



## Editorial

### The Revolutionary Impact of Modern Imaging Techniques on the Assessment and Management of Patients with Neurological Disorders

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The discovery of Xray by Roentgen in 1895 had a major impact on the practice of medicine in most organ systems but minimally influenced the practice of neurology for seven decades. The introduction of Xray Computed Tomography (XCT) by Hounsfield in 1971 changed dramatically the assessment of certain disorders of the brain. In particular, surgical and medical treatment of patients with traumatic brain injury has improved substantially. The use of contrast enhancement has improved the ability to detect lesions with blood-brain barrier abnormalities. This includes primary and metastatic brain tumors over the past four decades. However, the low sensitivity of CT scan in detecting soft tissue abnormalities has hindered its widespread use in many neurological disorders. Therefore, recently interest has shifted to novel approaches to overcome this deficiency.

Soon after, the invention of XCT, several reports appeared in the literature describing the potential use of Nuclear Magnetic Resonance (NMR) imaging of the brain and other organs as a means to assess soft tissue abnormalities. This methodology eventually led to the introduction of modern instruments based on the detection of NMR signals and reconstruction of tomographic images by 1980. The imaging modality was renamed Magnetic Resonance Imaging (MRI), and it has

dominated the field of neuroimaging over the ensuing years. The use of MRI has significantly influenced the practice of neurology and neurosurgery, and currently is the imaging method of choice in assessing brain disorders.

Despite the successes achieved by XCT and MRI, many conditions cannot be detected by these techniques, either early in their course or late. This deficiency stems from the fact that many brain abnormalities are due to alterations at the molecular level which may never translate to significant structural changes detectable by the methods. In recent years attempts have been made to overcome the low sensitivity of structural techniques by utilizing radiolabeled compound-based imaging.

The concept of imaging with radiolabeled preparations was introduced at the University of Pennsylvania in the late 1950's and led to the construction of imaging instruments in the early 1960's. This approach was initially achieved by the use of single gamma emitting radiolabeled tracers, and was primarily used to image blood-brain barrier abnormalities. The imaging modality is called Single Photon Emission Computed Tomography (SPECT). Over the years this technique has matured and become the modality of choice for the practice of conventional nuclear medicine world-wide. However, significant difficulties have been encountered in labeling single gamma emitting radionuclides to biologically important compounds. Therefore, major efforts have been directed at the utilization of positron emitting elements.

The paradigm shift from SPECT to imaging with positron emitting tracers occurred in the early 1970's at the University of Pennsylvania where investigators were assessing brain function with <sup>14</sup>C labeled deoxyglucose (CDG) in animals. This compound mimics glucose metabolism and is phosphorylated to CDG-6-phosphate which remains intracellular for an extended period of time. This tracer, along with a methodology called autoradiography, was shown to reveal brain function on a regional basis by the examination of post-mortem slices of the brain. Using physiologic stimuli such as tactile and visual activation, these investigators demonstrated the corresponding cortical sites in the brain with auto-radiographic images. Such observations resulted in a project to synthesize <sup>18</sup>F-deoxyglucose, which was initiated in 1973. By August

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1976, this compound (18F-deoxyglucose, FDG) was successfully synthesized tested in animals by investigators at the Brookhaven National Laboratory and subsequently was transported to the University of Pennsylvania for tomographic images of the brain and planar images of the whole body in human subjects. This major breakthrough in molecular imaging over the past 40 years has revolutionized molecular and functional imaging of normal and diseased brain in many disciplines. Investigators have demonstrated the role of FDG in better understanding of brain function in the resting and stimulated states. This has substantially improved our knowledge about brain function in normal aging. The practice of neurology and psychiatry has been affected by the use of FDG-PET, particularly in detecting cognitive abnormalities including dementias such as Alzheimer's disease and fronto-temporal dementias. This technique is used to detect seizure sites in frontal lobe epilepsy for surgical intervention. FDG-PET has become the most sensitive technique to assess traumatic brain injury and its change over time.

The major impact of FDG PET imaging has been in patients with cancer including brain tumors. This approach allows differentiation of low grade tumor from highly aggressive

cancers and thus better prognostication. It can differentiate recurrent tumor from radiation necrosis and now is the method of choice. FDG PET imaging has revolutionized the field of medical and radiation oncology, and oncology currently is the most important application of this method.

The impact of PET goes far beyond what has been achieved with FDG-PET imaging. We can now label many novel compounds to visualize molecular processes in the brain. For example, DOPA labeled with 18F (FDOPA) allows detection of presynaptic neuronal loss in the basal ganglia in patients with Parkinson's Disease, years ahead of clinical manifestation of the disease. Major efforts have been made to visualize amyloid plaques and Tau based tangles in the brain of patients with suspected Alzheimer's disease. Most pharmaceutical companies are now using PET imaging to develop new drugs directed neurological disorders.

Overall, the impact of PET has been more substantial than structural imaging such as CT and MRI. The potential for growth of PET imaging is enormous, and we expect the use of this technique will improve our ability to manage neurologic disorders in the future.