# Effects of Tissue-Specific Smoothing Approaches on Statistical Analysis in Quantitative MRI

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Abstract & Poster # 372

## Introduction

**Quantitative MRI (qMRI)** provides voxel-wise measurements of tissue properties related to myelin, iron and water content, making it a powerful tool for studying brain aging and microstructural alterations in vivo [1]. However, conventional **spatial smoothing** can introduce **partial-volume effects** and blur tissue boundaries, potentially affecting both statistical sensitivity and anatomical specificity [2].

Several **tissue-specific smoothing strategies** have been proposed to address these limitations, yet their relative impact on voxel-wise statistical analyses remains insufficiently characterized.

**Objective :** Compare 3 tissue-specific smoothing strategies:

- TWS: a linear tissue-weighted smoothing [2],
- gTSPOON: the generalization of a nonlinear tissue-masked compensated smoothing (TSPOON) [3] and
- SUSANs: an intensity-weighted tissue-masked smoothing based on the "Smallest Univalue Segment Assimilating Nucleus" (SUSAN) [4].

## Methods

**Data :** Analyses were performed on a publicly available lifespan qMRI dataset comprising quantitative maps (MTsat, PD, R1 and R2*) of 138 healthy participants (89F/49M, 19-75 years, mean age = 46.6) [5].

**Smoothing approaches :** TWS (Eq. 1), gTSPOON (Eq. 2) & SUSANs (Eq. 3)

Eq. 1
$$TWS(x) = \frac{(g * (\omega s(\phi)))(x)}{(g * \omega)(x)} \quad \text{with} \quad \begin{cases} TPM(x) > 0.05 \\ (g * \omega)(x) > 0.05 \end{cases}$$

Eq. 2
$$\underbrace{\frac{g * (M_{WM}\, s(\phi))(x)}{g * M_{WM}(x)}}_{=\text{TSPOON(x)}} \rightarrow \underbrace{\frac{g * (M_{TC}\, s(\phi))(x)}{g * M_{TC}(x)}}_{=\text{gTSPOON(x)}} \quad \text{with} \quad (g * M_{TC})(x) > 0.05$$

Eq. 3
$$SUSANs(x) = susan * (M_{TC} s(\phi))(x)$$

where $s(\varphi)$ are the quantitative maps warped into standard space, $w$ the modulated tissue weights, $g$* the Gaussian isotropic smoothing operator, $M_{TC}$ the "majority and greater than 20%" tissue mask and $susan$* = SUSAN smoothing operator.

**Analysis framework :**

- Age-related effects investigated separately in GM and WM
- Voxel-wise general linear models (reproducing Callaghan et al. [6])

**Statistical inference :**

- Parametric Random Field Theory (RFT) [7] with
  - Stationarity assumptions
  - Non-stationarity assumptions
- Non-parametric permutation-based inference [8]

**Additional analyses :**

- Voxel-wise log-likelihood (LL) maps: quantified GLM goodness-of-fit (independent of statistical thresholding)
- Bland-Altman analyses and spatial agreement metrics: compared smoothing approaches.

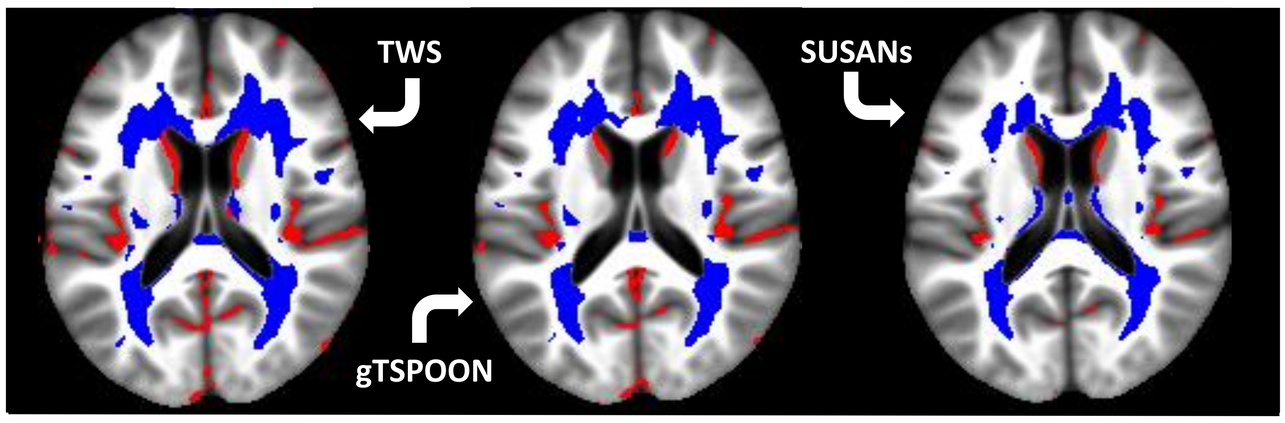


**Figure 1** Significant age-related MTsat decrease in GM and WM: non-parametric statistical maps thresholded at $p < 0.05$ (FWER-corrected).

