

# Repeatability of ultra-high-resolution Multi-Parametric Mapping across five 7T sites

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**INTRODUCTION:** “Why was this study/research performed? What unsolved problem are you addressing?”

Quantitative MRI provides access to markers of biologically-relevant tissue features and offers a standardised approach to imaging that can improve comparability across sites and time points<sup>1</sup>. This study sought to assess the repeatability of an ultra-high resolution (0.6mm isotropic) quantitative Multi-Parameter Mapping (MPM) protocol across five different 7T MR imaging sites.

**METHODS:** “How did you study this problem?”

A healthy volunteer (M, 34Y) underwent two MPM sessions with half an hour break in between (“scan” and “rescan”) on a Siemens MAGNETOM Terra, running VE12U-SP01 software, equipped with a single transmit, 32 channel receive head coil (Nova Medical). Imaging was repeated with the same volunteer, within 4 weeks, at five sites: University College London, UK (UCL); University of Cambridge, UK (CAM); Swiss Center for Musculoskeletal Imaging, Balgrist Campus, Switzerland (BAL); Max Planck Institute for Human Cognitive and Brain Sciences, Germany (CBS); and the University of Liege, Belgium (ULG).

The vendors’ automatic calibration, with three iterations, was used to set the transmitter reference voltage. This was followed by whole-brain B0 shimming (WIP1441), the outcome of which was used for all subsequent scans. The MPM protocol consisted of three 3D multi-echo gradient-echo scans with T1 (flip angle, FA = 20°), PD (FA = 5°) or MT weighting (4ms long Gaussian pulse, 2kHz off-resonance and 140° FA)<sup>2,3</sup>. Additional parameters: TR 19.50ms, 6 equidistant echoes with TE ranging from 2.3 to 14.2ms (reduced to 4 for MT-weighting), bandwidth of 469Hz/pixel, RF spoiling increment of 144° with 4pi dephasing per TR<sup>4</sup>, non-selective rectangular excitation pulse with a constant duration of 240μs across flip angles, GRAPPA factor 2 with 48 integrated reference lines in each phase-encoded direction, the total acquisition time of 9 minutes 10 seconds per volume. The transmit field, B1+, was mapped using a series of spin-echo and stimulated echo images (SESTE)<sup>5,6</sup> or via the Bloch-Siegert shift (BSS)<sup>7</sup>.

MPMs (MTsat, PD, R1, R2\*) were calculated using the hMRI toolbox<sup>3</sup>. This was repeated for each B<sub>1</sub> mapping method (only SESTE available from CAM). To assess repeatability, the intra-site coefficient of variation (CoV) was calculated as the difference relative to the mean on a voxel-wise basis expressed in percentage. Regions-of-interest (ROIs) for quantitative analysis were defined by merging the cortical and subcortical Harvard-Oxford atlases into 65

(anatomically defined) regions<sup>8</sup>. These were transformed to native space and restricted to voxels with a GM probability >80% via masking. The median CoV was extracted from each ROI.

## RESULTS: “Report the data, analyses and/or outcomes”

Figure-1 shows a single plane of each map from the scan and rescan sessions together with its CoV for each site. The quality of the parameter maps is generally good, however, distributed artefacts are visible in the  $R_1$  maps (e.g. Fig.1 arrows and discernible inter-hemispheric asymmetries).

Figure 2 shows the regional variation of the CoV. The highest CoV values, indicating worst repeatability, were observed for the MTsat map and within the temporal lobe. These findings were consistent across sites. Figure 3 shows the cumulative density of the median CoV values across ROIs and sites. 90% of ROIs had median( $\pm$  IQR) CoV values below 51.33( $\pm$  9.44)%, 9.78( $\pm$ 1.76)%, 21.73 ( $\pm$ 6.06)% and 26.61( $\pm$ 0.31)% for MTsat, PD,  $R_1$  and  $R_2^*$  respectively.

$B_1^+$  mapping was particularly challenging in the cerebellum due to low  $B_1^+$  efficiency and high off-resonance, more so for the SESTE method. Figure 4 shows the mean MPMs (across scan and rescan) for one site (BAL) for both BSS and SESTE, together with the corresponding plane from the  $B_1^+$  maps. The cerebellar region was very noisy and gave inconsistent or infeasible values, most visibly in the  $R_1$  map. Hence, the cerebellum was excluded from the CoV analysis. Low  $B_1^+$  efficiency also leads to higher CoVs in some parts of the temporal and occipital lobes.

