Emission Tomography: SPECT and PET

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ABSTRACT

Emission tomography is a medical image modality that utilizes molecules labelled with radionuclides, the *radiopharmaceuticals*, to obtain functional information about specific tissues or systems.
In SPECT, *Single Photon Emission Computerized Tomography*, the radionuclide decays by emitting one or more photons, while in PET, *Positron Emission Tomography*, the radionuclide emits a positron, in order to reach a lower energy level. Although the forms of energy emitted are different, the images are reconstructed from the information acquired by external detection of the emitted photons (SPECT) and the pair of annihilation photons (PET) in coincidence.
Due to the specificity and characteristics of these images, their information can be quantified, so that functional or metabolic parameters can be obtained for diagnostic or therapeutic purposes. However, in order to achieve reliable results, factors related to the instrumentation and patient conditions, as well as to the interactions between radiations and tissues and the reconstruction methods have to be considered carefully.
In this lecture, after the introduction of the fundamentals of nuclear medicine imaging, the basis of emission tomography acquisition and reconstruction will be presented. Some correction methods will be introduced in order to exemplify the current quantifications adopted in the clinical routine of molecular imaging.

Key words:
Emission tomography, functional imaging, iterative reconstruction, nuclear medicine, PET, quantification, SPECT.

I. INTRODUCTION

Emission tomography is a medical image modality that provides, basically, functional and/or metabolic information about an organ, a system or tissue. This is achieved by administrating radiopharmaceuticals to the patients and imaging the emitted radiation. The acquired information is useful not only for diagnostic purposes, such as detection of functional abnormalities or early identification of tumours, but also can be very helpful in therapy planning and follow-ups.

There are two types of emission tomography, depending on the decay mode of the chosen radionuclide: SPECT, *Single Photon Emission Computerized Tomography*, where the nucleus eliminates its energy by emitting one or more photons, and PET, *Positron Emission Tomography*, where the excess nuclear energy is emitted with a positron, anti-particle of electron. The tomograms are reconstructed from the external detection of the emitted photons or the pair of annihilation photons in coincidence.

II. IMAGE ACQUISITION

Radionuclide imaging is based on the principle that functional information can be obtained from external detection of spatial and temporal distributions of minute quantities of *radiopharmaceuticals* within the human body, under basically normal and non-invasive conditions.

A. Radiopharmaceuticals and Radionuclides

Radiopharmaceuticals are chemical compounds labelled with radionuclides, designed to provide information regarding specific physiological system. They are given to the patients by injection, orally or by inhalation, depending on their mechanisms of concentration in the organ or system under study. They can be presented as inorganic salt, gas, organo-metalic complex, organic molecule, etc.
Although there are no ideal radiopharmaceuticals, the following characteristics should direct the proper choice of an adequate compound: its concentration in the target organ or tissue should be higher than in non-target regions; the binding to the radionuclide should be strong enough for allowing the completion of the study; the radiation dose delivered to the patients should be as low as reasonably possible (ALARA principle) without degrading the diagnostic quality of the images; their preparation should be simple, convenient, fast and cost-effective; and they should interfere as least as possible with the normal physiological conditions of the patients.
There are several radionuclides presently in use in Nuclear medicine and they are produced either by

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nuclear reactors, as products of fission or neutron activation, or by particle accelerators (cyclotron or linear), as products of a nuclear reaction [(p,n), (p,2n), (d,n), (d,2n) or (α,2n)]. The radionuclide may also be a meta-stable daughter of a long-lived parent, eluted from a generator.

The most commonly used radionuclides in planar and SPECT imaging are listed in Table 1 and those in PET are presented in Table 2. Due to its facility in binding to a large number of molecules, as well as its physical properties and being available from generators, ^{99m}Tc (technetium 99m) is, by far, most widely used in Nuclear medicine. In the majority of PET studies, ^{18}F (fluorine 18), in the form of fluorodeoxyglucose (FDG), is administered to the patients as it has a longer half-live and does not need an on-site cyclotron for its production.

TABLE 1
COMMON γ EMITTER RADIONUCLIDES

Element	Half-life (h)	En γ (keV)	Production
^{99m}Tc	6.0	140	^{99}Mo generator
^{201}Tl	73	70-80; 135;167	cyclotron
^{67}Ga	78	93.5;184.5; 296;388	cyclotron
^{123}I	13.3	159; 285	cyclotron
^{131}I	8 days	284; 364;...	reactor (fission)
^{153}Sm	46.3	103; (also β$^-$)	reactor (n activation)

TABLE 2
COMMON β$^+$ EMITTER RADIONUCLIDES

Element	Half-life (mln)	En Max β$^+$ (MeV)	Production
^{11}C	20.4	0.959	cyclotron
^{13}N	9.96	1.197	cyclotron
O	2.07	1.738	cyclotron
^{18}F	109.8	0.650	cyclotron
Ga	68	1.899	cyclotron

B. Data Acquisition

Data acquisition in planar and SPECT imaging is fundamentally different from that in PET. In the former, the photons emitted by the nucleus, after traversing the human body, are detected and registered as a projection (2D distribution) by the scintillation camera. The projections are re-arranged as sinograms for tomographic reconstructions.