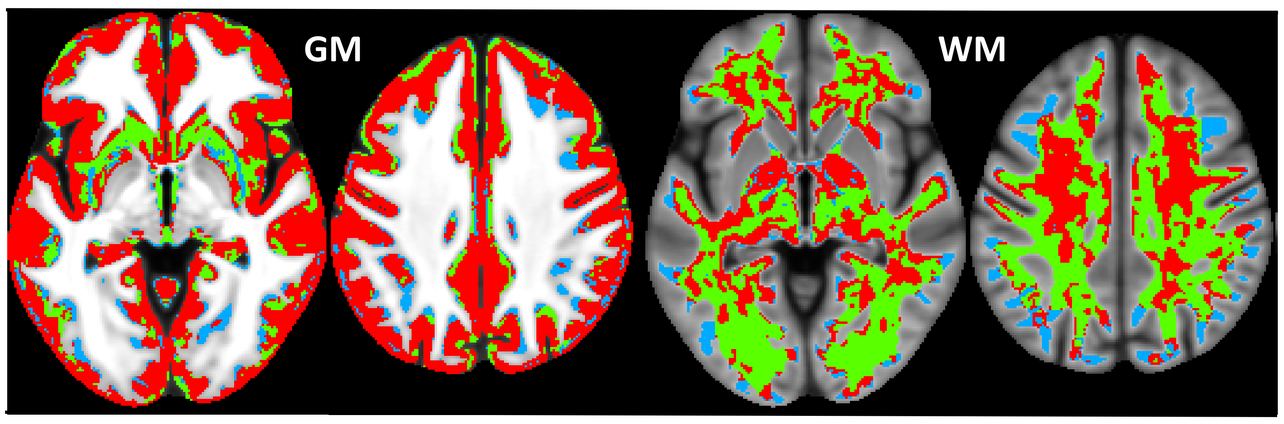


**Figure 2** Voxel-wise LL maps identifying regions with minimal GLM's residuals, for R2* maps smoothed using TWS, gTSPOON and SUSANs.

## Results

**Smoothing Comparison :**

- **Spatial distributions** (Fig. 1 and Tab. 1)
  - TWS and gTSPOON: similar age-related effect distributions across all qMRI parameters and tissue classes;
  - TWS: greater number of significant voxels/clusters, slightly lower T thresholds;
  - SUSANs: fewer significant voxels/clusters, markedly higher T thresholds;
  - Results: consistent across MTsat, PD, R1, and R2* maps.
- **Voxel-wise LL maps** (Fig. 2)
  - TWS: best model fit predominantly in GM (cortical ribbon),
  - gTSPOON: superior performance in homogeneous deep WM regions,
  - SUSANs: highest LL values at GM-WM interfaces (sulcal/gyral transitions), indicating improved preservation of sharp anatomical gradients.

**Inference Comparison :** (Tab. 1)

- Parametric inference (stationary/non-stationary RFT):
  - Nearly identical statistical thresholds, RESEL estimations, and spatial distributions of significant effects
- Non-parametric inference:
  - Lower T-thresholds
  - Larger extents of statistically significant voxels

| Inference | p<0.05 (FWE) | TWS | gTSPOON | SUSANs |
|---|---|---|---|---|
| Parametric RFT (stationarity) | # voxels | 70k / 76k | 51k / 68k | 21k / 54k |
| | # clusters | 1160 / 164 | 540 / 63 | 1002 / 631 |
| | T-threshold | 5.36 / 4.99 | 5.38 / 5.01 | 5.64 / 5.38 |
| Parametric RFT (non-stationarity) | # voxels | 70k / 76k | 51k / 68k | 21k / 55k |
| | # clusters | 1163 / 164 | 540 / 63 | 1002 / 637 |
| | T-threshold | 5.36 / 4.99 | 5.38 / 5.01 | 5.64 / 5.36 |
| Non parametric | # voxels | 78k / 93k | 57k / 83k | 24k / 63k |
| | # clusters | 1221 / 169 | 539 / 86 | 1120 / 596 |
| | T-threshold | 5.18 / 4.67 | 5.22 / 4.72 | 5.48 / 5.16 |

**Table 1** Overview of T-threshold values, and corresponding voxel and cluster counts derived from thresholded statistical MTsat quantitative maps in GM and WM.

## Discussion

Tissue-specific smoothing strategies substantially influence statistical sensitivity and voxel-wise model fitting in qMRI analyses.

- TWS and gTSPOON yield consistent results vs. SUSANs enhances model fit at tissue boundaries.
- Voxel-wise LL mapping revealed no uniformly optimal strategy, with each approach performing best in specific anatomical regions.

These findings highlight

- *smoothing as a region-dependent optimization problem,* and
- *non-parametric permutation-based inference as moderately more sensitive compared to RFT approaches.*

**References :** [1] Weiskopf N. et al. (2013), Frontiers in neuro-science. [2] Draganski B. et al. (2011), NeuroImage. [3] Lee J. E. et al. (2009), NeuroImage. [4] Smith S.M. and Brady J.M. (1997), International Journal of Computer Vision. [5] Callaghan M.F. and Phillips C. (2026), ds005851 on OpenNeuro. [6] Callaghan M.F. et al. (2014), Neurobiology of aging. [7] Friston K.J. (1994), Human Brain Mapping. [8] Nichols T.E. and Holmes A.P. (2002), Human Brain Mapping.

Scripts available at

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