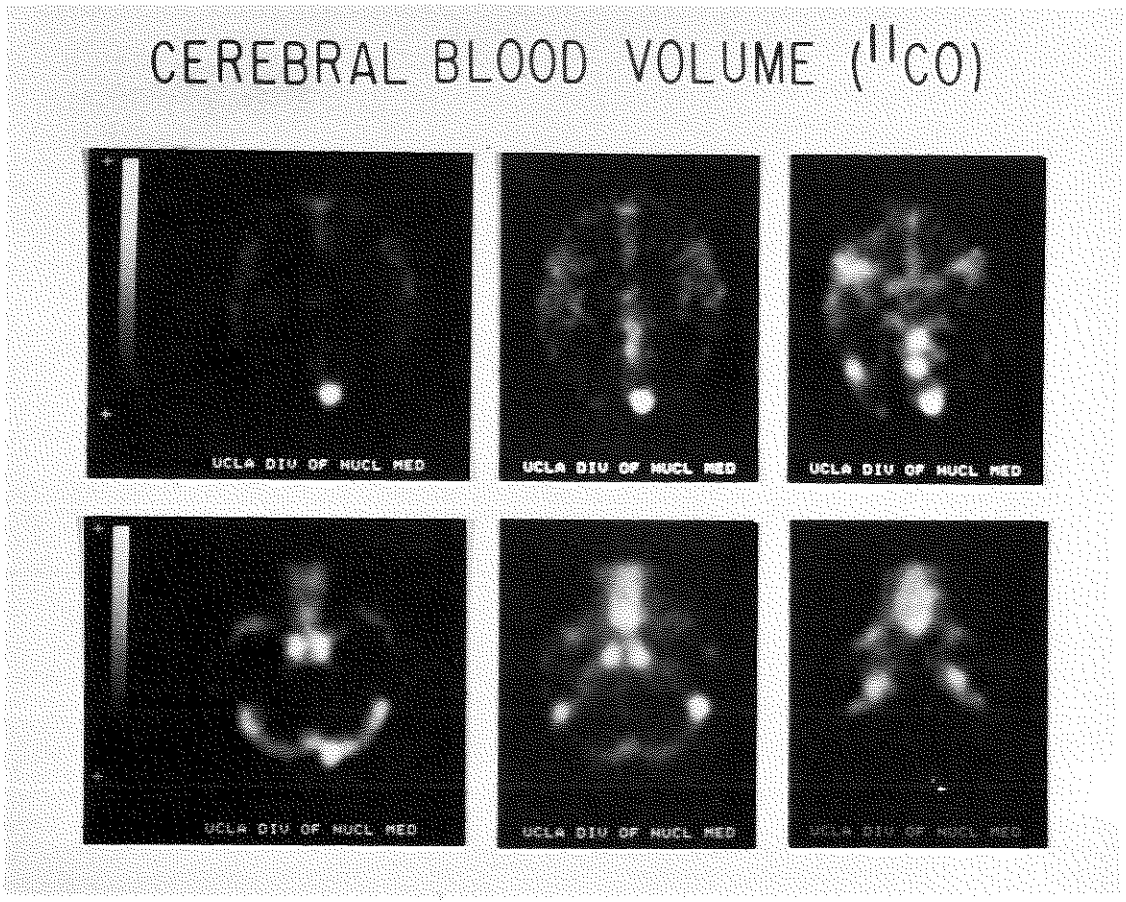

Fig. 7. — Cerebral blood volume study in a human subject from a single breath inhalation of ^{11}CO: the images show the cerebral blood volume distribution in tissue with the large vessels appearing as a dominant feature. (from M.E. Phelps et al., 59).

The investigation of heart physiology and disease is possible with the tomography of the myocardium after injection of $^{13}NH_3$ (31), ^{82}Rb (10), ^{11}C-glucose (42), ^{13}N-L-asparagine (28) or ^{11}C-palmitate (57) (fig. 6). The chambers of the heart may be visualized with ^{11}CO-red blood cells. Greater possibilities are opened in the examination of the heart by the use of high sensitivity tomographs and of gating systems (fig. 6).