In PET imaging, the pair of photons, produced by the annihilation of the positron with an electron inside the body and travelled in opposite directions, is detected in coincidence by a pair of scintillators and the coincidence events are used for image reconstruction. There are two systems available for collecting PET data: the PET scanner, constituted by rings of small scintillation detectors which surround the patient, and the camera based system, formed by a two-head camera that rotates around the patient while recording the coincidence events as pair of projections. In both systems, the data can be collected in 2-dimensional (2D) mode, with the insertion of angle limiting septa, in or 3-dimensional (3D) mode, without septa.

As in all imaging procedure, the inherent factors that affect the image quality can be divided in 3 groups: instrumental, physical and patient's dependent. The first one includes all characteristics of the imaging system; the physical factors refer to the properties and interactions of the radiations with the traversed tissues; and the patient factors include the physiological aspects as well as those related to the patient preparation and pharmaceutical pathway. Most of these factors have to be considered and corrected if one seeks for quantification, especially if absolute values are aimed.

Instrumental degradations can be minimized if adequate tuning and routine quality control tests are consistently performed. These should be done according to one of the well established and accepted protocols (NEMA, IAEA, IEC, AAPM, HPA, etc.), using standardized phantoms.

Pharmaceutical labelling defects can be reduced if proper quality control is carried out and kits are stored under recommended conditions.

Some of the patients' dependent aspects can be reduced with their careful preparation and radiopharmaceutical administration protocols strictly followed.

The effects of interactions between radiation and tissues, on the other hand, are unavoidable and should be compensated for adequately.

As the radioactive decay is a statistical process, Poisson noise is present in all data acquisition procedure and any further data handling should

take this fact into account. However, as the noise varies in opposition to the acquisition time and the amount of activity administered, its contribution to possible uncertainties can be diminished if one increases either parameter, regarding that it does not pose further burdens to the patient.

III. IMAGE RECONSTRUCTION

The basic problem of reconstruction in emission tomography is to estimate a volumetric radioactive distribution from a set of 2 dimensional projections (camera based acquisitions) or a set of lines of response (ring detectors based acquisitions). As the amount of data, or projections, is limited, there is not a unique solution. Due to the statistical nature of radioactive decay and detection process, the presence of noise in the acquire data is inevitable, so that an exact solution is not achievable. Furthermore, small differences between projections, due to instrumental, physical, statistical or clinical factors, may introduce significant alterations in the reconstructed slices, leading to an unstable solution.

Although all these facts show that tomographic reconstruction is an ill-posed problem, it is feasible to obtain a solution close to the given distribution, both in the visual and the quantitative aspects, so that a diagnostically reliable result is generally possible.

There are basically 2 approaches to solve the problem of reconstruction: analytical and iterative, each one presenting its own advantages and limitations. The choice of one or the other depends basically on the clinical objective of the study and the computational facilities supplied by the imaging system manufacturers. On the other hand, if research conditions are available, it is possible to achieve results customized to local necessities by developing appropriate corrections and introducing reconstruction parameters not available in the commercial systems.

A. Analytical Methods

The strategy adopted by the analytical methods is to obtain the tomographic slices by solving the inverse problem of the projections, that is, from the set of acquired data, which form the Radon transform, estimate the distribution by inverting this transform. The most well known of these methods is the Filtered Back Projection (FBP), based on the Central Slice Theorem (*one dimensional Fourier transform of a projection equals to the 2 dimensional Fourier Transform of the slice to be reconstructed*), and easy to be implemented. On the other hand, it does not take into account any of the factors that were mentioned before and considers the data noiseless. Therefore, it is necessary to perform radiation interactions correction either before or after the reconstruction.

In general, FBP is available in all commercial nuclear medicine imaging systems and the resulting images are adequate for the majority of routine clinical problems. However, when accurate quantification of dimensions and parameters are required, the errors introduced by this method can be unacceptable.

B. Iterative Methods

Iterative methods start from a guess estimation of the object (it could be a uniform source), which is projected by an operator, which includes the major characteristics of the whole imaging process, and the resulting projections are compared to the acquired set and difference images are generated. These images are then used to modify the guess solution and new projections are generated and compared. This iteration is continued until a certain criterion is reached and the original object is obtained.

Iterative methods that have been developed for tomographic reconstruction include: Algebraic Reconstruction Technique (ART), Simultaneous Iterative Reconstruction Technique (SIRT), Maximum Likelihood-Expectation Maximization (ML-EM) and others.

