Misclassified Tissue Volumes in Alzheimer Disease Patients With White Matter Hyperintensities
Importance of Lesion Segmentation Procedures for Volumetric Analysis

Naama Levy-Cooperman, BA; Joel Ramirez, MSc; Nancy J. Lobaugh, PhD; Sandra E. Black, MD

Background and Purpose—MRI-based quantification of gray and white matter volume is common in studies involving elderly patient populations. The aim of the present study was to describe the effects of not accounting for subcortical white matter hyperintensities (WMH) on tissue volumes in Alzheimer Disease patients with varying degrees of WMH (mild: n = 19, moderate: n = 22, severe: n = 18).

Methods—An automated tissue segmentation protocol that was optimized for an elderly population, a brain regional parcellation procedure, and a lesion segmentation protocol were applied to measure tissue volumes (whole brain and regional lobar volumes) with and without lesion segmentation to quantify the volume of misclassified tissue.

Results—After application of the tissue segmentation protocol and lesion analysis, mean total percentage misclassified volume across all subjects was 2% (17.9 cm³) of whole brain volume (corrected for total intracranial capacity). Mean percentage of misclassified tissue volumes for the severe group was 4.8% of whole brain, which translates to a mean volume 42.2 cm³. Gray matter volume was most overestimated in the severe group, where 6.4% of the total gray matter volume was derived from misclassified WMH. The regional analysis showed that frontal (41%, 7.4 cm³) and inferior parietal (18%, 3.25 cm³) lobes were most affected by tissue misclassification.

Conclusion—MRI-based volumetric studies of Alzheimer Disease that do not account for WMH can expect an erroneous inflation of gray or white matter volumes, especially in the frontal and inferior parietal regions. To avoid this source of error, MRI-based volumetric studies in patient populations susceptible to hyperintensities should include a WMH segmentation protocol. (Stroke. 2008;39:1134-1141.)

Key Words: MRI ■ Alzheimer disease ■ white matter hyperintensities

Over the past 25 years, the availability of MRI has progressed to a point where clinicians and researchers have an array of sophisticated image-processing techniques at their disposal. In structural neuroimaging, automatic segmentation algorithms can be used to obtain volumetric information derived from voxel intensity differences with a set of multi-modal MRIs of the brain. Segmentation techniques vary in approach but generally provide the same information—tissue volumes for gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF).1,2 There are numerous ways of obtaining brain tissue volumes in structural neuroimaging. Probability map registration involves the use of templates (eg, Talairach) in a software package.3 The Statistical Parametric Mapping (SPM) package uses a template-based approach where a scalar function of a spatially normalized image can be applied to groups of subjects, such as in voxel-based morphometry (VBM) techniques.4 Mathematical modeling such as discriminant analysis2,5 or Gaussian curve fitting1 apply mathematical models to generate intensity ranges for each brain tissue type. Artificial intelligence/fuzzy logic algorithms (eg, fuzzy c-means algorithm) involve procedures where class rules are generated by a blinded expert followed by an iterative clustering process where tissue labeling occurs based on the predefined class/tissue type rules.6,7 Still others use combinations of approaches creating multi-agent approaches8 or pattern recognition approaches.9

One limitation of many automatic tissue segmentation procedures is that they are generally based on T₁-weighted images. As such, they are not designed to account for the frequent presence of focal or diffuse signal changes seen on T₂-weighted images as hyperintensities in the cerebral white matter of both asymptomatic and cognitively impaired elderly individuals. These areas of increased signal intensity are typically referred to as white matter hyperintensities (WMH) and can be seen on T2-weighted, proton density (PD) spin...
and Fluid Attenuated Inversion Recovery (FLAIR) images. WMH may indicate the presence of small vessel ischemic vascular disease and are particularly common in individuals with cerebrovascular risk factors or stroke. However, the high prevalence of WMH observed in healthy individuals over 50 years of age suggests that they are a common age-related phenomenon. Unfortunately, because many segmentation procedures do not incorporate PD/T2 data, they cannot account for any change in T1-weighted contrast attributable to the presence of WMH.