The spatial dependance of the positron emission tomographs on the proximity of a cyclotron will probably be less constraining in the future, as a consequence of the availability of generator-produced positron emitters. ^{68}Ga ($T_{1/2}$ = 68 min.) may be produced by a ^{68}Ge generator ($T_{1/2}$ = 275 days) and may be used especially as ^{58}Ga-DTPA (69), ^{68}Ga-transferrin, $^{68}Ga(OH)_3$ particles, ^{68}Ga labeled macroagregated albumin and ^{68}Ga labeled red blood cells and platelets (65).

The positron emission transaxial tomography has developed tremendously in the last five years and offers a very valuable tool for opening nuclear medicine to up-to-now inaccessible fields of non-invasive physiological studies. The potential of these techniques for the investigation of physiological processes, metabolic pathways and pharmacodynamical problems is full of promise.

Résumé

La conception, l'élaboration et l'utilisation de tomographes transaxiaux d'émission se sont développées de manière considérable depuis les cinq dernières années. Ce progrès est le résultat, non seulement de l'avancement de la technologie nucléaire, mais aussi du développement de centres de recherches médicales avec cyclotrons et de l'effort de synthèse de nouvelles substances radiopharmaceutiques.

L'article revoit les principes de base de la tomographie transaxiale d'émission et les conditions d'application du concept de projection, dans le cadre de l'utilisation des émetteurs de positrons. La technique de superposition linéaire de rétroprojections filtrées est plus spécialement décrite, parmi les méthodes de reconstruction d'image qui peuvent être utilisées. La configuration des tomographes actuellement en fonction et celle des prototypes à l'étude sont brièvement décrites.

Les performances de ces tomographes, telles que la résolution spatiale, les capacités de comptage et le temps d'examen, sont discutées.

Une revue des principales applications actuelles de la tomographie transaxiale d'émission positronique illustre le fait que cette technique ouvre en médecine nucléaire un nouveau champ d'investigations, pour l'étude des processus physiologiques, des voies métaboliques et des problèmes pharmacodynamiques.

Samenvatting

Emissie reconstructie tomografie is een tak van de nucleaire technologie die de laatste vijf jaar een enorme vooruitgang heeft geboekt. Dit is het gevolg van de geleverde inspanningen om krachtiger detectietoestellen te bouwen voor de nucleaire geneeskunde, de verdere uitbreiding van het aantal onderzoekscentra met cyclotrons, en de groeiende belangstelling voor het samenstellen van radiofarmaca.

Het artikel heeft een overzicht van de grondbeginselen van de positron emissie reconstructie tomografie. De eisen i.v.m. de detectie worden gespecificeerd op basis van de toepasbaarheid van de projectievergelijking, en de unieke voordelen van de positron straalbronnen worden onderstreept. Van de wiskundige methoden die eventueel gebruikt kunnen worden bij de reconstructie van het beeld, wordt meer in het bijzonder de techniek van lineaire superpositie van gefilterde terugprojecties beschreven. De opmaak van tomografieën die thans op biochemisch terrein gebruikt worden, evenals de configuraties van de onderzochte prototypes, worden kort geschetst.

Er wordt een bespreking gegeven van enkele bestaande of wenselijke verwezenlijkingen van emissie tomografieën, zoals ruimtelijke resolutie, telmogelijkheden en onderzoekstijd.

Een overzicht van de toepassingen van de positron emissie tomografie maakt duidelijk dat deze techniek voor de nucleaire geneeskunde de weg opent naar het totnogtoe ontoegankelijk onderzoek van fysiologische processen, metabolische processen en farmaco-dynamische problemen.