## DISCUSSION: “How do you interpret the results?”

The repeatability of the MPM measures was generally good and consistent across sites and the results were in line with the CoV values reported for high-resolution (0.8mm) MPMs at 3T<sup>9</sup> but higher for MTsat, which had the lowest repeatability. PD was most reproducible while  $R_1$  and  $R_2^*$  were intermediate. Spatially, repeatability was lowest in temporal and occipital cortices.

Distributed artefacts were observed in the  $R_1$  maps. These may be caused by intra-scan motion, though no obvious motion artefacts were visible in the FLASH volumes. Inter-scan motion can also lead to substantial variation in transmit and receive fields at 7T and may have contributed to spatially varying error in  $R_1$ . Off-resonance conditions are challenging for the FLASH volumes and particularly the  $B_1^+$  mapping techniques used. SESTE uses an EPI readout with low resolution making it vulnerable to distortions and intra-voxel dephasing. BSS uses a matched FLASH readout but is phase-based and contaminated by higher-order  $B_0$  inhomogeneity effects. These effects reduced the repeatability (e.g. temporal lobe, Figure 2) and led to substantial artefacts in the cerebellum (Figure 4).

## CONCLUSION: “What is the relevance to clinical practise or future research?”

This study assessed the repeatability of an ultra-high-resolution (0.6mm) MPM protocol by scanning the same individual twice at 5 different 7T sites. The repeatability of the maps was good and consistent at all sites. Further investigations are required to evaluate inter-scanner and inter-individual variability. This study can serve as a baseline for the assessment of other protocols.

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## Synopsis

Repeatability is key to the utility of quantitative MRI, which promises standardised measures with biological relevance. Here we tested a candidate ultra-high resolution (0.6mm isotropic) multi-parameter mapping protocol at five 7T sites. Repeatability was good, with  $B_0$  and  $B_1^+$  field inhomogeneities being the limiting factor. MTsat had the lowest repeatability and PD the highest.  $R_1$  and  $R_2^*$  were intermediate. Repeatability was also lowest in temporal and occipital cortices. These observations were consistent across sites.

