Dementias Platform UK PET-MR harmonisation clinical study: initial results

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BACKGROUND

The combination of positron emission tomography (PET) and magnetic resonance imaging (MRI) provides complete assessment of patients' brains for early diagnosis of Alzheimer's disease (AD) and essential imaging biomarkers for stratification or as a response biomarker in clinical trials. Such trials are important to clarify which patient groups will benefit from emerging biological therapies, such as aducanumab and other antibodies against amyloid or tau deposits.

In the UK, the Medical Research Council therefore funded installation of multiple hybrid PET/MR scanners, creating a unique national network includes 8 PET/MR scanning sites within the Dementias Platform UK (DPUK) to perform advanced brain research and clinical trials. The aim of this ongoing study is to harmonise scanning across these scanners and quantify the measurement variability within each site (repeatability) and across sites (reproducibility).

METHODS

The ongoing prospective, repeated measures study design consists of scanning twice 45 elderly volunteers who underwent testing to ensure their cognitive (MMSE, GDS-15) and physical health. Simultaneous PET/MR scanning was performed twice for each participant involving 3 Siemens and 5 GE scanning sites, with each participant randomised into one of three groups: (1) repeatability (same site, same scanner), (2) intra-scanner reproducibility and (same scanner, different site) (3) inter-scanner reproducibility (different site and scanner, **Table 1**). Two PET radiotracers are being used , [^{18}F]flutemetamol (174.7 MBq, range: 134 to 196.5 MBq) and [^{18}F]florbetaben (279.3 MBq, range: 258.9 to 311.3 MBq), and test-retest scans were always done with the same tracer.

		Flutemetamol	Florbetaben	Total
Repeat	GE	4	1	5
	Siemens	2	1	3
Intra-scanner	GE	2	0	2
	Siemens	0	1	1
Inter-scanner		4	2	6
Total		12	5	17

Table 1: Breakdown of participant by randomisation group and tracer

PET data were acquired from 60-120 minutes post injection, with both standard (T1, T2, T2*) and advanced MR (ASL, DWI, rsfMRI, qSM) sequences acquired simultaneously. Data acquired 90-110 min p.i. were reconstructed for visual inspection and quantitative analysis using MR-derived μ-maps (Brain HiRes in Siemens MMR and ZTE in GE Signa) for attenuation correction within OSEM image reconstruction with 4 iterations and 28 or 21 subsets, with no time-of-flight (TOF). Standard centiloid (CL) procedures (Klunk *et al*., 2015) were used for analysis of cortical amyloid tracer binding which determine the ratio of the cortical to whole cerebellum activity concentration, which was then mapped into the CL scale to correct for differences between radiotracers. Test-retest variability was analysed by correlation plots. The reconstructions done on the scanner were 12 x 5 min frames, with the images that were created for visual assessment the 20 min period closest to 90-110 (GE data).

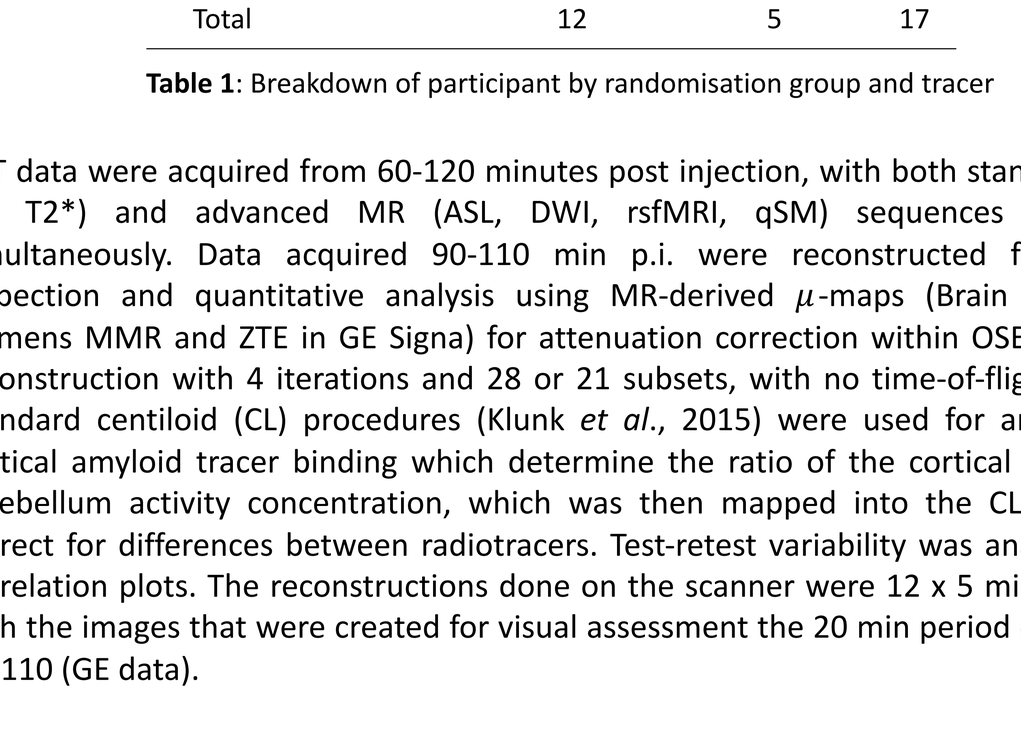

Figure 1: Positive (top) and negative (bottom) test-retest amyloid PET scans

CONCLUSIONS

Very good test-retest was observed for most participants (less than 10 points on the centiloid scale, median 4), similar to previously reported for PET/CT (Battle *et al*., 2018, Miki *et al*., 2017, Joshi *et al*., 2012, Villemagne *et al*., 2011, Vandenberghe *et al.* 2010). However, problems with attenuation correction can occur and cause larger test-retest differences. Thus, careful inspection of individual attenuation maps is recommended.