References

1. AMBROSE J.: Computerized transverse axial scanning (tomography): part 2: Clinical application. *Brit. J. Radiol.*, 64: 1023-1047, 1973.
2. ANGER H.O.: The scintillation camera for radioisotope localization. In: HOFFMAN G. and SHEER K.E., *Radioisotope in der Lokalisationdiagnostik*, Schattauer-Verlag, Stuttgart, 1967, 18-21.
3. BATES R.H.T. and PETERS T.M.: Towards improvements in tomography. *N. Z. J. sci*, 14: 883-896, 1971.
4. BRACEWELL R.N.: Strip integration in radio astronomy. *Aust. J. Physiother.*, 9: 198-217, 1956.
5. BRACEWELL R.N. and RIDDLE A.: Inversion of fan-beam scans in radio astronomy. *Astrophys. J.*, 150: 427-434, 1967.
6. BROWNELL G.L. and SWEET W.H.: Localization of brain tumors *Nucleonics*, 11: 40-45, 1953.
7. BROWNELL G.L., BURNHAM C.A., WILENSKY S., ARONOW S., KAZEMI H., STRIEDER D.: New developments in positron scintigraphy and the application of cyclotron-produced positron emitters. In: *Med. Radioisotope Scintigraphy, I.A.E.A.*, Vienna, 1969, p. 163-176.
8. BROWNELL G.L. and BURNHAM C.A.: MGH positron camera. In FREEDMAN G.S., *Tomographic imaging in nuclear medicine, Society of Nuclear Medicine*, New-York, 1973, p.154.
9. BROWNELL G.L., BURNHAM C., AHLUWALIA B., ALPERT N., CHESLER D., COCHAVI S., CORREIA J., DEVEAU L.: Positron imaging instrumentation. *IEEE Trans. Nucl. Sci.*, NS24: 914-916, 1977.
10. BUDINGER T.F., YANO Y., HOOP B.: A comparison of 82 Rb^+ and 13 NH_3 for myocardial positron scintigraphy. *J. nucl. Med.*, 16: 429-431, 1975.
11. BUDINGER T.F.: Quantitative nuclear medicine imaging: application of computers to the gamma camera and the whole-body scanner. In: LAWRENCE J.H., *Recent advances in nuclear medicine*, Grune & Stratton, New York, 1974, p. 41-130.
12. BUDINGER T.F. and GULLBERG G.T.: Three-dimensional reconstruction in nuclear medicine. *IEEE Trans. Nucl. Sci., N.S. 21: 2-20, 1974.*
13. BUDINGER T.F. and GULLBERG G.T.: *Transverse section reconstruction of gamma-ray emitting radionuclides in patients. In:* TER-POGOSSIAN M. et al., *Reconstruction tomography in diagnostic radiology and nuclear medicine*. University Park Press, Baltimore, 1977, p. 315-342.
14. BURNHAM C.A. and BROWNELL G.L.: A multicrystal positron camera. *IEEE Trans. Nucl. Sci.*, NS-19: 201, 1972.
15. CHESLER D.A.: Positron tomography and three dimensional reconstruction technique. In: FREEDMAN G.S., *Tomographic Imaging in Nuclear Medicine*. Society of Nuclear Medicine, New York, 1972, p. 176-183.
