Using Brain Perfusion SPECT with Q.Brain for Identifying Progression to Alzheimer's Disease

Along with increased life expectancy comes a growing incidence of neurodegenerative diseases, such as Alzheimer's disease (AD). Pathologically, AD is characterized by the presence of amyloid deposition and neurofibrillary tangles along with the loss of cortical neurons and synapses.[1] People afflicted with this disorder have a gradual deterioration of cognition, behavior and function.[2] Recent advancements in therapies, such as cholinesterase inhibitors, have been shown to provide greater benefits in patients who start therapy early in the course of AD.[3]

At the National Center for Neurology and Psychiatry, Hiroshi Matsuda, MD, PhD, Director of the Integrative Brain Imaging Center, utilizes a multi-modality approach along with behavioral and psychological examinations to diagnose dementia and AD—and differentiate these neurodegenerative diseases from other psychological disorders such as delirium or depression. Diagnosing dementia cannot be determined by one type of examination, as it is possible for a person with higher levels of education and knowledge to fall within normal ranges in a cognitive neurological exam (known as cognitive reserve). Rather, it requires combining several types of examinations such as a psychological exam, family interviews, blood tests, review of medical history, and imaging exams using CT, MRI and SPECT.

"To make a confident and early diagnosis of Alzheimer's or dementia, we must perform various tests and judge comprehensively," Dr. Matsuda says. He adds that one primary challenge in this type of diagnosis is the ability to predict if a patient is moving from mild cognitive impairment (MCI) to AD.

According to Dr. Matsuda, while the concept of MCI may be heterogeneous, there is an increased recognition that the most common subtype, amnestic MCI, likely progresses to AD. Medications such as cholinesterase inhibitors have been shown to delay the progression of AD; however, when this course of treatment is delayed there are fewer demonstrated benefits compared to when starting treatment earlier in the course of AD.[3,4]

Essential information on a patient's typical behavior is collected through family interviews to help separate dementia, delirium and depression. Cases of sudden cognitive dysfunction progression and REM sleep behavior disorders are highly suggestive of Lewy Body Disease, a progressive dementia caused by abnormal microscopic deposits that damage brain cells over time.

Medical imaging, such as SPECT, can help support a neurologic exam and provide an early differential diagnosis that referring physicians seek in order to commence with appropriate therapy, Dr. Matsuda explains. Roughly 150 brain SPECT exams are performed each month at his center to help detect dementia and differentiate it from other neurological or psychological disorders.

"CT is the first imaging exam to eliminate the absence of physical factors, such as a brain tumor or cerebral infarction, that could account for cerebrovascular dementia," he adds. A voxel-based specific regional analysis system (VSRAD) using MRI is also often employed to analyze atrophy of the hippocampus. However, Dr. Matsuda believes the initiation of treatment based on MRI without an accompanying SPECT study is less than ideal.

