

RADIONUCLIDE IMAGING

Pages with reference to book, From 151 To 153

Syed Farooq Akber (Institute of Medical Science, University of Toronto, Ontario, Canada.)

Radionuclide imaging is a powerful medical diagnostic tool to monitor physiologic functions, as well as to evaluate distribution of radiopharmaceutical tracer within identifiable organs. This highly sensitive technique enables one to determine areas of abnormal tissues, but is not overly specific in defining the nature or importance of the abnormalities.

Initially, radionuclide tracer technique was designed to measure pathophysiological processes. Subsequently, the application and improvement of this technique has revolutionized research methods, led to a better understanding and insight of many fundamental biological processes and add new dimension in diagnostic information previously inaccessible. The availability of non-diffusible radionuclide tracers with high activity, short lived nuclides, improved scintillation cameras with rapid sequential imaging and memory capabilities and analog to digital processing have led to the development of the study of the dynamics of physiological function. This resulted in important physiological understanding of renal, cardiovascular, cerebral and pulmonary function.

In clinical nuclear medicine, radionuclides which are produced in nuclear research reactors or in accelerators (cyclotron) are labeled to a chemical compound. This upon administration to a patient, will localize within a specific organ. A chemical compound has specific receptor sites within the target organ and radionuclide acts only as an indicator of the physiological path of the chemical compound. Diagnostic information is abstracted from the radiopharmaceutical diluted in metabolic pathways. However, radionuclide imaging techniques do not depict structural anatomy like ultrasound, X-ray computed tomography (XCT) or conventional radiographs. It is the only established noninvasive technique available to investigate organ physiology, although recently Nuclear magnetic resonance (NMR) imaging technique has shown its capability to probe organ physiology and anatomy without ionizing radiation.¹

The gamma photons emanating from the nuclides inside the human body are detected externally by an Anger scintillation camera, a rectilinear scanner, single photon emission computed tomography (SPECT) or positron emission computed tomography (PET). The effective half-life of a radiocompound in the body is determined by the Physical half-life of the nuclide and the biological half-life of the clearance of a radiocompound from the body. It is therefore, important that radionuclides of appropriate energy and short physical half-life should be used. This facilitates an injection of a higher dose for better statistics, without enhancing the radiation exposure to the patient. However, the radiocompound tracers should be nontoxic and be taken up differently by normal and abnormal tissues. The radiocompound tracer activities are monitored within the organ by averaging either over time or count rate. Physical constraints of scintillation camera and rectilinear scanner restrict the spatial resolution and usually allows lesion of 1 to 2 cm in size to be resolved.

The instrument side of the radionuclide imaging is stagnant and no significant improvements have been made in either Anger scintillation cameras or rectilinear scanners. However, the availability of portable nuclear generators such as Technetium-99m (Tc-99m) have greatly enhanced the practicality of radionuclide imaging. PET has the disadvantage that since every hospital cannot afford to have a cyclotron, the use of PET scanners are accessible to only few large medical centers. It is therefore, apparent, that radionuclide imaging will be largely dependent on the state of the art-Anger scintillation cameras, rather than rectilinear scanners because the latter are becoming obsolete due to the better performance of Anger scintillation cameras and the inherent difficulties of rectilinear scanners such as low sensitivity and small depth response and cannot compare to the Anger scintillation camera for dynamic rapid sequential imaging.

The success of the PET scanner depends on the availability of a cyclotron to produce radionuclides of the basic organic building block elements such as oxygen, nitrogen, carbon, plus other elements such as fluorine. Despite the high cost of PET scanners and cyclotron, it has nevertheless, opened a new vista of radionuclide imaging. It enables one to monitor biochemical and physiological processes *in vivo*, including regional blood flow, oxygen consumption, metabolic glucose rate and the utilization of various substrates for energy metabolism and neuroreceptor mapping. The success of PET radionuclide imaging will enable the clinical radiochemist to label these compounds with single gamma emitting radionuclides such as Tc-99m, I-123, and Tl-201 in order to perform tomographic studies with SPECT, even though the above nuclides are poor competitors when compared to PET radionuclides such as C-11, N-13, O-15, and F-18. SPECT images are far inferior in resolution to those obtained by PET.

With currently available radiotracers and detectors it is possible to scan externally most of the organs of the human body. Despite the many advances that have been made in radionuclide imaging in recent years, the introduction of new tracers into clinical practice is declining. An analysis in 1977 on the status quo in radionuclide imaging, prompted Bennett² to state "that nuclear medicine needs some new ideas in radiopharmaceuticals--- the cheaper, the better."

The introduction of new radiopharmaceuticals will result in increased application of radionuclide imaging. There have been a few developments in radiopharmaceutical in the past decade that have resulted in commercial products This include thallium 201 for myocardial perfusion imaging and Tc-99m hepatobiliary agents for cholescintigraphy. The introduction of iodine-123 (I-123) in radionuclide imaging has provided new incentive to label biogenic amines, antibodies and free fatty acids. While biogenic amines and free fatty acids have already found their way onto clinical diagnostic inventories, antibodies for *in vivo* detection of tumors now seem ready for clinical trials.

In recent years uptake, turnover and clearance of biogenic amines have been demonstrated in the living beings³⁻⁵. The most promising of all bioamines is N-Isopropyl-I-123-P-Iodoamphetamine (IMP). IMP binds to nonspecific sites after intravenous administration in the brain in accordance with regional cerebral blood flow. It has also been used to study cerebrovascular disorders and metabolic activities of the brain. SPECT evaluation of the brain, using IMP, demonstrated a significant and sensitive role for IMP in the evaluation of Alzheimer's disease⁴. IMP has a reduced uptake in the posterior temporal and parietal regions in patients with such disease.

IMP also binds to high affinity sites located on the membranes of pulmonary endothelial cells. Analysis of the metabolic functions of the lung-especially the lung's effect on the concentration of circulating IMP-has opened a new vista of lung research using radionuclide imaging into the study of metabolic functions mechanism of extraction and physiological perturbation⁶⁻⁸

It is indeed fascinating to note that today in nuclear medicine no area holds more promise than the development of radionuclide labeled monoclonal antibodies. The labeling of radionuclide with antibody is critical in the sense that the technique of labeling does not alter the antibody molecule to the extent that it lost the desired specificity and affinity. A method such as conjugation by which a bifunctional chelate can be used to bind the radionuclide with antibody is therefore, needed.

The technique using monoclonal antibodies to deliver radiotracers to a tumor may not be limited to diagnosis but may be applicable for immunotherapy as well. By incorporating yttrium-90, which is a beta emitter suggests the possibility of treating localized tumors within an organ. Research on this aspect is in the offing and in the not too distant future, we may have antibodies labeled with suitable isotopes for the diagnosis and therapy of tumors in the human body.

Compared to other imaging modalities, radionuclide imaging will have a difficult time competing with NMR imaging. Radionuclide imaging, nonetheless, have a unique contribution to make to NMR imaging because of its emphasis on physiological and anatomical parameters. Radionuclide imaging can ameliorate the understanding of NMR imaging and conversely NMR imaging can help to distinguish regions of interest to be studied by radionuclide imaging. For example, in brain scan of

NMR, we cannot see metabolic processes very vividly while in radionuclide imaging, we can observe the metabolic pathways of biological radiotracer such as biogenic amine receptors and 2deoxyglucose metabolism. Radionuclide imaging and NMR imaging will be complementary modalities in the future. It appears that if radionuclide imaging is to play a pivotal role in diagnostic imaging, improvements have to be made in instrumentation and new effective tracers have to be introduced in clinical practice to make radionuclide imaging a more comprehensive modality.

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