16. CHO Z.H., CHAN J.K., ERICKSSON L., SINGH M., GRAHAM S., MAC DONALD N.S. and YANO Y.: Positron ranges obtained from biomedically important positron-emitting radionuclides *J. nucl. Med.*, 16: 1174-1176, 1975
17. CHO Z.H., CHAN J.K. and ERICKSSON L.: Circular ring transverse axial reconstruction of radionuclide distribution. *IEEE Trans. Nucl. Sci.*, NS-23: 613-622, 1976.
18. CHO Z.H., COHEN M.B., SINGH M., ERICKSSON L., CHAN J., MAC DONALD N. and SPOLTER L.: Performance and evaluation of the circular ring transverse axial positron camera (CRTAPC). *Medical radionuclide imaging. I.A.E.A.*, Vienna, 1977, p. 269-290.
19. COMAR D., CARTRON J.C., MAZIERE M. and MARAZANO C.: Labeling and metabolism of methionine-methyl-^{11}C. *Eup. J. nucl. Med.*, 1: 11-14, 1976.
20. CORMACK A.M.: Reconstruction of densities from their projections, with applications in radiological physics. *Phys. in Med. Biol.*, 18: 195-207, 1973.
21. DERENZO S.E., ZAKLAD H. and BUDINGER T.F.: Analytical study of a high-resolution positron ring detector system for transaxial reconstruction tomography. In: TER-POGOSSIAN M.M., *Reconstruction tomography in diagnostic radiology and nuclear medicine*, University Park Press, Baltimore, 1977, p. 343-358.
22. DE ROSIER D.J. and KLUG A.: Reconstruction of three-dimensional structures from electron micrographs. *Nature*, 217: 130-134, 1968.
23. EICHLING J.O., HIGGINGS C.S. and TER-POGOSSIAN M.M.: Determination of radionuclide concentrations with positron CT scanning (PETT). Concise communication. *J. nucl. Med.*, 18: 845-847, 1977.
24. FIRNAU G., NAHMIAS C. and GARNETT S.: The preparation of [^{18}F]-5-fluoro-DOPA with reactor-produced fluorine-18. *Int. J. appl. Radiat.*, 24: 182-184, 1973.
25. FOWLER J.S., FINN R.D., LAMBRECHT R.M. and WOLF, A.P.: The synthesis of ^{18}F-5-fluorouracil. *J. nucl. Med.*, 14, 63-64, 1973.
26. FOWLER J.S., ANSARI A.N., ATKINS H.L., BRADLEY-MOORE P.R., MAC GEGOR R.R. and WOLF A.P.: Synthesis and preliminary evaluation in animal of carrier-free ^{11}C-1-dopamine hydrochloride. *J. nucl. Med.*, 14: 867-869, 1973.
27. FREEDMAN G.S.: Tomography with a gamma camera. *J. nucl. Med.*, 11: 602-604, 1970.
28. GELBARD A.S., CLARKE L.P., LAUGHLIN J.S.: Enzymatic synthesis and use of ^{13}N-labeled L-asparagine for myocardial imaging. *J. nucl. Med.*, 15: 1223-1225, 1974.
29. GRAHAM L.S., MACDONALD N.S., ROBINSON G.D. and LLACER J.: Effect of positron energy on spatial resolution *J. nucl. Med.*, 14: 401-402, 1973.
30. HOFFMANN E.J., PHELPS M.E., MULLANI N.A., HIGGINGS C.S. and TER-POGOSSIAN M.M.: Design and performance characteristics of a whole body transaxial tomograph. *J. nucl. Med.*, 17: 493-502, 1976.