The pathophysiological origins of WMH are diverse and include multiple cerebrovascular and neuropathological factors, ranging from so-called “incomplete” infarction, dilation of perivascular spaces, gliosis, demyelination, clasmatodendrosis (cytoplasmic swelling and vacuolation of astrocytes), and small deep white matter microcystic and lacunar infarcts. Recently, harmonization standards have been recommended for research involving cognitive impairment related to vascular factors, which include suggestions for qualitative measurement of WMH. The present study emphasizes the need for similar guidelines in studies that attempt quantitative brain measures in individuals with dementia because of the ubiquity of white matter disease in the elderly.

Given that automated tissue segmentation techniques segment the whole brain into gray, white, and CSF volumes, the absence of an additional WMH segmentation procedure could potentially inflate volumes in some of these tissue types. Thus, depending on the signal intensities and the features of the segmentation algorithm, WMH would be allocated to the GM, WM, or CSF volumes. This study quantifies this misallocation in an Alzheimer Disease (AD) dementia population with varying degrees of cerebrovascular disease to investigate this potential error. A robust T1-weighted segmentation protocol, combined with a brain regional parcellation technique, and a semiautomated lesion segmentation protocol was used to determine: (1) the types of misclassification, (2) the extent of misclassified tissue volumes, and (3) the brain regions most affected.

### Methods

#### Participants

Subjects in the present study were part of the Sunnybrook Dementia Study and were recruited from the Cognitive Neurology Clinic at Sunnybrook Health Sciences Centre, a University of Toronto academic healthcare institution. Patients were excluded for this study if they had concomitant neurological disorders including clinical stroke or Parkinson disease; history of signifi-
cortex head trauma, psychotic disorder unrelated to dementia, psychoactive substance abuse, or major depression. Patients in this study had the historical profile typical of AD with insidious onset of short term memory loss and gradual decline. The patients were enrolled in a longitudinal observational study using the same standardized protocol. All patients received a comprehensive clinical evaluation, including detailed medical history, neurological examination, routine laboratory investigation, and neuropsychological testing with a standardized test battery. The presence of cerebrovascular risk factors was ascertained including: arterial hypertension, diabetes, hyperlipidemia, and cardiac disorders such as coronary artery disease. All patients in this study met National Institute of Neurological and Communicative Disorders and Stroke–Alzheimer Disease and Related Disorders Association criteria for probable or possible AD, and Diagnostic and Statistical Manual of Mental Disorders - Fourth Edition criteria for dementia. “Possible AD” diagnosis was based on the presence of sufficient subcortical cerebrovascular disease to contribute to dementia, but not enough to meet criteria for Vascular Dementia (VaD). For this study, patients were excluded if they met the National Institute for Neurological Disorders and Stroke–Association Internationale pour la Recherche et l’Enseignement en Neurosciences criteria for possible or probable VaD, which requires focal neurological signs in addition to imaging evidence of CVD. Presence of silent cortical strokes on MRI also excluded the patient.

A consensus derived rating scale developed under the auspices of the European Task Force in Age-Related white Matter Changes was used to rate WMH severity (ARWMC) and subclassify patients by severity of WMH (Reported $\kappa = 0.67$; Our Group $\kappa = 0.89$). The ARWMC was selected because it was designed to address some of the reliability problems encountered with previous scales. Details of this scale have been published elsewhere, and the ARWMC has shown promise in a study of WMH progression in AD. Severity of WMH was rated on PD and T2-weighted MR images in 5 regions in each hemisphere: frontal, parieto-occipital, temporal, basal ganglia, and infratentorial. WMH were accepted if they appeared on both PD- and T2-weighted images and if they were at least 5 mm in diameter. Severity was graded from 0 (none) to 3 (severe) based on the appearance of the WMH. A measure of global severity was derived by summing the ratings for the 5 regions.

