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Guest Editorial
Evaluating Pathology in the Brain With Nuclear Medicine

Neuronuclear imaging studies, particularly using positron emission tomography (PET) and single-photon emission computed tomography (SPECT), have advanced our understanding of the biologic function and molecular interactions, as well as the pathologic changes, occurring in the human brain in numerous ways. These studies have enabled us to monitor or measure processes as diverse as cerebral blood flow, metabolism of glucose, utilization of oxygen, uptake of amino acids, penetration of the blood–brain barrier, rate of various enzymatic activities, accumulation of aberrant proteins, as well as levels of synthesis, presynaptic uptake, synaptic entry, and postsynaptic binding of neurotransmitters and neuromodulators in functioning brain tissue. In doing so, they cast light on pathologic events in ways that inform us about underlying causes, diagnoses, prognoses, therapeutic responses that have occurred, and responses to possible therapeutic options that are likely to occur (or not occur) in individual patients.

In this issue of *Seminars in Nuclear Medicine*, most of the topics (evaluations for brain death, epilepsy, cognitive decline, brain tumors) were selected for inclusion to provide critical review of the current status of neuronuclear imaging applications that have become clinically well-established and to point toward future directions in which those applications may be expanded. The other topics (neuroimaging for central motor dysfunction, mood disorders) have been selected, among a wide array of potential contenders, based on how epidemiologically important the conditions that they represent are, coupled with there being a sufficient base of data surrounding the pertinent imaging studies to point to the likelihood of increasing interest in their clinical utility in the future.

The first article presents the current state of the art for deriving maximal reliable information from SPECT and PET studies of patients with epilepsy intractable to medical therapy, who are undergoing evaluation for neurosurgical candidacy. In addition to the use of commonly employed perfusion and metabolic agents, the potential role of a variety of tracers of neurotransmitter/neuromodulator systems is discussed, and the value of image quantification and statistical analysis methods is examined. The contributions that dedicated small-animal imaging methods are poised to make to the understanding of epilepsy, and to the acceleration of translational drug studies, are also considered.

Both initial characterization and post-treatment monitoring of primary brain tumors have always been challenging to adequately assess through neuroimaging, and the development of effective treatments for most kinds of brain tumors has been even more challenging. As related in the second article, significant progress in meeting both of these challenges is being made, partly through the study of how best to employ newer imaging agents, and through the advent of new therapeutic strategies. The latter development has heightened the importance of being able to accurately evaluate patients with brain tumors early, identifying the most appropriate candidates for new treatments or combination regimens that may have a favorable impact on slowing or halting progression of an often deadly disease, while allowing earlier discontinuance of treatments that will be ineffective for those individuals.

Among all the clinical indications for which radiologists and nuclear medicine physicians read brain PET scans, the demand is greatest for those pertaining to Alzheimer's disease and related disorders. This demand is driven by the high (and growing) prevalence of those conditions, coupled with the problem that the differential diagnosis for causes of cognitive impairment is wide, and often difficult to distinguish clinically. In the third article, progressive changes in the brain observed with PET, seen in people ranging from those who experience no or very mild symptoms and are clinically considered to be normal for their age, to those suffering from full-blown dementia, are examined, as is the role of PET in assisting with the differential diagnosis of the underlying cause for cognitive decline.

Nowhere is the role of nuclear medicine in making life and death decisions more apparent than when neuronuclear imaging is used in the evaluation of brain death. The fourth article describes the various radiotracers and techniques that are available to assist with that evaluation, and particularly examines the meaning of discordance of nuclear imaging with results of clinical studies. In addition to the insights offered in the text, the figures presented here bring together

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an outstanding mix of structural imaging, functional imaging, and clinical information for the cases they illustrate.

As with the cognitive decline described in the third article, motor dysfunction is also often attributable to neurodegenerative disease, while being accompanied by a differential diagnosis that can be difficult to sort through clinically, particularly in its early stages. The fifth article examines neuronuclear imaging studies explicitly aimed at illuminating changes in the brain associated with central movement disorders. Their potential utility with respect to drug development, as well as in direct clinical application, is explored.

The single most disabling neuropsychiatric condition, in terms of the sheer number of people-years affected, is depression. The last article articulates the roles that neuronuclear imaging can play in its evaluation. A special focus of this article is the refinement of the monoaminergic model of depression, which brain PET imaging is helping to elucidate.

In my editorial role, I greatly appreciate the efforts expended and expertise shared by the authors who have contributed to this issue, illuminating the present power and future potential of nuclear medicine to assess pathology in living brain matter. Over the past 3 decades, the conceptual framework within which the evaluation and management of neurologic/psychiatric conditions occur has evolved considerably, in parallel with developments in neuroimaging. The articles in this issue delineate the diverse roles of nuclear medicine in improving our understanding of these conditions, as well as the health of patients suffering from them.

Daniel H.S. Silverman, MD, PhD
Guest Editor