



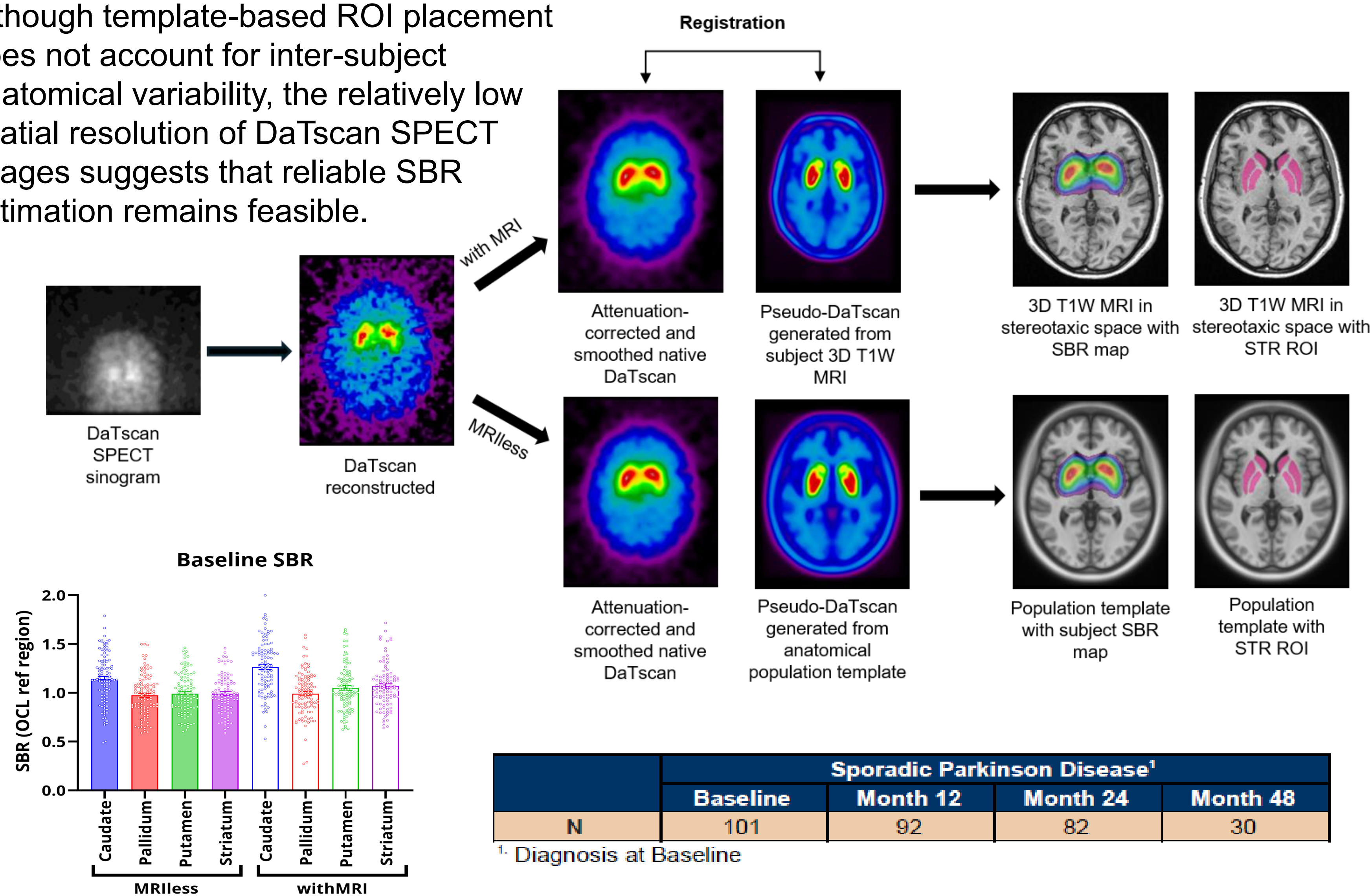
Introduction

In clinical trials, SBR (Striatal Binding Ratio), estimated from DaTscan SPECT images, supports subject selection, stratification, randomization, and efficacy assessment. For example, by confirming presynaptic dopaminergic deficits, DaTscan can help exclude participants with scans without evidence of dopaminergic deficit (SWEDD). SBR analysis often relies on an MRI-based anatomical reference for the definition of regions-of-interest (ROIs) in the DaTscan images. However, MRI adds cost, complexity, and patient burden, so a DaTscan SPECT-only workflow would improve access and efficiency in the context of clinical trials.

Methods

We previously developed a robust, fully automated DaTscan-to-MRI registration method in our PIANO™ image processing platform that relies on a 6-parameter (rigid-body) transformation of the DaTscan to the subject's MRI scan. In this work, we generalize this approach to estimate a 9-parameter affine transformation between any DaTscan image and a non-subject anatomical reference (population template), allowing estimation of SBR without a subject-specific MRI scan.

Although template-based ROI placement does not account for inter-subject anatomical variability, the relatively low spatial resolution of DaTscan SPECT images suggests that reliable SBR estimation remains feasible.