The following criteria were applied to classify patients into Severe, Moderate, or Mild WMH subgroups. Severe WMH patients had extensive periventricular or deep white matter hyperintensities (visual rating scale score of 3 [diffuse involvement] in 2 areas and 2 [beginning confluence] in 2 other areas). Moderate WMH patients had a score of 1 (focal lesions) in more than 1 area or a score of 2 (beginning confluence) in any area. Subjects with minimal (ie, no more than 1 small focal, nonlacunar hyperintensity) or no WMH were designated as having Mild WMH.

### Healthy Elderly Control Group
Twenty healthy elderly controls (NC) [Mean±SD age: 71.5±7.8] who underwent the same imaging protocol and segmentation procedure were also included in the study for additional gray matter volume comparisons. Controls were volunteers from the community.

### MRI Protocols
Magnetic resonance (MR) images were acquired on a 1.5 Tesla Signa scanner (GE Medical systems) in compliance with the consensus panel imaging recommendations on Vascular Cognitive Impairment. Three image sets were acquired in the same imaging session: T1-weighted (an axial 3D SPGR with 5ms TE, 35ms TR, 1 NEX, 35° flip angle, 22×16.5 cm FOV, 0.859×0.859 mm in-plane resolution, and 1.2 to 1.4 mm slice thickness depending on head size), PD and a T2-weighted (interleaved axial dual-echo spin echo with TEs of 30 and 80 ms, 3 seconds TR, 0.5 NEX, 20×20 cm FOV, 0.781×0.781 mm in-plane resolution, and 3 mm slice thickness).

### Image Analysis
Brain extraction and automated tissue segmentation was accomplished using a modified version of previously described methods. All images were coregistered to the T1-weighted image using the automated image registration package (AIR, v.5.223). The PD/T2 images were used to extract brain and subdural CSF, then the masked T1 was segmented using a T1-based segmentation whereby local intensity histograms are fitted to 4 Gaussian curves to derive cut-offs for classifying each voxel as WM, GM, or CSF. It is a robust and reliable tissue segmentation protocol optimized for elderly and AD populations (Phantom: coefficient of agreement=0.97, Scan-Rescan differences: Global <1% of TIC, Local <0.15% of TIC).

Brain region parcellation was accomplished using a modified version of our previously described methods for semiautomated brain region extraction (SABRE). SABRE is a highly reliable method which parcellates each individual brain into 26 brain regions proportional to individual head sizes (Interclass Correlation range: 0.97 to 0.99 for individual tissue classes in each region). A set of

### Table 1. Demographic Characteristics of the Sample (n=59)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Mild WMH</th>
<th>Moderate WMH</th>
<th>Severe WMH</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Subjects</td>
<td>19</td>
<td>22</td>
<td>18</td>
<td>ns</td>
</tr>
<tr>
<td>Men/women</td>
<td>13/6</td>
<td>6/16</td>
<td>5/13</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Age, y</td>
<td>74.8 (5.8)</td>
<td>75.6 (6.3)</td>
<td>78.2 (6.6)</td>
<td>ns</td>
</tr>
<tr>
<td>MMSE</td>
<td>24.3 (3.7)</td>
<td>23.6 (3.7)</td>
<td>24.5 (4.0)</td>
<td>ns</td>
</tr>
<tr>
<td>YOE</td>
<td>14.1 (4.4)</td>
<td>13.3 (3.6)</td>
<td>13.0 (3.3)</td>
<td>ns</td>
</tr>
<tr>
<td>ARWMC score</td>
<td>1.0 (0.9)</td>
<td>8.7 (3.7)</td>
<td>16.7 (3.1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

$\chi^2$ and 1-way ANOVA group comparisons. Numbers are mean (SD).