RESULTS

As of 16 FEB 2022, the data of 17 participants, of which there were 10 females and 7 males, with mean age of 72.2 (range of 66-81), mean MMSE of 29 (range 28-30), have been analysed and are included in this report, as detailed in table 2.

Exemplary test-retest scans are shown for a positive and a negative case in **Figure 1**. Test-retest intra-class correlation was 0.92 and 0.98 without a single outlier (see **Figure 2** for scatter and Bland-Altman plots, with different colours indicating scanner groups). The outlier with a very large difference between first and second scan was due to an erroneous μ-map (large and clear artefacts observed in the μ-map) used in attenuation correction.

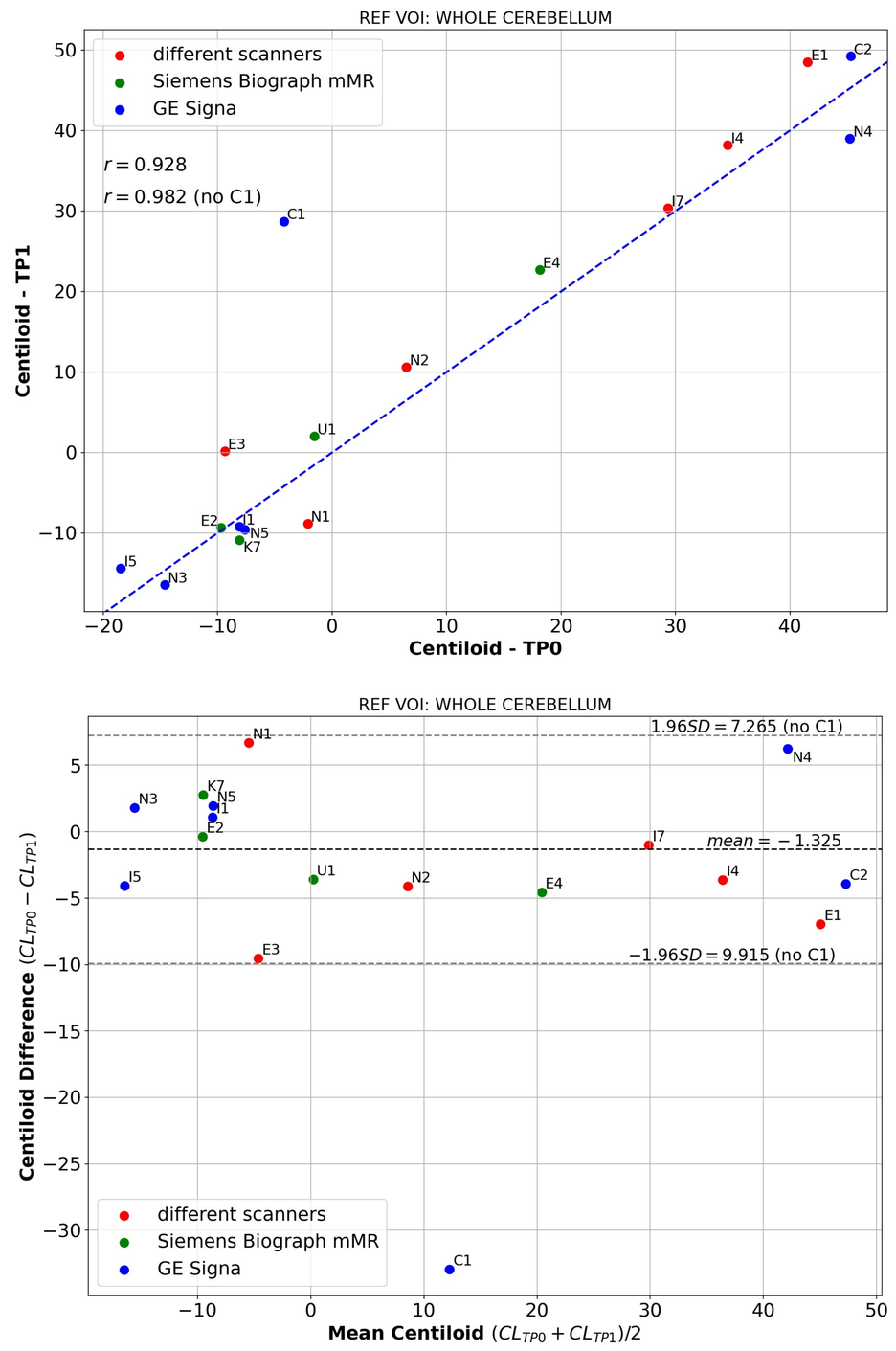

Figure 2: Scatter (top) and Bland-Altman (bottom) plots of the 17 test-retest scans. Scanner groups are shown in different colours and the text symbols correspond to participant identifiers.

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ACKNOWLEDGMENTS

The study is funded by an MRC partnership grant (MR/N025792/1). Partners also receive support from other individual grants, and Alliance Medical is providing part of tracer doses as in-kind support.