Answers to Peer-review

1. Peer review point 1: Describe relationship between AD and CAA

Cerebral β-amyloid angiopathy (CAA) occurs when β-amyloid is deposited in the vascular media and adventitia. It is a common pathology in the brains of older individuals and is known to co-exist with other causes of cognitive decline. CAA has been shown to contribute to changes in early AD pathogenesis; CAA is present in 2-3% of the AD brains of which half of them have a severe form. Therefore it is possible that vascular change and neuritic plaque deposition are not just parallel processes but reflect additive pathological cascades. CAA also predisposes towards cerebral infarction and cerebral haemorrhage, though the clinical effects of CAA in AD are mostly silent, or at least are ''masked'' by the greater degree of neuronal dysfunction induced by senile plaque (SP) formation and neurofibrillary degeneration. CAA has been shown to contribute to changes in early AD pathogenesis, therefore, in order to correctly diagnose the dementia subtype, robust cognitive assessment, and dedicated neuroimaging is required to actively search for other causes of cognitive impairment.

2. Peer review point 2: Describe scales used

Several scales have been used to describe the examination of the patient to review his conscious level, as well as various forms of cognitive testing. A Glasgow Coma Scale score, which is used to review levels of consciousness was 13 (15 is the highest score and the patient scored 2 points less due to his ‘confused’ speech). An Abbreviated Mental Test Score (AMTS) used to assess cognition at the bedside was low at 2/10 (a score of less than 7 would prompt more sensitive cognitive testing). As prompted by the low AMTS , further more detailed cognitive tests were carried out: he scores 10/30 on a Montreal Cognitive Assessment (MoCA) (a score of 26 or over is normal); and, he scored 62/100 on an Addenbrookes Cognitive Examination 3 (ACE3), affecting mainly memory and fluency

domains (a score of 88 and above is normal, below 83 is abnormal, and between 83 and 87 is inconclusive).

3. Peer review point 3: Application to AI?

There are two primary methods of AI in use in medical imaging. The first uses pre-defined features/equations as an input into sophisticated machine learning models, which then use this input to define characteristics of images. The second (deep learning) uses imaging data as its input without any prior definition by humans. This method can reduce noise, minimise artefact and enhance image quality in MRI imaging. By using an age and sex matched standardised database, it can highlight statistically significant variations from the norm and therefore provide objective assessment of disease which is more accurate, sensitive and specific than a radiologist reporting[1]. This method of AI has huge potential in the diagnosis of cognitive impairment, and more specifically AD, as it can identify features of disease much earlier than clinicians and can also remove cognitive biases clinicians face when reviewing large quantities of ambiguous images[2], such as in this case.

References

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2. McDonald RJ, Schwartz KM, Eckel LJ, Diehn FE, Hunt CH, Bartholmai BJ, Erickson BJ, Kallmes DF. The effects of changes in utilization and technological advancements of cross- sectional

imaging on radiologist workload. Acad. Radiol 2015;22:1191–1198. PMID: 26210525.

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