

C. Farrell  
F. Chappell  
P. A. Armitage  
P. Keston  
A. MacLulich  
S. Shenkin  
J. M. Wardlaw

## Reply to 'Does assessing brain atrophy on an individual patient basis need correction to peak brain volume or a surrogate?'

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C. Farrell · F. Chappell ·  
P. A. Armitage · P. Keston ·  
J. M. Wardlaw (✉)  
Division of Clinical Neurosciences,  
Western General Hospital,  
Bramwell Dott Building, Crewe Rd,  
Edinburgh, EH4 2XU, UK  
e-mail: joanna.wardlaw@ed.ac.uk

A. MacLulich · S. Shenkin  
Department of Medicine for the  
Elderly, The University of Edinburgh,  
Edinburgh, UK

Dear Editor,

The authors raise an important point that is not infrequently overlooked in studies of both whole brain and regional brain volume changes with ageing, namely that whole and regional brain volumes should be adjusted for maximum lifetime brain volume, a surrogate for which is intracranial volume. Interestingly, this adjustment is something that radiologists do intrinsically when subjectively assessing an individual brain for volume loss. However, in image processing, the brain is typically extracted from the skull, and unless intracranial volume is measured and used to adjust the brain volume figures, the results may be biased.

The cases included in our paper (Farrell et al., Eur Radiol 2008 Aug 9 Epub ahead of print) describing the development of a normal template for ages 65–70 and 75–80 did have intracranial volume assessed, and this was described in the original publications from which we derived these “truly” normal cases to form our

template. The template as described in our paper is primarily intended for use by radiologists when reporting clinical studies. For this purpose, we presented the 5th through to 95th centile equivalent images from each age group, because the “averaged” images, as derived using a standard linear affine transformation, are too blurry to be used in any meaningful way for subjective rating. However, if the volume data for 65–70 or 75–80 year olds were to be used for comparison with volume data from other cohorts, then a correction for intracranial volume would have to be included in the calculation, and it would be better to use a non-linear transformation.

We are in the process of testing the volume template, re-derived using a non-linear affine transformation, in a different cohort for this very purpose. We are also deriving white matter volume using methods that are independent of Statistical Parametric Mapping.

Joanna Wardlaw and Paul Armitage on behalf of the co-investigators.