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

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Background: Quantitative magnetic resonance imaging (qMRI) enables interpretable measurements of the brain's physical properties. However, its interpretability is affected by the partial volume effect induced by Gaussian smoothing. To address this issue, tissue-specific smoothing approaches, such as Tissue-Weighted Smoothing (TWS) in qMRI (Draganski et al., 2011) and Tissue-SPecific smOOthing compenSated (TSPOON) (Lee et al., 2009), designed for white matter in diffusion tensor imaging, have been proposed. The tissue weighting in TWS and TSPOON relies on modulated warped tissue probability maps. TWS preserves the continuous nature of these maps, while TSPOON uses them to create tissue-specific binary masks, representing tissue density.

Methods: The generalization of TSPOON (GTSPOON) to all tissue classes was enabled by implementing generalized tissue-specific masks (Callaghan et al., 2014). TWS and GTSPOON were used to reproduce results from Callaghan et al.'s study involving 138 participants, allowing a quantitative comparison of the two smoothing approaches. Additionally, the differences induced by the choice of smoothing were systematically investigated.

Results: Large brain regions were significantly affected by the choice of smoothing approach, particularly at the boundaries between gray matter and white matter. The reproduced results showed that significant regions identified using TWS were larger and more numerous than those identified using GTSPOON. The statistical thresholds applied to T-values were generally higher with GTSPOON compared to TWS, whereas the effective smoothing was greater with TWS than with GTSPOON. These findings were consistent across all quantitative parameters.

Conclusion: This study demonstrates that the tissue-specific smoothing approach TWS is more sensitive, whereas GTSPOON results in greater specificity and more robust smoothing. The choice of smoothing approach depends on the type of study being conducted (e.g., population-based or longitudinal studies favor TWS, while confirmatory studies favor GTSPOON). These findings underscore the critical impact of smoothing on statistical outcomes in qMRI studies.

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Quantitative MRI (qMRI) provides interpretable maps of the brain's physical properties. However, when smoothed with a standard Gaussian kernel, their interpretability is affected by partial volume effect at the border of tissue classes, e.g. grey and white matter (GM and WM). To address this issue, tissue-specific smoothing approaches, such as "Tissue-Weighted Smoothing" (TWS) (Draganski et al., 2011) and "Tissue-SPecific smOOthing compeNsated" (TSPOON) (Lee et al., 2009) have been proposed, designed respectively for qMRI in GM/WM and diffusion tensor imaging in WM only. TWS and TSPOON rely on GM/WM tissue probability maps, respectively using the continuous tissue density values or a binarized version, i.e. tissue-specific masks.

First the TSPOON approach was generalized (GTSPOON) to all tissue classes, using both GM and WM tissue-specific masks (Callaghan et al., 2014). Then TWS and GTSPOON were used to reproduce results from Callaghan et al.'s age regression study involving 138 participants (19-75y), allowing a quantitative comparison of the two smoothing approaches. Additionally, the differences induced by the two smoothing approaches were systematically investigated.

Large brain regions were significantly affected by the choice of smoothing approach, particularly at the boundaries between GM and WM. The statistically significant regions identified using TWS were larger and more numerous than those identified using GTSPOON. The FWER statistical thresholds applied were generally higher with GTSPOON compared to TWS, whereas the effective smoothing was larger with TWS than with GTSPOON. These findings were consistent across all quantitative parameters.

This study demonstrates that the TWS approach is overall more sensitive, whereas GTSPOON is more specific and leads to more robust smoothing. The choice of smoothing approach depends on the type of study being conducted (e.g., population-based or longitudinal studies favor TWS, while confirmatory studies favor GTSPOON). These findings underscore the critical impact of smoothing on statistical outcomes in qMRI studies.