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>
> *Dr. Hiroshi Matsuda*

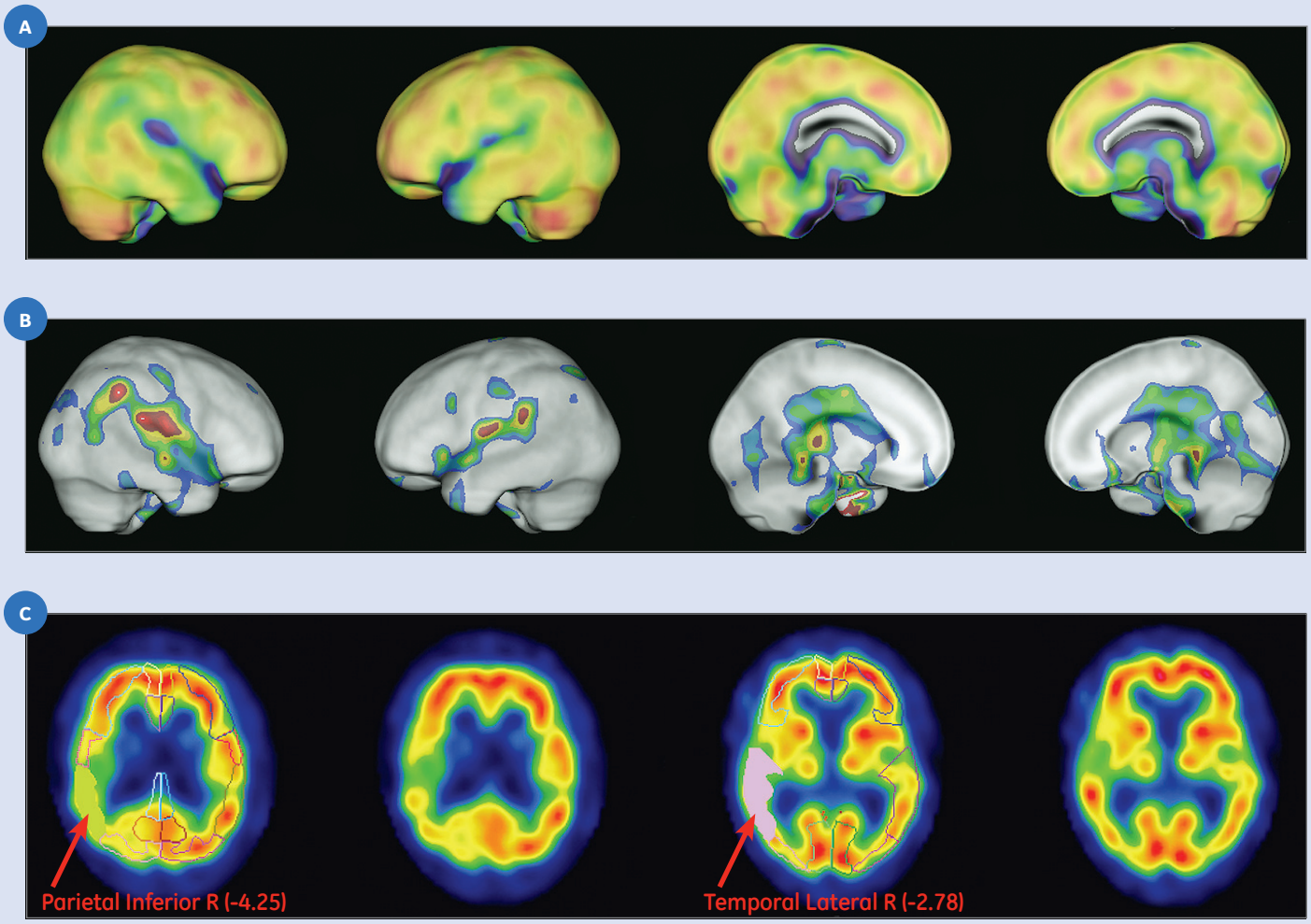

Figure 1. A 78-year-old woman with slowly progressive memory impairment over the last five years. Mini-mental state examination score 24. (A) Q.Brain result with perfusion image registered to the MNI space atlas; (B) Results from Q.Brain statistical analysis. (C) Perfusion analysis across the regions demonstrate areas of significant hypoperfusion, marked with arrows and z-scores. Evidence of perfusion reduction in right temporoparietal cortex and bilateral posterior cingulate cortices, compatible with mild cognitive impairment due to Alzheimer's disease.

"Brain perfusion SPECT can clearly show clinical findings in patients who are in their 40s and 50s," Dr. Matsuda explains. "However, in patients who are in their 70s, it may be difficult to differentiate mild dementia from AD. Therefore, a final diagnosis should be based on information from a combination of MRI and SPECT imaging test results. When used together, MRI and SPECT can provide a differential diagnosis in 70-80% of patient cases."

Adding amyloid PET imaging enhances the confidence and reliability of a diagnosis by further reducing false positives. However, PET FDG scans indicated for dementia are not presently reimbursed in Japan.

Statistical analysis (z-score) of brain SPECT data is frequently utilized by Dr. Matsuda and his colleagues at National Center for Neurology and Psychiatry. Quantitation of cerebral blood flow using a Patlak Plot and software such as Q.Brain can also help Dr. Matsuda differentiate between the types of dementia, such as AD or vascular dementia.