### Table 2. Total Misclassified Tissue by Group

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Total (n=59)</th>
<th>Severe WMH (n=18)</th>
<th>Moderate WMH (n=22)</th>
<th>Mild WMH (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percent</td>
<td>2.04</td>
<td>4.83</td>
<td>1.33</td>
<td>0.27</td>
</tr>
<tr>
<td>Volume, cm³</td>
<td>17.9 (0.2–86.5)</td>
<td>42.2 (18.1–86.5)</td>
<td>11.4 (0.2–24.3)</td>
<td>2.5 (0.2–6.3)</td>
</tr>
<tr>
<td>Grey Matter</td>
<td>2.73</td>
<td>6.41</td>
<td>1.68</td>
<td>0.3</td>
</tr>
<tr>
<td>Percent</td>
<td>14.2 (0.1–78.0)</td>
<td>34.7 (13.0–78.0)</td>
<td>8.4 (0.2–18.5)</td>
<td>1.6 (0.1–4.6)</td>
</tr>
<tr>
<td>Volume, cm³</td>
<td>3.7 (0.04–17.2)</td>
<td>7.5 (3.3–17.2)</td>
<td>3.0 (0.04–7.6)</td>
<td>0.9 (0.05–2.6)</td>
</tr>
</tbody>
</table>

Values in parentheses indicate range. Percent MRI measures are expressed as mean percent of supra-tentorial total intracranial capacity (ST-TIC).
easily identified landmarks were traced on the masked T1 images using the 3D rendering and region of interest (ROI) modules in the ANALYZE software package (Biomedical Imaging Resource, Mayo Foundation): the central sulcus, sylvian fissure, parieto-occipital sulcus, anterior commissure, and posterior commissure. An in-house program (written in C++) combined these landmarks with the Talairach proportional grid system to generate individualized maps of 13 lobular regions in each hemisphere.

White matter hyperintensity segmentation was accomplished using previously described methods. This semiautomated procedure used an intensity cutoff based on a weighting of the PD and T2 images to define putative WMH. The output was then manually edited by a trained operator who accepted relevant hyperintensities (based on concurrent evaluation of PD and T2 weighted images) to generate final lesion volumes (ICC range for 26 SABRE brain regions: 0.96 to 0.99). WMH containing cystic fluid-filled/infarcted tissue, which segmented as CSF on the T1-weighted image, were included as a subcategory of lacunar volumes.

These procedures generated 2 segmented images in T1-acquisition space: (1) original (GM, WM, and CSF), and (2) with lesion (GM, WM, CSF, and WMH). These 2 images were compared globally and regionally to determine: (1) the volume of misclassified tissue and