The two major advantages of these methods that are responsible for better images (less artefacts, lower noise level, enhanced lesion delectability) and more accurate quantification are: possibility of including geometric and interaction models in the projector and noise modelling and treatment.

The critical points regarding the iterative methods are: a very large system of equations to be dealt with (for a 128x128x128 set of data, there are 2,097,152 equations with the same number of unknowns); iterative inversion of this large system; choice of a "distance" that should be minimized by the "best" solution; convergence can be slow and noise level increases with the number of iterations; need of high performance computing facilities in order to allow for routine application of these methods.

An accelerated version of ML-EM, the Ordered Subset Expectation Maximization (OS-EM) is,

presently, the only iterative method available in most commercial emission tomographic systems.

IV. IMAGE QUANTIFICATION

To quantify means to obtain a *number* that could describe some characteristic of an object. In medicine, quantification may lead to determination of normal ranges, identification and classification of abnormalities, estimation of functional or metabolic activities, planning and follow-up of therapies, amongst other objectives. The aimed quantity can be an absolute or a relative one. In the case of nuclear medicine, one can estimate the absolute radioactive concentration per unit volume in PET, or the relative activities within different regions of the patient, or in different time intervals, or between different patients and normal subjects in both SPECT and PET. One can also evaluate the function of the heart by calculating, for example, the ventricular ejection fraction, the regional perfusion and contraction. Volumes and dimensions can also be quantified if accurate geometrical calibration factors are available.
In the clinical routine, however, when only relative comparisons or a broad overview of the function are requested, most corrections are not performed and a qualitative result is presented to the referring physician.

A. Corrections

In order to obtain reliable quantification in SPECT and PET, some basic corrections or compensations are required. Although the basis of corrections is fundamentally the same for both modalities, in practice, they can differ as the instrumentation is not the same, the radiopharmaceuticals have distinct pathways and the radionuclides have different physical characteristics.
i – *Instrumental:* non-uniform and variable response of the imaging system (planar and tomographic spatial uniformity, non-linearity, non-uniform axial sensitivity, non-stationary geometric resolution, partial volume effect, etc.). These imperfections can be partially corrected with normalizing tables during acquisition; further compensations can be included in the projector used in the reconstruction process.
It is important that geometrical and sensitivity calibrations are measured accurately, so that dimensions and activities can be quantified in both 2D and 3D acquisitions.

ii – *Physical:* scatter and attenuation of the emitted radiations by the human body and decay of the radionuclide. The latter is usually corrected during acquisition, as the decay constant and the time lag between injection and data collection are known. The scatter fraction, which degrades the image contrast and incorporates events in misplaced positions, can be corrected either by adopting a protocol that also acquires this component to the images, or by estimating the scatter distribution with an accepted physical model. The attenuation, which leads to a significant loss of detected events, is corrected, nowadays, with the patient's own attenuation coefficients map, reconstructed from a set of transmission projections. Some systems have a radioactive source for this purpose, while others are supplied by a CT scanner.
In PET, it is necessary to correct for the random coincidence events, which can almost double the number of collected counts, depending on the acquisition mode, 2D or 3D and the electronic collimation implemented by the manufacturer. Usually it is corrected during the acquisition process.
iii – *Statistical:* The statistical nature of the acquired data can be taken into account in iterative methods that have this information incorporated in the projector. In the FBP reconstruction procedure, the noise is not corrected, but only smoothed out by using an adequate filter in place of the ramp in the filtering phase. In general, relative quantifications are acceptable when only smoothing is carried out. For example, in a FBP reconstructed synchronized SPECT myocardial perfusion study, noise can be smoothed out by adopting the Butterworth filter with critical frequency equals to 0.7 Nyquist frequency and order 4, the resultant polar maps provide diagnostically reliable information about the degree of blood supply and the motility in different regions of the myocardium.

B. Validation

As in any measuring and quantifying system, it is essential that testing of the reconstruction and quantification methods is performed, so that their performance, limitations and accuracies can be validated. These tests should start with simulated data, then, physical phantom studies and, finally, clinical studies.
Different approaches for simulating nuclear medicine studies had been developed. However, due to the many physical processes involved in emission tomography, the Monte Carlo method, which is a random sampling technique, has been

widely applied to simulate all the stages, from the emission of photons or positrons to the acquisition of the projections, passing through the interactions of these particles with the body and the detecting system. Specific characteristics of any intermediate stage, including the statistical nature of the radioactive decay and interactions, can be included in the modelling, so that realistic situations can be achieved.

There is not a unique test to be executed or parameter to be evaluated in all procedures. The choice will depend on the study and the accuracy aimed. On the other hand, if appropriate knowledge on instrumentation and radiopharmaceuticals, physical factors and reconstruction algorithms, fundamentals of physiology and clinical protocols is available, accurate and reliable results can be produced to enhance the diagnostic potential of emission tomography.

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