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*Reply:*

T.P. Tanpitukpongse and J.R. Petrella

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**REPLY:**

**W**e thank Dr Haller for his recent letter regarding our publication, “Predictive Utility of Marketed Volumetric Software Tools in Subjects at Risk for Alzheimer Disease: Do Regions Outside the Hippocampus Matter?”

We restricted our study to NeuroQuant (CorTechs Labs, San Diego, California) and Neuroreader (Brainreader, Horsens, Denmark) because they have received FDA 510(k) marketing clearance and physicians are likely to use them in everyday practice. Also, these packages use a probabilistic atlas-based segmentation on non-uniformity-corrected 3D T1-weighted images to derive absolute volumes of a variety of cortical and subcortical structures (and are not voxel-based morphometry–derived gray matter concentrations, as stated by Dr Haller).

We fully agree with Dr Haller that areas outside the medial temporal lobe play a role in the evolution of Alzheimer disease (AD); indeed, we and others have previously documented the value of using multiple markers, including other brain regions.<sup>1,2</sup> Nevertheless, the earliest synaptic lesions in AD are thought to be in the medial temporal lobe, and MR imaging hippocampal volumes are one of the markers used in newer diagnostic criteria for mild cognitive impairment (MCI) due to AD.<sup>3</sup>

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Clearly, MCI and dementia are heterogeneous in their pathology, presentation, and outcomes; using multiple anatomic and molecular biomarkers will no doubt help us better personalize diagnosis and therapy.<sup>4</sup>

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**T.P. Tanpitukpongse**  
UNC Rex Healthcare  
Raleigh, North Carolina  
**J.R. Petrella**  
Duke University Health System  
Durham, North Carolina