## Quantifying 3D-MRF Reproducibility Across Subjects, Sessions, and Scanners Automatically Using MNI Atlases

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**Target Audience:** Clinicians and researchers interested in; leveraging Magnetic Resonance Fingerprinting (MRF) as a source of population-scale structural and tissue property datasets via data aggregation, and reproducibility of MRF quantitative maps and clinically-accepted qualitative approaches across scanners, sites, and subjects.

**Purpose:** In prior studies where offline reconstruction of 2D acquisitions were evaluated using manually-drawn ROIs, Magnetic Resonance Fingerprinting (MRF) has been shown to reliably and reproducibly quantify T1 and T2 in phantoms and in-vivo. However, performing such analysis for 3D-MRF has been limited by the intensive offline computation needed for MRF reconstruction, complicating regional comparisons against standard imaging methods.

In this work, we implemented a fully-automatic online 3D-MRF reconstruction and crossmodality registration for comparison of 3D-MRF's reproducibility against clinical qualitative acquisitions in standard MNI-152 atlas regions. We then performed an intra- and inter-scanner reproducibility study to quantify whether in-vivo 3D-MRF reproducibility meets or exceeds MPRAGE and TSE. The same study is performed to determine whether map reproducibility across sessions and scanners supports subject or population data aggregation.

**Methods:** Ten healthy volunteers were imaged on different days across two 3T scanners with different software (Siemens MAGNETOM Vida XA20 and XA31) Each scan session consisted of three "sets" of three "series" of images: 3D-MRF FISP with a B1 mapping prescan, 3D-MPRAGE, and multislice 2D-TSE. All with a field of view of 250x250x150mm<sup>3</sup> and a spatial resolution of 1x1x2.5mm<sup>3</sup>. First, an "original" set of images was acquired, followed immediately by a "repetition" set. Finally, subjects were removed from the scanner completely, sent back into the bore, and a new localizer and final "reposition" set were acquired. The procedure was repeated on the second scanner within a week.

TSE and MPRAGE datasets were reconstructed online by the scanner.3D-MRF was reconstructed online by a custom Gadgetron Kubernetes cluster utilizing the FIRE (Siemens)



mean ± std dev (bias ± agreement)	Intrascanner		Interscanner
	Same-Session (Original vs Repetition)	Cross-Session (Original vs Reposition )	Cross-Session (All vs All)
T1 (%)	0.95 ± <u>4.12</u>	-0.40 ± <u>4.49</u>	-0.73 ± <u>4.55</u>
T2 (%)	1.50 ± <b>6.08</b>	1.01 ± <b>6.04</b>	-2.08 ± <u>6.27</u>
T1/T2 (%)	-0.54 ± <b>6.12</b>	-1.41 ± <u>5.95</u>	1.35 ± <u>6.68</u>
MPRAGE (%)	2.55 ± <b>12.33</b>	-0.35 ± <u>11.79</u>	0.28 ± <u>12.38</u>
TSE (%)	-0.36 ± <b>20.83</b>	-1.62 ± <b>24.47</b>	2.28 ± <b>28.80</b>
MPRAGE/TSE (%)	2.87 ± <b>21.33</b>	1.22 ± <b>24.12</b>	-2.03 ± <b>27.34</b>

interface prototype, which managed raw data transfer and returned quantitative maps to the scanner. All sets were exported to header-complete DICOMs and converted to NIFTI using dcm2niix. A fully-automated registration and region extraction pipeline performed analysis afterwards. For registration purposes, synthetic T1w/T2w contrasts were generated from MRF maps, then images from all sets were linearly registered to the first scanner's "original" MPRAGE image series via FLIRT. Finally, the first scanner's "original" MPRAGE set was registered to MNI-152 via FNIRT, saving transformation and warp matrices. Atlas label maps were then generated for each atlas/subject/scanner/set combination by transforming the atlas label map into the subject space. Twelve well-defined, homogenous regions from the Harvard-Oxford subcortical atlas were selected and regional means/differences were compared to evaluate reproducibility

**Results:** The consistent bias and standard deviations of T1/T2 indicate in-vivo 3D-MRF is reproducible whether a scan is repeated immediately (T1: 1.25±4.33%, T2: 1.88±6.18%), after reposition of the subject on the same scanner (T1: 0.43±4.49%, T2: 1.31±4.88%), or on a different scanner/day (T1: -0.57±4.90%, T2: -3.28±5.34%). Although MPRAGE and TSE are qualitative acquisitions, and therefore not expected to produce reliable quantitative output, consistent intra-regional contrasts were expected. However, unpredictable differences were observed for repetitions (MPRAGE: 6.56±14.21%, TSE: -0.43±23.11%), repositions (MPRAGE: -0.98±12.67%, TSE: -2.25±26.87%), and scanners (MPRAGE: 1.10±13.75%, TSE: 3.74±32.30%).

**Discussion:** The apparent reproducibility of in-vivo 3D-MRF offers multiple opportunities: intrascanner and interscanner variations are negligible such that data from many sessions, scanners, and sites can potentially be treated as a single dataset for inference or other deep learning processing. Similarly, intrasubject cross-scanner comparisons are likely valid. Meanwhile, the questionable regional repeatability of conventional imaging contrast ratios casts doubt on the reliability of metrics like T1w/T2w ratio, even within the same scan session.

**Conclusion:** We evaluated the reproducibility of 3D-MRF versus clinical-standard MPRAGE and TSE acquisitions for ten subjects across three acquisition sets on two scanners via a fully-automated registration and regional analysis framework. T1 and T2 quantitative maps from 3D-MRF were found to be highly reproducible across scanners and sessions, with no significant difference between repeating a scan immediately on the same scanner, repeating a scan after repositioning the subject and reshimming, and repeating a scan on a different scanner entirely. Importantly, the reliability of the resulting maps suggests that synthetic contrast generation based on MRF maps may allow for system- or session-agnostic T1/T2 weighted contrasts with reproducibility exceeding the current clinical standard.

