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WHAT IS THE PURPOSE OF EMISSION COMPUTED TOMOGRAPHY IN NUCLEAR MEDICINE?

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WHAT IS THE PURPOSE OF EMISSION COMPUTED TOMOGRAPHY IN NUCLEAR MEDICINE?

Is radionuclide Emission Computed Tomography (ECT) a mathematical and physical concept, an instrument, a radionuclide tracer technique, a research or diagnostic procedure, a new or old concept? Is it a,b, etc, none of the above or all of the above? To a greater extent it is or will be all of the above.

Computed tomography (CT), goes by many names composed of combinations of words; section, tomography, transverse, transverse-axial, transaxial, computed, computerized, reconstruction, etc. but probably the most important terms are reconstruction and tomography. This can be appreciated from the fact that the fundamental approach of CT is exact (or near exact) 3-dimensional (3D) reconstructio of a tomographic section from a series of one dimensional projections of an object. Reconstruction can be accomplished in the transaxial or longitudinal direction or at any angle between these two extremes. The mathematical techniques (algorithms and assumptions of reconstruction tomography are common to both x-ray and radionuclide CT and are reviewed elsewhere (1-3).

The important physical factors which must be taken into account in ECT are: i) uniform or near uniform detector resolution and response (efficiency) with depth; ii) accurate correction for photon attenuation; iii) removal or significant reduction of scatter radiation to assure detector response represents the linear sum of activity viewed and provide high contrast and sensitivity; iv) accurate detector positioning and sampling (both linear and angular) to provide optimum reconstructed image quality and v) detection system with high efficiency to meet the demanding statistical requirements of CT. Where these factors have been presented in the literature, the explicit and quantitative relationships among them, and the manner in which they effect the quality of the ECT image has yet to be determined.

A number of ECT systems have been or are being constructed at this time (TABLE 1). These systems can be separated into two categories: (a) systems which employ single photon counting (SPC) such as scanners and cameras for ^{99m}Tc, ^{131}I, ^{123}I, etc. and (b) systems which employ annihilation coincidence detection (ACD) of positron emitting radionuclides. During the past several years there have been many discussions, presentations and published papers which have discussed advantages and disadvantages of each of these techniques. From all of this there are several points which appear, at least more clear than others. Approximately an equal number of investigators and commercial companies have chosen to pursue each approach.* To date, in human subjects, SPC systems have been used primarily for brain, whereas ACD has been used for whole body studies. This primarily results from the fact that the methods for maintaining a relative constant resolution with depth (eg. summing or geometric mean of opposing views) and approximation methods (or no method) for attenuation correction with SPC have so far only proven to be viable in small, uniform and symmetrical objects like the head (2,4-6). However, ACD provides a method in which attenuation is fundamentally a slow <u>varying</u> function,

* The only commercially available tomographs at this time are the ACD systems from ORTEC Inc. and the Cyclotron Corp.

correctable by an exact or near exact technique even as object size and local variation in attenuation becomes large (7,8). ACD also provides resolution and high contrast which is depth independent as the object size increases (7-10). The unique capability of ACD to collect data with the high geometric efficiency of a fan beam (transaxial CT; data collection in x, θ) or a cone beam (direct 3-D tomography; data collection in x, y, θ and ϕ, where ϕ is perpendicular to angle of rotation, θ) consistent with the assumptions of reconstruction tomography is also advantageous. SPC has the advantage, as discussed by Kuhl et al (4), Keyes et al (5), Jaszczak et al (6), and others, in that it can be used with either existing or new radiopharmaceuticals labelled with ^{99m}Tc and other commercially available radionuclides. This is contrasted to the disadvantage of ACD in the requirement of an on-site accelerator for studies employing ^{11}C, ^{13}N and ^{15}O. As has been discussed earlier (11) this disadvantage is however offset to some degree by the availability of a commercial generator system of ^{68}Ge-^{68}Ga, the generator system of ^{82}Sr-^{82}Rb and ^{18}F (commercially available). These positron emitting radionuclides could be used to label a wide variety of presently employed radiopharmaceuticals and for development of new labelled compounds to be used with the imaging advantages of ACD.

