Alternative-Based Thresholding: A Simulation Study
Jasper Degryse 1*, Ruth Seurinck 1, Joke Durnez 1, and Beatrijs Moerkerke 1

Abstract
In fMRI research, researchers often aim to investigate activation in specific functional regions of interest (fROIs). Current statistical methods tend to localize fROIs inconsistently, only avoiding the detection of false activation. Avoiding to miss true activation is however equally important in this context. We discuss a new procedure (Durnez et al., 2013) that complements classical testing with evidence against activation and evaluate the technique for defining fROIs using simulated data.

Keywords
fMRI, fROI, Accuracy

Introduction
When analyzing fMRI data, a statistical test to find evidence against the null of no activation is performed in each voxel. Due to the huge number of voxels, this induces a multiple testing problem leading to an explosion of false positives. In response, thresholding is typically made very conservative to control the Type I error rate. However, power or the ability to detect activation is then dramatically reduced, leading to a large number of Type II errors. Durnez et al. (2013) present an ABHT procedure that combines classical testing with evidence against a pre-specified alternative to reduce the amount of false negatives (FN) and reliably identify inactive voxels. We conducted a simulation study to evaluate the performance of this new method.

1. Methods
Let $\Delta$ represent the signal in a single voxel. The alternative-based thresholding (ABHT) procedure combines a $p_0$-value measuring evidence against $H_0: \Delta = 0$ and a $p_1$-value measuring evidence against $H_a: \Delta = \Delta'$ (Figure 1).

Considering both $p$-values over all voxels, results into a layered statistical parametric map (LSPM) with three distinct layers. One layer represents voxels with evidence against $H_0$ and in favor of $H_a$ ($p_0 < \alpha$ and $p_1 > \beta$), suggesting activation (dark blue region in Figure 1). A second layer contains voxels with evidence against $H_a$ and in favor of $H_0$ ($p_0 > \alpha$ and $p_1 < \beta$), suggesting absence of activation (light blue region in Figure 1). Thirdly, voxels that are consistent with both the null and alternative hypothesis or provide evidence against both hypotheses, do not allow reliable conclusions on the presence or absence of activation and belong to the uncertainty layer (yellow region in Figure 1). Finally we have voxels that are statistically significant under the null, but whose activation is not large enough to be considered active under the alternative, the practically insignificant voxels (orange region in Figure 1).

We simulated 299 single subject data sets (resolution: $30 \times 30 \times 30$; voxel size: $2\text{mm} \times 2\text{mm} \times 2\text{mm}$; activation: $< \beta$), suggesting absence of activation (light blue region in Figure 1).
Figure 2. False positives (Type I errors) and False negatives (Type II errors) for both the classic testing procedure and the ABTP.

For all combinations of ES and σ the same trends were found in the LSPM. Figure 2 compares classical null hypothesis testing with the LSPM with ES = 1.5 and σ = 20 (SNR = 0.075). The number of FP in the LSPM corresponded with uncorrected testing with α = 0.05, but dropped to that of the FDR corrected testing when α = 0.001. Importantly, the overall number of FN in the LSPM was lower than in both the uncorrected and FDR corrected classical testing procedure. With increasing β or decreasing τ, the number of FN increased and the number of FP decreased. The uncertainty layer consisted of more voxels as α and β decreased and τ increased. The number of truly inactive voxels in this layer was consistently larger than the number of truly active voxels for all parameter values (Figure 3). On average the uncertainty layer was
Figure 3. The number of voxels in the uncertainty layer (above) that are truly active (left bottom) or truly inactive (right bottom).
Figure 4. Visual presentation of the LSPM. The greener the voxel is, the more it occurred in the layer that is shown over all simulations.