Quantitative SPECT Leads to Improved Performance in Discrimination Tasks Related to Prodromal Alzheimer's Disease

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We investigated the impact of the quantitation and reconstruction protocol on clinical tasks. The performance of standard clinical reconstruction procedures in discrimination tasks related to the diagnosis of prodromal Alzheimer's disease (AD) was compared with the performance of a quantitative approach incorporating improved corrections for scatter, attenuation, intrinsic spatial resolution, and distance-dependent spatial resolution. **Methods:** Seventeen normal controls (normal group), 56 subjects who did not have dementia, who did have memory problems, but who did not develop AD within 5 y of follow-up (questionable group), and 27 subjects who did not have dementia, who did have memory problems, and who did develop AD over the follow-up period (converter group) were considered in this study. ^{99m}Tc-hexamethylpropyleneamine oxime SPECT and MRI studies were performed for each subject at baseline. The standard quantitation protocol (STD), routinely used in our clinic, consisted of Compton window scatter correction followed by filtered backprojection with attenuation correction using a uniform attenuation map. In the improved quantitative approach (QUAN), projections were corrected for scatter by use of a general spectral method and reconstructed by use of ordered-subset(s) expectation maximization, incorporating corrections for collimator response and attenuation using both a uniform attenuation map (QUANunif) and a nonuniform attenuation map (QUANnonunif). Mean SPECT activity concentration and MRI volume were estimated for 7 structures: rostral anterior cingulate gyrus, caudal anterior cingulate gyrus, posterior cingulate gyrus, hippocampus, basal forebrain, amygdala, and the banks of the superior temporal sulcus. Data were analyzed by pairwise discriminant analysis, and performance in binary group discrimination was measured by correlated receiver-operating-characteristic analysis. **Results:** The use of QUANnonunif yielded a small but systematic improvement in discrimination accuracy for normal versus converter groups (accuracy or area under the receiver-operating-characteristic curve [Az], 0.965), normal versus questionable groups (Az, 0.973), and questionable versus converter groups (Az, 0.881) compared with the results obtained with QUANunif (Az, 0.955, 0.962, and 0.866, respectively). Discrimination performance was significantly lower ($P < 0.05$) with STD than with QUAN in all 3 tasks (Az with STD, 0.906, 0.878, and 0.768, respectively). MRI volume estimation led to a lower overall performance in all 3 tasks than did QUANnonunif (Az with MRI, 0.947, 0.917, and 0.872, respectively). **Conclusion:** Improved quantitative image reconstruction with accurate compensation for scatter, attenuation, and variable collimator response led to significantly better performance in discrimination tasks related to the diagnosis of prodromal AD than did standard clinical reconstruction procedures. The use of a nonuniform brain attenuation map yields a small improvement in discrimination accuracy.

Key Words: quantitative brain SPECT; prodromal Alzheimer's disease; iterative reconstruction; attenuation correction; scatter correction; resolution recovery

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Scatter, attenuation, and variable collimator response corrections are required for quantitative brain SPECT. In most clinical brain studies, however, uniform attenuation of the brain is assumed, and scatter and variable collimator response are ignored. Several studies have compared uniform and nonuniform attenuation correction schemes for quantitation in SPECT (*1–4*). These studies used simple phantoms or patients for whom no gold standard was available.

It is known that established Alzheimer's disease (AD) is characterized by perfusion abnormalities; the most consistent finding in mildly or moderately impaired patients with probable AD is decreased perfusion, compared with that in controls, in the temporoparietal association neocortex (*5–8*). There is currently great interest in determining whether perfusion abnormalities precede overt disease. Identification of brain perfusion patterns that predict the subsequent development of AD has practical as well as theoretic significance; early prediction of AD would make it possible to implement strategies to prevent or delay dementia. Decreased perfusion in the posterior cingulate gyrus in pro-

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Representative Results:

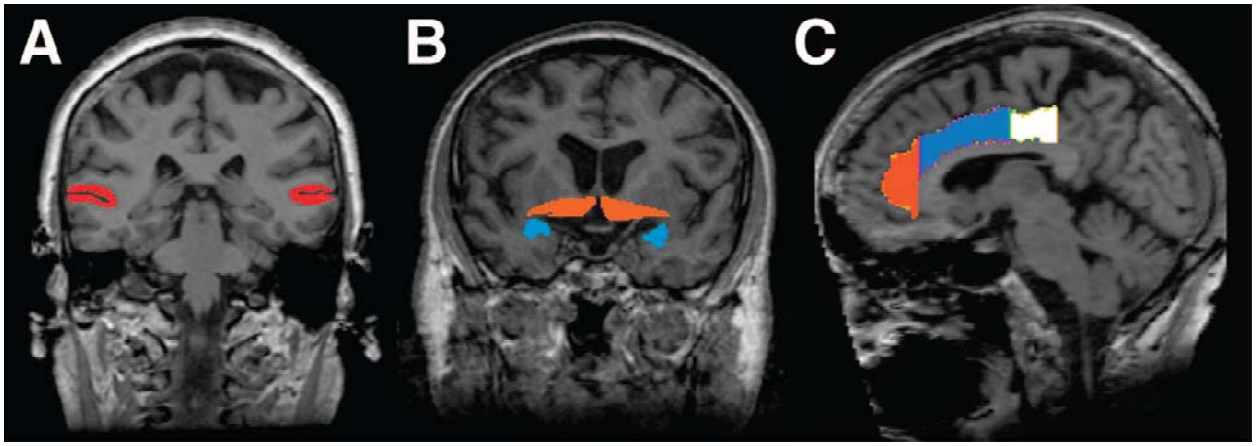

FIGURE 1. Locations of 6 VOIs defined on MR images used in SPECT-based discrimination tasks. (A) Banks of superior temporal sulcus (red). (B) Basal forebrain (orange) and amygdale (blue). (C) Rostral anterior cingulate gyrus (orange), caudal anterior cingulate gyrus (blue), and posterior cingulate gyrus (white).

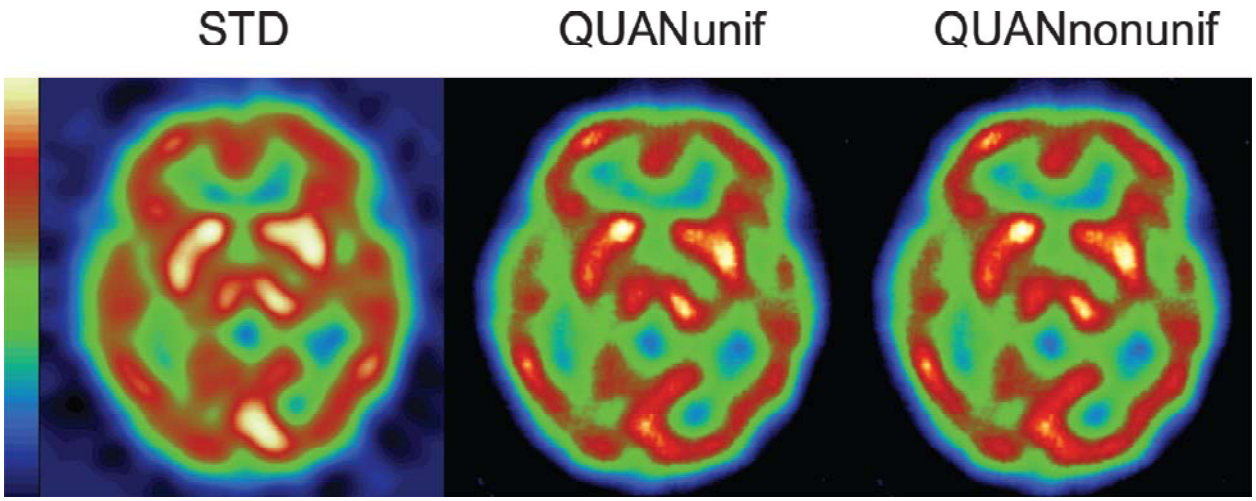

FIGURE 3. Transverse slice of a converter study reconstructed with STD, QUANunif, and QUANnonunif.