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## Figures

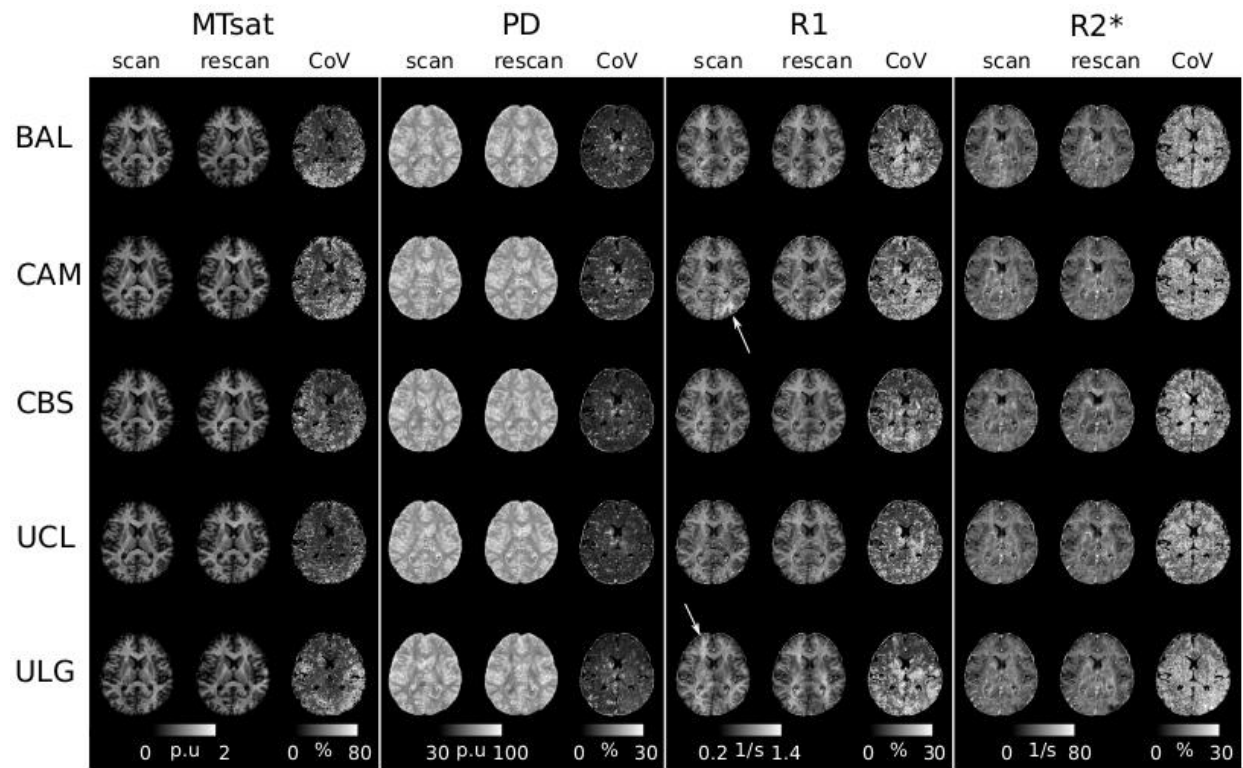


Figure 1 shows scan, rescan and CoV for the four quantitative parameter maps for 5 sites (B1 method - SESTE). Note the different scales for the MTsat CoV.