Cost is certainly another factor which must be considered. Keyes et al (5) have indicated that one of the motivations for using a camera for ECT is the lower cost resulting from the use of conventional technology. However, the "Humongotron" does not provide a convincing case in this direction. As a complete system, there are no expected cost differences between a SPC or ACD tomograph since the majority of cost factors are common to both systems. Cost does become a significant factor when one considers the desire to have an on-site capability for producing ^{11}C, ^{13}N, ^{15}O, etc. This matter must be resolved by clearly and definitively establishing the true bottom line cost for a compact, self shielded, reliable, simple to use cyclotron (or some other type of accelerator) consistent with the criteria and needs of a clinical environment (eg. not a flexible research machine). To this end, the National Cancer Institute has recently released a request for proposals (RFP) to design and build such a medical accelerator.

Keyes et al (5) have also discussed the advantage of being able to simultaneously record multiple slices with the gamma camera. However, this is really a cost-design decision as to whether the total system efficiency is oriented to maximize it in the 2-D projection (eg. like the camera) or the transaxial plane (eg. like most specifically designed transaxial tomographs). The latter has the tomographic advantage of being able to perform a single slice rapidly to minimize artifacts from movement of activity, organ or patient and the general advantage of maximizing the detector efficiency to the organ of interest (eg. much of a camera field of view includes regions above and below the organ which may not be important and thus a portion of system efficiency is lost). Even though all the ECT systems have the capability (or potential) to also provide a conventional 2-D projection image (eg. 2-D scan) the camera systems typically provide a higher efficiency and a stationary full field view in this imaging mode.

At this point there still remain advantages and disadvantages to SPC and ACD tomography and more definitive data are needed to clarify the individual points of concern. However, if we assume that the physical factors, instrument design and cost factors have been resolved, one must ask what is the objective of ECT. Is it to produce a better instrument, improve image contrast and spatial description

of lesions, improve detection rates etc? The answer to this question may rest in the understanding of what ECT allows one to do that couldn't be done before. Probably, the most important factor is the capability to tomographically section an organ into a map of quantitative tracer concentration with high resolution and accuracy. Thus added to image improvement from the removal of the superimposition of information in 2-D imaging and improvement in image contrast, is a means to measure physiologic function that has not existed in the past. ECT can be thought of as a technique for performing "in vivo autoradiography." The physiologic ECT models for this technique can be derived from autoradiographic and other existing models which can be put into a form consistent with the criteria of ECT.

The question has arisen frequently whether ECT can perform dynamic studies. In the conventional approach to dynamic studies such as blood flow with rapid time sampling the answer is probably negative because of statistical limitations. It should be remembered that in tomography one is trying to detect accurately the activity in very small volumes (eg. 1 or 2 cm cubes). In a conventional cerebral blood flow study with a gamma camera the image of the whole organ is severely limited statistically without imposing the added requirement of approximately an equivalent number of counts for each selected transaxial slice of the organ. If tomographic studies of dynamic processes are to be accomplished by rapid time sampling, the ECT must be: (i) able to collect all necessary angular and linear samples in a time short compared to tracer clearance rate (ii) efficient enough to collect required number of counts per plane to form an acceptable image and (iii) simultaneously record all planes required or subject patient to multiple isotope injections.

Thus it would appear that conventional dynamic studies and ECT are somewhat at odds. However, the term dynamic studies refers to a broader category of function measurements which can be accomplished by approaches which are consistent with ECT. This can be achieved by (a) rearranging the present dynamic models (differential equation rate models) to an accumulation (integral equations) model. Many of these models exist in the field of quantitative autoradiography and others can be developed by reformulation of existing dynamic models. For example, we have used an autoradiographic model and the MARK IV tomograph to measure the cross sectional distribution of the cerebral glucose metabolic rate in units of mg glucose utilized/min/100 gms with ^{18}F-2-deoxyglucose (12,13); (b) using labelled compounds which accumulate and are retained in tissue in proportion to blood flow, metabolism, etc. in which tissue concentration is static or slowly changing at time of measurement; (c) maintaining a static distribution with steady state infusions; (d) using dynamic models when the rate of the process is slow compared to ECT measurement time; (e) multiple short time sampling of repetitive motion of the heart.