<table>
<thead>
<tr>
<th>Regions</th>
<th>Total (n=59)</th>
<th>Severe SH (n=18)</th>
<th>Moderate SH (n=22)</th>
<th>Mild SH (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Percent</td>
<td>Volume, cm³</td>
<td>Percent</td>
<td>Volume, cm³</td>
</tr>
<tr>
<td>Sup Frontal</td>
<td>1.23</td>
<td>0.60 (0–5.1)</td>
<td>3.51</td>
<td>1.7 (0.02–5.1)</td>
</tr>
<tr>
<td></td>
<td>0.42</td>
<td>0.2 (0–1.2)</td>
<td>0.02</td>
<td>0.01 (0–0.06)</td>
</tr>
<tr>
<td>Mid Frontal</td>
<td>4.497</td>
<td>5.1 (0–21.0)</td>
<td>10.29</td>
<td>11.6 (2.7–21.0)</td>
</tr>
<tr>
<td></td>
<td>3.11</td>
<td>3.5 (0–6.7)</td>
<td>0.65</td>
<td>0.7 (0–2.5)</td>
</tr>
<tr>
<td>Inf Frontal</td>
<td>0.338</td>
<td>0.1 (0–0.9)</td>
<td>0.87</td>
<td>0.2 (0–0.9)</td>
</tr>
<tr>
<td></td>
<td>0.18</td>
<td>0.04 (0–0.2)</td>
<td>0.06</td>
<td>0.02 (0–0.1)</td>
</tr>
<tr>
<td>Med Inf Frontal</td>
<td>0.492</td>
<td>0.1 (0–0.8)</td>
<td>1.15</td>
<td>0.2 (0–0.8)</td>
</tr>
<tr>
<td></td>
<td>0.07</td>
<td>0.1 (0–0.3)</td>
<td>0.0 (0–0.0)</td>
<td>0.02 (0–0.1)</td>
</tr>
<tr>
<td>Med Sup Frontal</td>
<td>0.845</td>
<td>0.4 (0–3.4)</td>
<td>2.42</td>
<td>1.0 (0.05–3.4)</td>
</tr>
<tr>
<td></td>
<td>0.24</td>
<td>0.1 (0–0.5)</td>
<td>0.02</td>
<td>0.01 (0–0.05)</td>
</tr>
<tr>
<td>Med Mid Frontal</td>
<td>2.390</td>
<td>0.9 (0–13.5)</td>
<td>4.43</td>
<td>2.7 (0.03–13.5)</td>
</tr>
<tr>
<td></td>
<td>2.17</td>
<td>0.3 (0–1.1)</td>
<td>0.85</td>
<td>0.006 (0.05)</td>
</tr>
<tr>
<td>Sup Parietal</td>
<td>4.376</td>
<td>6.4 (0–31.7)</td>
<td>10.75</td>
<td>15.5 (7.2–31.7)</td>
</tr>
<tr>
<td></td>
<td>2.78</td>
<td>4.0 (0–9.1)</td>
<td>0.49</td>
<td>0.8 (0–2.5)</td>
</tr>
<tr>
<td>Inf Parietal</td>
<td>1.434</td>
<td>1.4 (0–13.2)</td>
<td>3.32</td>
<td>3.3 (0.02–13.2)</td>
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<tr>
<td></td>
<td>0.88</td>
<td>0.8 (0.1–2.2)</td>
<td>0.24</td>
<td>0.2 (0–1.1)</td>
</tr>
<tr>
<td>Occipital</td>
<td>1.344</td>
<td>1.4 (0–13.2)</td>
<td>3.3 (0.02–13.2)</td>
<td>3.3 (0.02–13.2)</td>
</tr>
<tr>
<td></td>
<td>0.88</td>
<td>0.8 (0.1–2.2)</td>
<td>0.24</td>
<td>0.2 (0–1.1)</td>
</tr>
<tr>
<td>Ant Temporal</td>
<td>0.134</td>
<td>0.1 (0–1.7)</td>
<td>0.46</td>
<td>0.0 (0–1.7)</td>
</tr>
<tr>
<td></td>
<td>0.00</td>
<td>0.0 (0–0.01)</td>
<td>0.01</td>
<td>0.0 (0–0.01)</td>
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<tr>
<td>Post Temporal</td>
<td>0.930</td>
<td>1.6 (0–6.1)</td>
<td>2.05</td>
<td>3.5 (0.6–6.1)</td>
</tr>
<tr>
<td></td>
<td>0.78</td>
<td>1.3 (0.1–3.9)</td>
<td>0.10</td>
<td>0.2 (0–0.7)</td>
</tr>
<tr>
<td>Ant BG/Thal</td>
<td>0.782</td>
<td>0.1 (0–0.9)</td>
<td>1.41</td>
<td>0.2 (0–0.9)</td>
</tr>
<tr>
<td></td>
<td>0.65</td>
<td>0.1 (0–0.5)</td>
<td>0.36</td>
<td>0.0 (0–0.9)</td>
</tr>
<tr>
<td>Post BG/Thal</td>
<td>0.212</td>
<td>0.1 (0–1.18)</td>
<td>0.61</td>
<td>0.1 (0–1.2)</td>
</tr>
<tr>
<td></td>
<td>0.07</td>
<td>0.01 (0–0.09)</td>
<td>0.02</td>
<td>0.0 (0–0.07)</td>
</tr>
</tbody>
</table>

Values in parentheses indicate range.
Percent MRI measures are expressed as mean percent of total regional capacity (TRC).
the regions most affected by misclassified WMH. See Figure 1 for a graphical description.