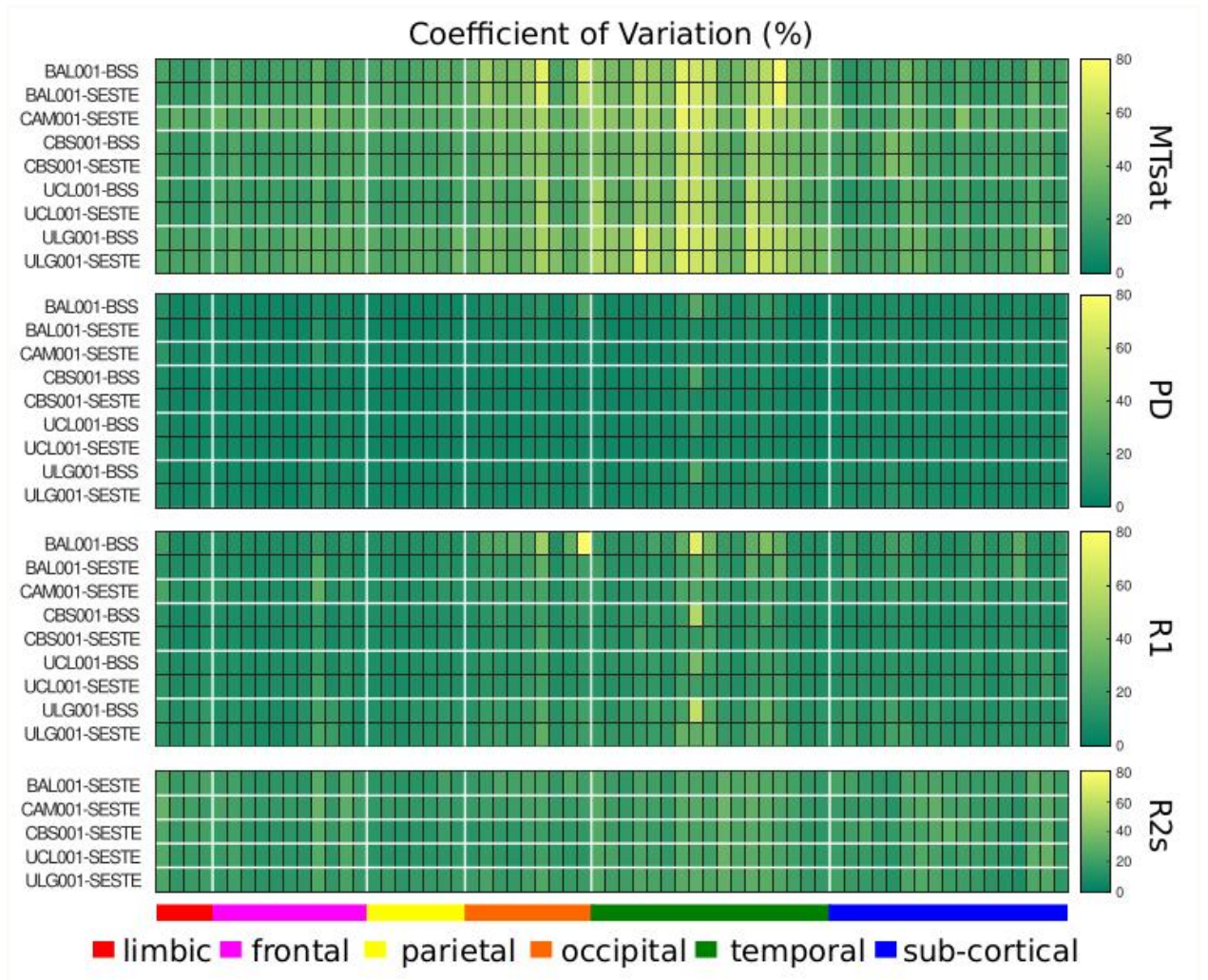


Figure 2 shows a heatmap of median CoV (in %) estimated at each ROI for each study site and for two B1+ mapping methods for the four quantitative maps. The ROIs are arranged by brain region, which is colour coded at the bottom.

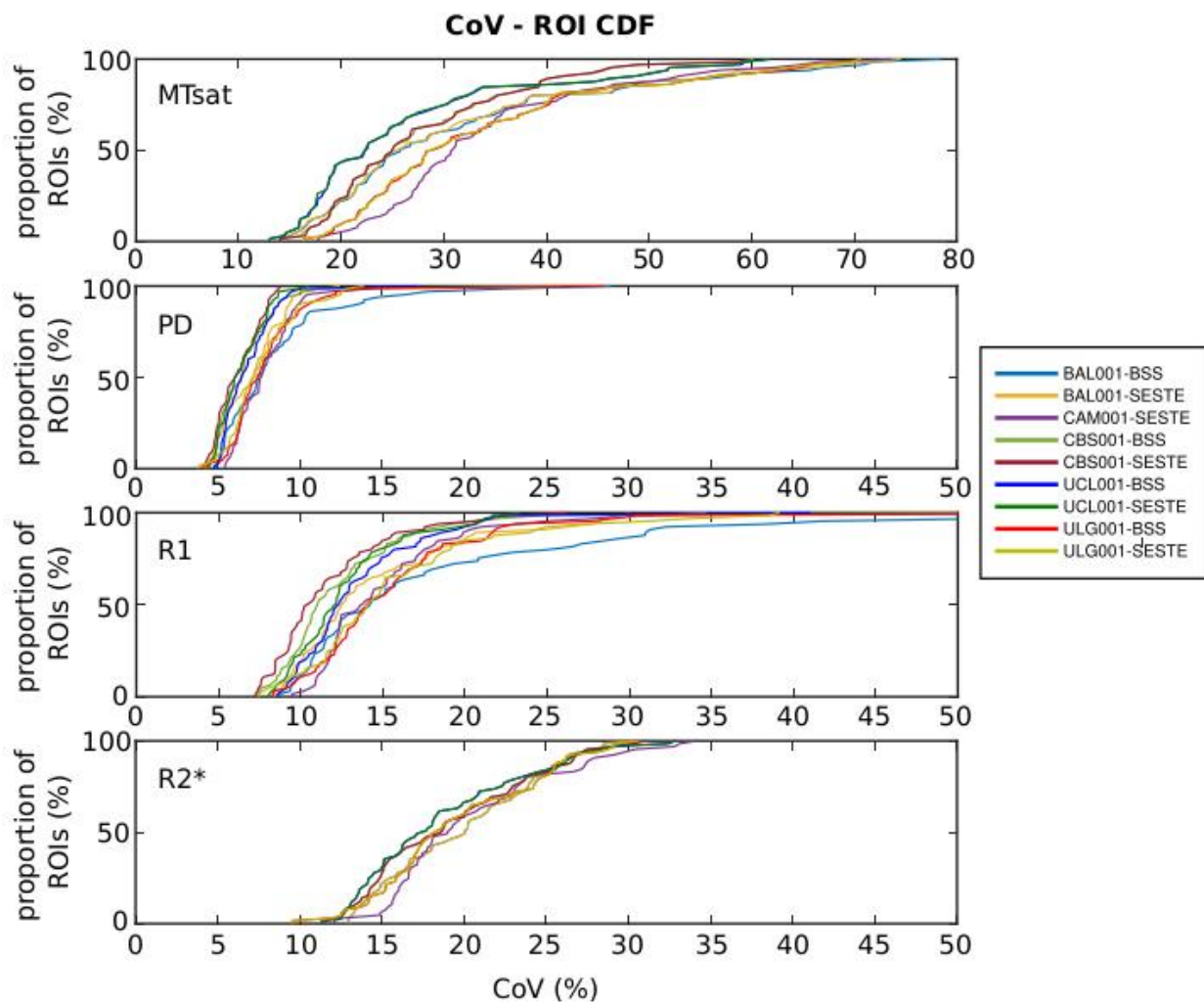


Figure 3 shows a Cumulative Distribution Function depicting the frequency of median CoV(%) values over ROIs for each site and B1 correction method.