The advent and rapid growth of x-ray CT has posed a significant challenge to Nuclear Medicine. However, the approach to CT can be divided into two categories: a) "morphologic tomography" with x-ray CT and b) "physiologic or function tomography" with ECT. Useful application of the former is advanced well ahead of the latter and efforts should be put forth to develop the unique capabilities of ECT to provide quantitative information about blood flow and volume (vascular perfusion, vasodialation, vasoconstriction, vasoparalysis, autoregulation, etc.), metabolism (cell viability, metabolic shunts, aerobic/anaerobic ratios, metabolic acidosis, etc.) substrate and ion transport and wide variety of other function indicators. The success of this approach is very much dependent on the availability of labelled

compounds whose properties are consistent with the above objectives. This aspect lends support to the concept of developing an accelerator based generator system for routine production of ^{11}C, ^{13}N, and ^{15}O because of the capability to synthesize chemically a wide variety of labelled natural substrates, analogues, drugs, etc. with biosynthetic (enzymatic and photosynthetic) and organic reactions. Thus, the chemical labelling capabilities and the types of labelled compounds produced will also play a determining role in the success of ECT and the selection of SPC or ACD.

ECT is a mathematical and physical concept, an instrument, a radionuclide tracer technique, a research procedure and it is certainly both an old (Kuhl began his work in the late fifties) and a new concept. It also has great and unique potential as a diagnostic technique. It is interesting that the basic principles of medical CT were exemplified and developed in Nuclear Medicine by Kuhl and coworkers and the concept of "physiologic or function tomography" provides a technique to advance the original charter of Nuclear Medicine in the use of radionuclides for the measure of metabolism and physiologic function.

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TABLE I: EMISSION TRANSAXIAL TOMOGRAPHS*

INSTITUTION OR COMPANY	APPLICATION	TYPE	DETECTION* MODE	TYPICAL SCAN++ TIME
Searle & Baylor	Head	Single Head Camera	SPC	20 min+
Univ of Aberdeen	Body	Single Head Camera	SPC	15 min+
Univ of Michigan	Body	Single Head Camera	SPC	20-30 min+
Donner Lab, Univ of Calif.	Body	Single Head Camera	SPC	30 min+
Univ of Aberdeen	Body	Sq. Array Scanner	SPC	3-15 min
UCLA (MARK IV)	Head	Sq. Array Scanner	SPC	1-5 min
Univ of Aberdeen & J & P Engineering Co	Body	Dual Head Scanner	SPC	15 min
UCLA & Ortec Inc (ECAT)	Body	Hexagonal Array Scanner	ACD	20-120 sec**
Washington Univ (PETT III, IV)	Body	Hexagonal Array Scanner	ACD	3-8,1-4 min***
Mass.Gen.Hosp. & Cyclotron Corp.	Body	Dual Head Mutl. Detector	ACD	10 min+
Searle & Univ of Chicago	Body	Dual Head Camera	ACD	10 min+
UCLA (CRTAPC)	Body	Circ. Array Scanner	ACD	20-60 sec
Montreal Neurol. Inst.	Head	Circ. Array Scanner	ACD	2-10 min
Donner Lab., Univ of Calif.	Body	Circ. Array Scanner	ACD	3 min

* SPC represents Single Photon Counting as employed in conventional scanners and scintillation cameras.
ACD represents Annihilation Coincidence Detection of positron emission.

\+ Simultaneous multiple planes

*** 4 simultaneous planes

++ Scan times given are not under the condition of the same image noise, resolution and dose.

** 10 sec scan capability.

* Adapted from table 2 reference 3