Acquisition
^{99m}Tc - ECD 600 MBq inj.
LEHR
3 min. continuous mode * 6 rot = 18 min.
Chang AC, scatter correction

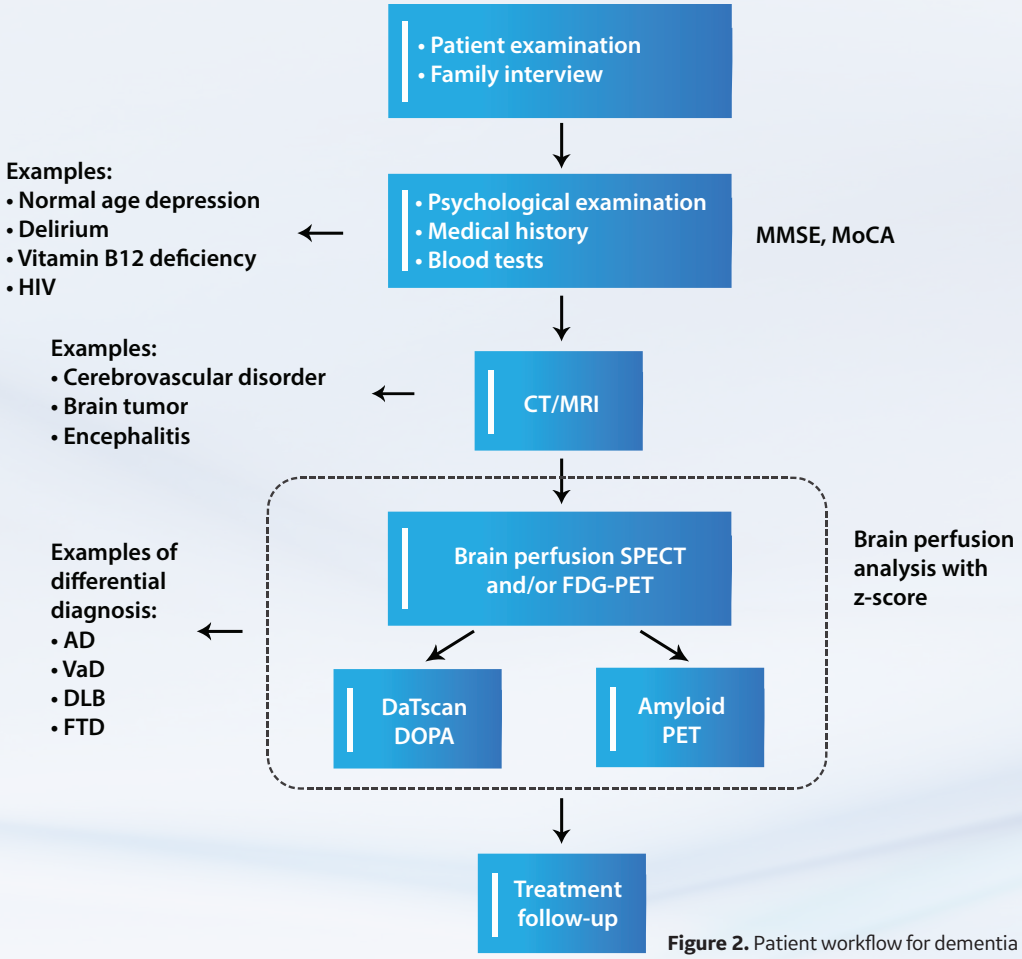

Figure 2. Patient workflow for dementia diagnosis.

In addition, cases of diffused flow reduction often indicate depression rather than dementia.

Furthermore, the use of 3D stereotactic surface projection (3D-SSP) for SPECT data analysis does not require structural images, rather it utilizes data from the medial and lateral brain surfaces. Processed data can then be used for intersubject comparisons with either t or z statistics; this technique has been used frequently in the cross-sectional studies of dementia. However, 3D-SSP can lose information that SPECT inherently provides.

Another technique commonly utilized in Japan is tomographic z-score mapping, an automated voxel-by-voxel analysis of z-score values as a volume of interest (VOI) that also incorporates statistical parametric mapping.

Q.Brain is a software solution used by Dr. Matsuda that enables evaluation of both 3D-SSP and quantitative analysis of z-scores to help identify patients with early onset of AD. Q.Brain standardizes individual brain shapes through its registration to a standard atlas while preserving functional information. With Q.Brain, numeric uptake values are added to reports and compared to a normal patient database, since visual inspections or VOI techniques may not be sufficient for accurate diagnosis.

Published studies suggest that using SPECT studies for regional cerebral blood flow analysis in patients with MCI may help predict those who will progress to AD.[5,6] ■

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