31. HOOP B., BURNHAM C.A., CORRELL J.E., BROWNELL C.L., SMITH T.W. and SANDERS C.A.: Myocardial imaging with $^{13}NH_4$ and a multicrystal positron camera. *J. nucl. Med.*, 14: 181-183, 1973.

32. HOOP B., LAUGHLIN J.S. and TILBURY R.S.: Cyclotrons in nuclear medicine. In: HINE G.J. and SORENSON J.A., *Instrumentation in nuclear medicine*, Academic Press, New York, 1974, p. 407-457.

33. HOUNSFIELD G.N.: Computerized transverse axial scanning (tomography). Part I: description of system. *Brit. J. Radiol.*, 46: 1016-1022, 1973.

34. JONES T., CHESLER D.A. and TER-POGOSSIAN M.M.: The continuous inhalation of oxygen 15 for assessing regional oxygen extraction in the brain of man. *Brit. J. Radiol.*, 49: 339-343, 1976.

35. KEYES J.W., KAYS D.B. and LEES D.E.B.: Applied comparisons of methods for radionuclide transverse section tomography. *Proc. 1st World Congress in Nuclear Medicine*, Tokyo, 1974, p. 1281-1283.

36. KEYES J.W., ORLANDEAN N. and HEETDERKS W.J.: The humongotron, a scintillation camera transaxial tomograph. *J. nucl. Med.*, 18: 381-387, 1977.

37. KUHL D.E. and EDWARDS R.Q.: Image separation radioisotope scanning. *Radiology*, 80, 653-662, 1963.

38. KUHL D.E. and EDWARDS R.Q.: The MARK III scanner: A compact device for multiple-view and section scanning of the brain. *Radiology*, 96: 563-570, 1970.

39. KUHL D.E., EDWARDS R.Q., RICCI A.R. and REIVICH M.: Quantitative section scanning using orthogonal tangent correction. *J. nucl. Med.*, 14: 196-200, 1973.

40. KUHL D.E., REIVICH M., ALAVI A., NYAZY I. and STAUM M.M.: Local cerebral blood volume determined by three-dimensional reconstruction of radionuclide scan data. *Circulat. Res.*, 36: 610-619, 1975.

41. KUHL D.E., EDWARDS R.Q., ALAVI A., REIVICH M. and ROTHENBERG H.: Radionuclide computerized tomography for brain study. In: TER-POGOSSIAN M.M. et al., *Reconstruction tomography in diagnostic radiology and nuclear medicine*, University Park Press, Baltimore, 1977, p. 281-291.

42. LIFTON J.F. and WELSH M.J.: The preparation of glucose labeled with 20-minute half-lived carbon-11. *Radiat. Res.*, 45: 35-40, 1971.

43. MUEHLLEHNER G.: A tomographic scintillation camera. *Phys. in Med. Biol.*, 16: 87-96, 1971.

44. MUEHLLEHNER G.: Positron camera with extended counting rate capability. *J. nucl. Med.*, 16: 653-657, 1975.

45. NEW P.F., SCOTT W.R., SCHNUR J.A., DAVIS, K.R. and TAVERAS J.M.: Computerized axial tomography with the EMI scanner. *Radiology*, 110, 109-123, 1974.

46. OPPENHEIM B.E.: More accurate algorithms for iterative 3-dimensional reconstruction. *IEEE Trans. Nucl. Sci.*, NS21: 72-77, 1974.

47. PAXTON C.R. and AMBROSE J.: The EMI scanner. A brief review of the first 650 patients. *Brit. J. Radiol.*, 47, 530-565, 1974.

48. PHELPS M.E., HOFFMAN E.J., HUANG S.C. and TER-POGOSSIAN M.M.: Effect of positron range on spatial resolution. *J. nucl. Med.*, 16, 649-652, 1975.

49. PHELPS M.E., HOFFMAN E.J., MULLANI N.A. and TER-POGOSSIAN M.M.: Application of annihilation coincidence detection to transaxial reconstruction tomography. *J. nucl. Med.*, 16: 210-224, 1975.

50. PHELPS M.E. and HOFFMAN E.J.: Resolution limits of positron cameras. *J. nucl. Med.*, 17, 757-758, 1976.

51. PHELPS M.E., HOFFMAN E.J., MULLANI N.A., HIGGINGS E.S. and TER-POGOSSIAN M.M.: Some performance and design characteristics of PETT III. In: TER-POGOSSIAN et al., *Reconstruction tomography in diagnostic radiology and nuclear medicine*. University Park Press, Baltimore, 1977, p. 371-392.

52. PHELPS M.E., HOFFMAN E.J., HUNG S.C. and KUHL D.E.: ECAT, a new computerized tomographic imaging system for positron-emitting radiopharmaceuticals — 1978. In press.

53. RAICHLE M.E., LARSON K.B., PHELPS M.E., GRUBB R.L., WELCH M.J. and TER-POGOSSIAN M.M.: In vivo measurement of brain glucose transport and metabolism employing glucose ^{11}C. *Amer J. phys.*, 228: 1936, 1975.

54. ROBERTSON J.S., MARR R.B. and ROSENBAUM M.: Thirty-two crystal positron transverse section detector. In: FREEDMAN G.S., *Tomographic imaging in nuclear medicine, Society of Nuclear Medicine*, New York, 1973, p. 142-153.