Imaging data were obtained from the Parkinson's Progression Markers Initiative (PPMI) database. Longitudinal analyses included only Parkinson's disease (PD) participants. The cohort was 68/33 male/female at baseline, with a mean age of ~61 years. SBR was estimated using the occipital lobe as the reference region. Baseline SBR is shown as mean $\pm$ SEM for the striatum, putamen, caudate, and pallidum, comparing DaTscan SPECT processing with and without MRI.

Results

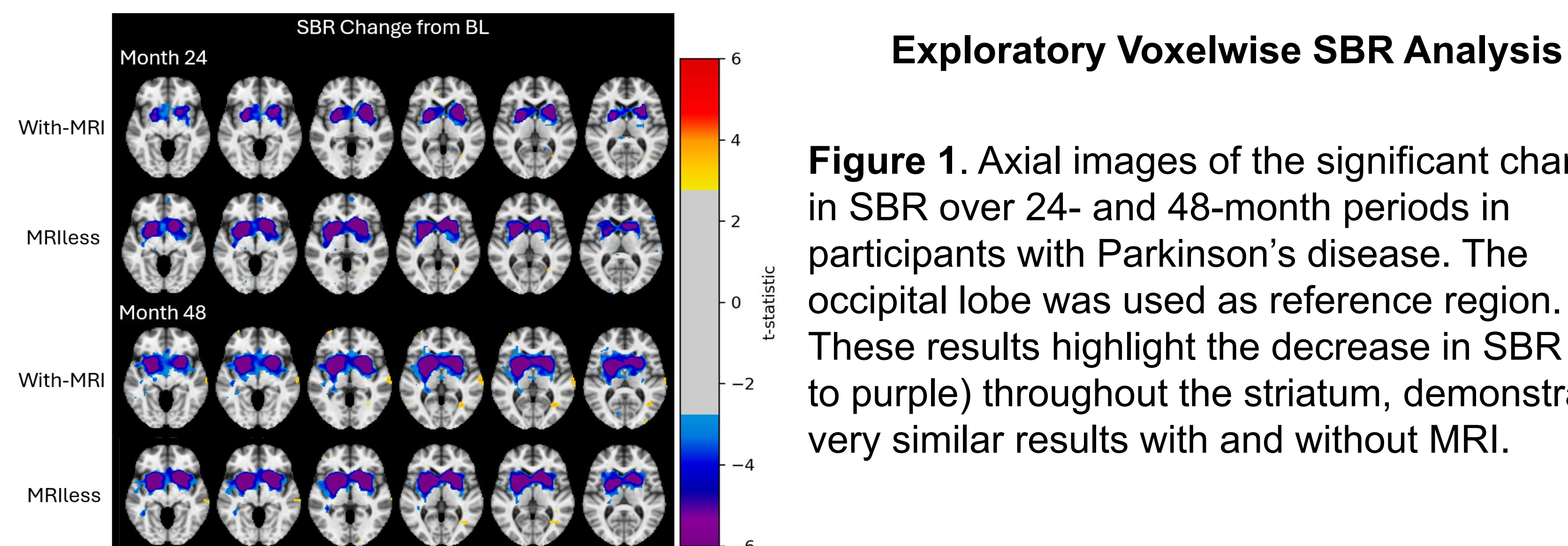


Figure 1. Axial images of the significant change in SBR over 24- and 48-month periods in participants with Parkinson's disease. The occipital lobe was used as reference region. These results highlight the decrease in SBR (blue to purple) throughout the striatum, demonstrating very similar results with and without MRI.