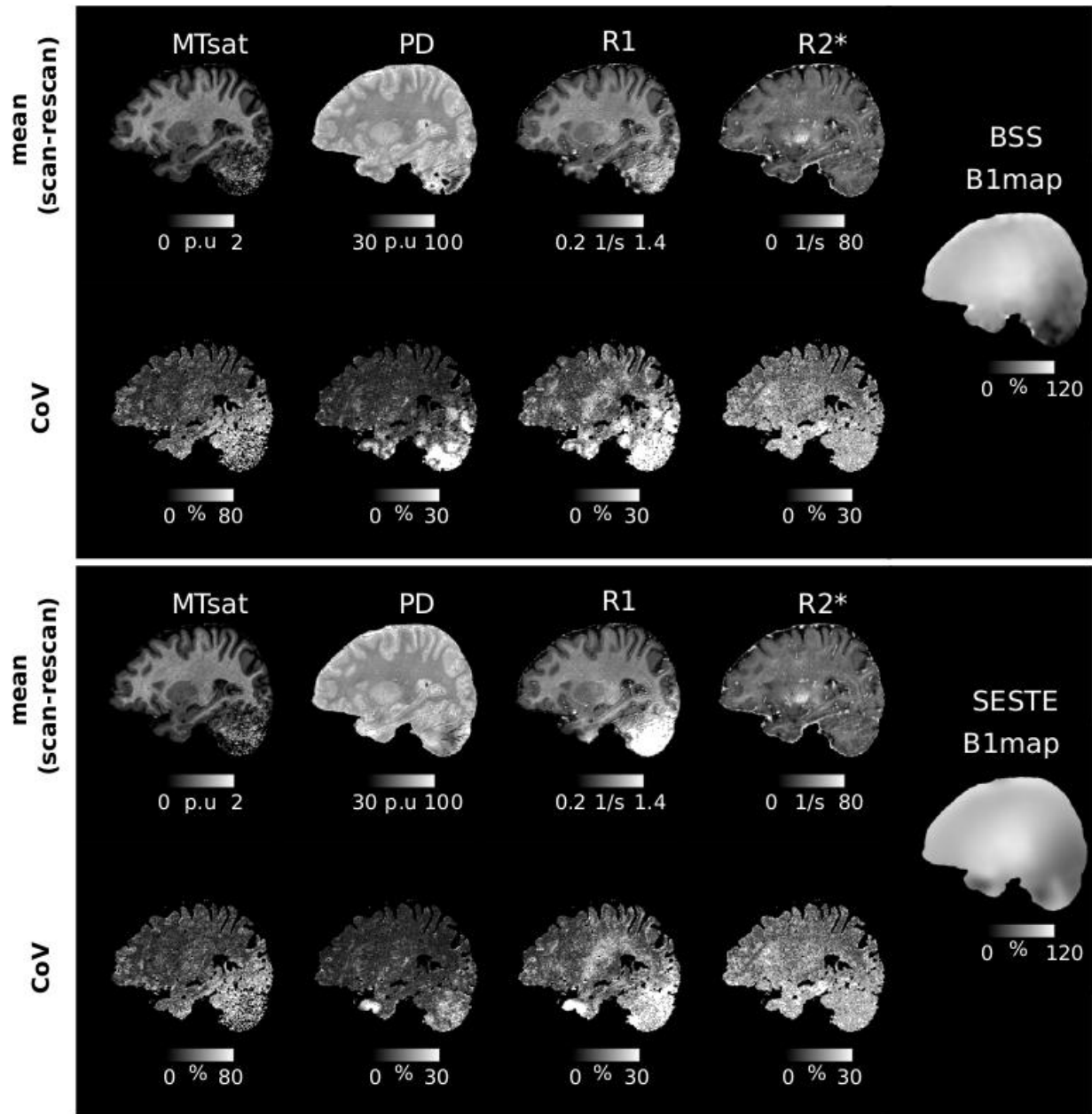


Figure 4 shows the mean of each MPM for the site BAL, the corresponding CoVs and the respective B1+ maps (based on Bloch-Siebert shift: BSS or spin-echo and stimulated echo pairs: SESTE).