55. SILVESTER D.J., CLARK J.C. and PALMER A.J.: The future of accelerator-produced radiopharmaceuticals. In: *Proc. of the 1st World Congress of nuclear medicine*. World Fed. of Nuclear medicine and biology. Tokyo, 1974, p. 181-190.

56. SNYDER D.L. and COX J.R. Jr.: An overview of reconstructive tomography and limitations imposed by a finite number of projections. In: TER-POGOSSIAN M.M. et al., *Reconstruction tomography in diagnostic radiology and nuclear medicine*. University Park Press, Baltimore, 1977, p. 3-32.

57. SOBEL B.E., WEISS E.S., WELCH M.J., SIEGEL B.A. and TER-POGOSSIAN M.M.: Detection of remote myocardial infarction in patients with positron emission transaxial tomography and intravenous ^{11}C-palmitate. *Circ.*, 55: 853-857, 1977.

58. STRAATMANN M.G. and WELCH M.J.: Enzymatic synthesis of nitrogen-13 labeled amino acids. *Radiat. Res.*, 56: 48, 1973.

59. TER-POGOSSIAN M.M., PHELPS M.E., HOFFMAN E.J. and MULLANI N.A.: A positron-emission transaxial tomograph for nuclear imaging (PETT), *Radiology*, 114: 89-98, 1975.

60. TER-POGOSSIAN M.M., PHELPS M.E., BROWNELL G.L., COX J.R., DAVIS D.O. and EVENS R.G.: Reconstruction tomography in diagnostic ra-

diology and nuclear medicine, University Park Press, Baltimore, 1977.

61. TER-POGOSSIAN M.M., PHELPS M.E., HOFFMAN E.J. and COLEMAN R.E.: The performance of PETT III. In: TER-POGOSSIAN M.M. et al., *Reconstruction tomography in diagnostic radiology and nuclear medicine.* University Park Press, Baltimore, 1977, p. 359-369.
62. TER-POGOSSIAN, MULLANI N.A., HOOD J., HIGGINS C.S. and CURRIE C.M.: A multislice positron emission computerized tomograph PETT IV yielding transverse and longitudinal images. *J. Radiol.:* In press.
63. WALTERS T.E., SIMON W., CHESLER D.A., CORREIA J.A.: Iterative convolution for radionuclide tomography with correction for internal absorption. In: TER-POGOSSIAN M.M. et al., *Reconstruction tomography in diagnostic radiology and nuclear medicine.* University Park Press, Baltimore, 1977, p. 309-314.
64. WELCH M.J. and TER-POGOSSIAN M.M.: Preparation of short half-lived gases for medical studies. *Radiat. Res.*, 36: 580, 1968.
65. WELCH M.J., THAKUR M.L., COLEMAN R.E., PATEL M., SIEGEL B.A. and TER-POGOSSIAN M.M.: Gallium-68 labeled red cells and platelets: new agents for positron scintigraphy. *J. nucl. Med.*, 18: 558-562, 1977.
66. WELCH M.J.: Radiopharmaceuticals and other compounds labeled with short-lived radionuclides. Pergamon Press, New York, 1977.
67. WOLF A.P., CHRISTMAN D.R., FOWLER J.S. and LAMBRECHT R.M.: Synthesis of radiopharmaceuticals and labeled compounds using short-lived isotopes. In: *Radiopharmaceuticals and labeled compounds,* vol. I, IAEA, Vienna, 1973, p. 313.
68. WRENN F.R., GOOD M.L. and HANDLER P.: The use of positron-emitting radio-isotopes for the localization of brain tumors. *Science,* 113: 525-527, 1951.
69. YANO Y.: Preparation and control of 68 Ga-radiopharmaceuticals. In: *Radiopharmaceuticals from generator-produced isotopes, IAEA, Vienna, 1971, p. 117-125.*

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