SBR Correlation by Timepoint

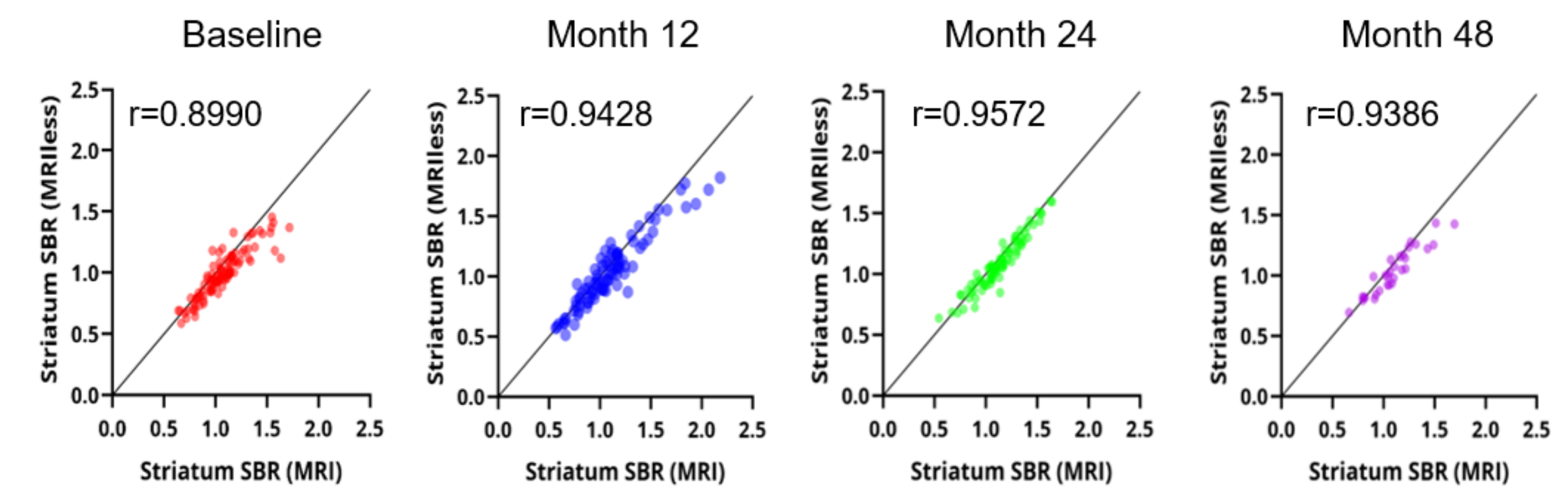


Figure 2. Correlation showing, by timepoint, the association between the SBR data produced with and without the use of an MRI anatomical reference. The line of equivalency is displayed.

SBR Change over Time

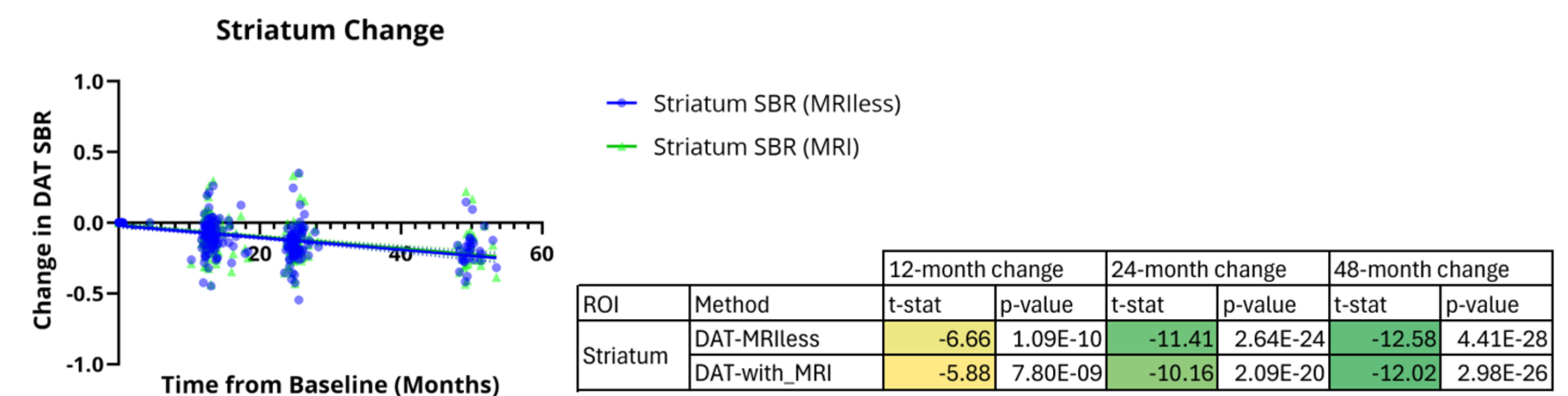


Figure 3. The graph shows regional SBR changes over 48 months. The table summarizes t-statistics and p-values, showing significant changes by 12 months. The mixed-effects model included 82 participants with up to 24 months of follow-up data and 30 with up to 48 months follow-up data. Both methods showed similar SBR change over time.

Sample Size Analysis

ROI	Method	PIANO 12-month change				PIANO 24-month change				PIANO 48-month change			
		20%	40%	60%	80%	20%	40%	60%	80%	20%	40%	60%	80%
Striatum	DAT-MRIless	610	154	68	40	282	72	32	18	158	40	18	10
	DAT with MRI	888	222	100	56	350	88	40	22	238	60	28	16

Table 1. Sample size estimates per arm required to observe a 20-80% reduction in SBR in a treated group compared to an untreated group. The table highlights that for both methods, fewer than 50 participants per arm are needed to detect a 60% or 80% reduction of the observed SBR after 24 months.

Advantages

An MRI-less DaTscan workflow has several advantages while still supporting screening, randomization, and longitudinal SBR analysis:

- **Cost and efficiency:** Reduces trial costs for screening and randomization.
- **Patient experience:** Reduces scanning, improves comfort, and decreases burden.
- **Operational logistics:** Facilitates scheduling and patient management, especially at clinical sites without both DaTscan SPECT and MRI scanning capabilities.

Conclusions

DaTscan SBR quantification without the use of a subject-specific anatomical MRI reference is feasible and yields results comparable to MRI-based analysis. This approach has the potential to substantially reduce cost, logistics, and patient inconvenience, supporting the broader adoption of DaTscan quantification in Parkinson's disease clinical trials.

Acknowledgements

Data used in the preparation of this presentation was obtained from the Parkinson's Precision Medicine Initiative (PPMI) database (<https://ida.loni.usc.edu>).