Results
Fifty-nine patients were included in the study (24 males and 35 females; mean±SD age, 76.2±6.3 year), with a mean educational level of 13.6±3.7 year. The mean±SD MMSE score across all participants was 23.8±3.8, indicating mild to moderate AD. There were more women in the groups with severe and moderate WMH (χ²=10.1, P<0.01). Characteristics of the participants by severity of WMH are given in Table 1.

Percentage Misclassified Tissue Volumes
Percent of misclassified tissue was calculated for overall parenchyma, separated by tissue type (GM, WM) and by brain region. The mean percent misclassified tissue was greatest in the patients with severe hyperintensities (4.8%), which translates to a volume of approximately 42.2 cm³. Misclassified volumes for all 3 severities combined were 2% (17.9 cm³) of total parenchyma. Slightly greater percentages of misclassified tissue were segmented as GM, with 6.4% of total brain GM misclassified in the group with severe hyperintensities compared to 1.2% of total brain WM misclassified in the same group. This translates to a volume of approximately 34.7 cm³ and 7.5 cm³, respectively. Overall percentage and volumes of misclassified tissue for gray and white matter according to severity are listed in Table 2.

Data for misclassification relative to brain region is given in Table 3. Misclassified volumes were largest in the middle frontal and inferior parietal regions, particularly in the Severe WMH group where 10% of these regions were misclassified—translating to volumes of approximately 11.6 cm³ and 15.5 cm³ respectively. These same regions were also the most strongly affected when the data were collapsed across WMH group, with 4% of these regions being affected by misclassified tissue volumes.

Expressed as a proportion of total misclassified volumes, misclassified volumes were greatest in the middle frontal, inferior parietal and occipital regions (see Table 3 and Figure 2). The frontal region (comprising both middle and medial frontal regions) accounted for approximately 41% misclassified tissue across all 3 groups, and 40% misclassified in the severe group. These percentages translate to actual volumes of approximately 7 cm³ and 17 cm³. Inferior parietal also accounted for a large percentage of misclassified tissue yielding 33% (6.4 cm³) of the misclassified volumes in the entire group, and 37% in the severe group (15.5 cm³). No hemispheric differences were seen in any of the regions. Lobular volumes of different tissue types were normalized to the supratentorial total intracranial capacity (ST-TIC) and expressed as a percentage. Uncorrected mean volumes expressed in cm³ are provided simply to give a volumetric impression to the extent of misclassified tissue volumes.

In an additional analysis, we compared GM volumes in a group of 20 NC who underwent the same imaging protocol and segmentation procedure. As shown in Figure 3, GM volumes in the NC group were compared to our group of AD patients, with and without WMH segmentation. As expected, we found that with WMH correction, the NC group had significantly larger GM volumes than the AD patients (F(3,78)=6.05, P=0.001). Bonferroni posthoc analysis revealed greatest differences in volume when NC GM was compared to the moderate WMH (P=0.001) and severe WMH groups (P=0.015). When the groups were compared without WMH correction, a significant difference was also found (F(3,78)=5.84, P=0.001), but posthoc analyses revealed very different contrasts. Differences between the NC and moderate WMH remained (P=0.03), but inflation of the GM volume in the severe WMH group abolished the group difference (P=1) originally present with separate WMH segmentation. In fact, the GM mean volume of the severe WMH group exceeded that of the NC group. As shown in Figure 4, similar results
were found for the Middle Frontal region ($F_{A76}=16.7$, $P<0.001$) where the GM inflation in the severe WMH group was even more pronounced when compared to the normal controls ($P<0.001$).

