Bilateral Spatial FIltering: Refining Methods For Localizing Brain Activation In The Presence Of Parenchemal Abnormalities.

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Introduction:

Functional magnetic resonance imaging (fMRI) is an increasingly important method for pre-surgical mapping. Accurate localization of relevant functional areas by anatomical landmarks alone becomes difficult in the presence of mass effect and abnormal signal associated with brain tumors. The threshold level for activation in most fMRI experiments has been fundamentally conservative, trying to avoid type I errors (errors of specificity) at a cost of greater type II errors (errors of sensitivity). A frequent approach to maximize sensitivity is to use smoothing filters, most commonly a Gaussian algorithm. However, it is known that smoothing may introduce false positive activations. A potential consequence of false positive activity projected onto tumor tissue is incomplete surgical resection.

Given these concerns, we have modified the standard Gaussian method of spatially filtering fMRI data, taking advantage of *a priori* knowledge that activation localizes to cortex. Rather than maintaining a constant filter width over the entire brain volume, a bilateral filter effectively reduces the width of the smoothing kernel at any sharply contrasting spatial borders, such as those between cortex, edema, and tumor. Thus, bilateral filters should minimize type I errors (false positive errors of activation) at tumor interfaces and increase the significance of detected brain activation. This may translate into increases in sensitivity and specificity for weak functional activation signals.[1]

Methods:

Acquisition and paradigm: Functional MR data was acquired using a standard head coil on a 1.5T Siemens MR system. A total of 120 gradient-echo EPI data sets were collected using (TE50/TR2500, 128^2 matrix, 240 mm^2 FOV, 20 axial 5 mm slices, 1 mm gap). We used a simple block design finger-tapping task consisting of 6 cycles, 40 volumes per cycle. A physiologic "baseline" dataset was created by concatenating the blocks of non-activated time-series data. To simulate activation of select voxels, a hemodynamic response function[2] was convolved with the block design, scaled to a 3% signal change based on the mean of the time series, and then added to the time series. *In vivo* and simulated data analysis was performed on fMR images from a 30 y.o. patient with known low grade glioma in the right frontal-parietal lobe. Ether a standard spatial Gaussian filter or a bilateral filter was applied (both with 8 mm FWHM) prior to statistical analysis using t-test. The threshold level of activation was set at $p \leq 10^{-6}$ (approximate Bonferroni correction for total number of voxels).

Bilateral filter: The output of a standard Gaussian filter is related to input by convolution of a Gaussian response function with each input data point in the image: $J_s = \frac{1}{k_s} \sum_{p \in \Omega} f(p-s) I_p$

where I_p is the input image, J_s is the output image, $f(p\text{-}s)$ is the Gaussian convolution kernel, and k_s is a normalization factor.[2] The bilateral filter modifies this approach by adding an "edge stopping" function which decreases the weight of voxels which have intensities significantly different from their neighbors (i.e. voxels at an "edge"). This results in a function: $J_z = \frac{1}{k_s} \sum_{p \in \Omega} f(p-s) g(I_p - I_s) I_p$, here $g(I_p - I_s)$ is also a Gaussian function. The resulting filter smoothes voxels that are near each other and similar in intensity but avoids smoothing across tissue boundaries and in regions of sharp interfaces. The effect is similar to that found using anisotropic diffusion filtering.[3]

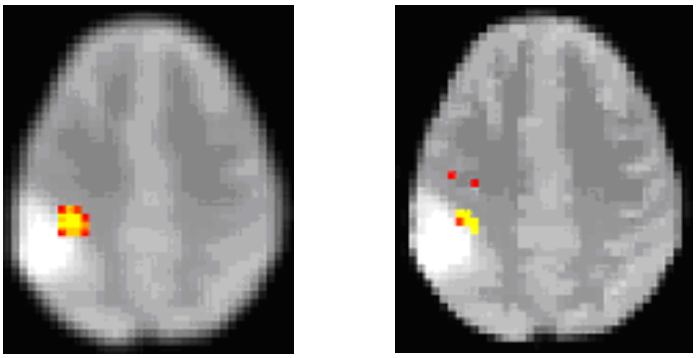

Fig1: Simulated 3% signal imposed on physiologic dataset. Five contiguous voxels simulating activation were placed at the edge of the tumor. The Gaussian filter introduced 10 false positive activations at the tumor margin (left) while the bilateral filter introduced no positive activations at the tumor margin (right). The bilateral filter introduced 2 false positive activations remote from the tumor.

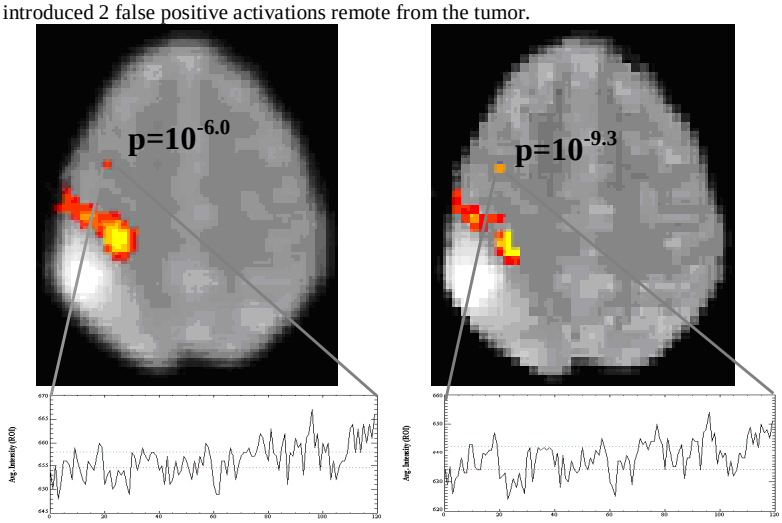

Fig 2. *In vivo* and simulated activation. The large cluster of activation at the tumor margin representing *in vivo* activation is less blurred using the bilateral (right) compared to Gaussian (left) filter. In addition, we superimposed a single voxel of simulated activation data (3% signal) anterior to the motor gyrus. The p value is lower using bilateral compared to the Gaussian ($10^{-6.0}$ vs. $10^{-9.3}$). The signal intensity time course shown for simulated data shows increased activation SNR using the bilateral filter.

Results:

Figure 1 shows a comparison of Gaussian versus bilateral filtering for a simulated 3% activation signal in 5 contiguous voxels superimposed on the physiologic baseline dataset. The Gaussian filter introduced 10 false positive voxels at the tumor margin. In contrast, the bilateral filter introduced no false positive voxels at the tumor margin, although it introduced 2 false positive voxels remote from the neoplasm. This demonstrates that the bilateral filter can more accurately localize activation in the presence of abnormal anatomy. Figure 2 is a hybrid figure demonstrating *in vivo* brain activation during left finger tapping; superimposed on this time course is a simulated 3% activation signal in a single voxel anterior to the activated brain. The *in vivo* data shows more precise localization to gray vs. white matter using the bilateral compared to Gaussian filter, suggesting improved spatial accuracy. In addition, the signal intensity time course of simulated data illustrates how the bilateral filter improves the significance level of a single activated voxel (Gaussian filter: $p=10^{-6.0}$, bilateral filter $p=10^{-9.3}$). This increased sensitivity may become critical depending on the threshold level.

Conclusion: Bilateral filtering can more accurately localize activated brain in regions of abnormal tissue such as brain tumors. Compared to standard Gaussian smoothing, this gain is achieved by decreasing false positive activation, at the same time improving sensitivity to small volumes of activation.

References:

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