**Discussion**

The results of this study suggest that clinical investigators using only a T1-weighted MRI acquisition to derive brain tissue volumes by tissue classification techniques from elderly populations should be aware of the pitfalls. In the absence of a WMH or lesion segmentation, investigators can expect up to a 5% inflation attributable to misclassification. In particular, T1-based segmentations can result in a 6% inflation of GM volumes. This misclassified GM volume translates to a volume of approximately 35 cm$^3$ (for reference a standardized ping pong ball is 32.7 cm$^3$). Furthermore, the additional comparison between healthy elderly and AD patients revealed that in individuals with large volumes of WMH, GM volumes may appear to be in the normal range if not properly segmented.

WMH are a very common finding among individuals with CVD and coexisting AD. They are particularly common in individuals with cerebrovascular risk factors or stroke, but they also occur in healthy individuals over 50 years old and are increasingly prevalent with aging, suggesting they are an age-related phenomenon. One large population based study reported the prevalence of WMH to be approximately 95% in an elderly sample, with the proportion of WMH increasing with age. Similar numbers were reported in the Cardiovascular Health Study, a large ($n=3301$) study of community dwelling elderly, suggesting that only 4.4% of patient MRI scans were free of any abnormal signal in the white matter.

Although the present results are based on a modest sample of subjects with varying degrees of white matter disease, they are comparable to results from larger studies. The mean total cranial volume for this sample ($n=59$) was 1198.9 cm$^3$. These volumes are comparable to those recently reported in the Framingham Heart Study ($ST-TIC=1262.8 \text{ cm}^3$, $n=2200$), a large community-based sample study. They also reported similar WMH volumes expressed as a percentage of total intracranial volume in subjects with white matter disease (Moderate and Severe: 3.08%, Framingham: 3.04%).

The present data indicate that regional measures of tissue atrophy in elderly populations based only on T1 segmentation...
should be interpreted with caution, especially when examining the middle frontal, medial frontal, and inferior parietal regions. In this study, up to a quarter of the frontal regions were affected by misclassified tissue volumes, and similar findings were seen in parietal regions. These regions have been previously reported to be clinically relevant in individuals with Alzheimer disease and with subcortical hyperintensities. Specifically, Tulberg et al (2004) conducted a PET study in which higher frontal and parietal WMH were associated with reduced frontal regional PET glucose metabolism and low scores on executive function tasks. Another study suggested that both the volume of WMH and the total cortical GM volumes were correlated with reduced regional cerebral glucose metabolism primarily in the dorsolateral prefrontal cortex, suggesting that WMH and GM volumes both correlate with cognitive functions usually attributed to frontal regions. The purpose of the present study was to demonstrate the need for a standardized protocol and deployment of a WMH segmentation program when planning an MRI-based volumetric study in an elderly population. Whether dealing with normal elderly controls, or patients with AD, cerebrovascular disease, or mixed diseases, clinical researchers now have a selection of automated and semiautomated lesion segmentation protocols to choose from to minimize the problem of misclassified tissue volumes in individuals with WMH. Novel unified multispectral segmentation algorithms may better solve the problem of misallocated tissue attributable to WMH; however, to our knowledge there are currently no such programs that include a WMH segmentation. Currently, to implement quantitative measures of WMH, MRI scanning protocols must include additional T2-weighted, PD, or FLAIR images. In compliance with the consensus imaging recommendations for Vascular Cognitive Impairment, we suggest similar standards for AD studies attributable to the high prevalence of subcortical ischemic vascular disease.

**Acknowledgments**

We thank Dr Fuqiang Gao and Christopher Scott for their assistance in data collection.

**Sources of Funding**

The research reported in this article was supported by the K.M. Hunter Graduate Scholarships, the L.C. Campbell Cognitive Neurology Research Unit, the Canadian Institutes of Health Research, Alzheimer Society of Canada, and the Alzheimer Association.
Disclosures

None.

References

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*Stroke*. 2008;39:1134-1141; originally published online March 6, 2008;
doi: 10.1161/STROKEAHA.107.498196

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

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