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Bilateral spatial filtering: Refining methods for localizing brain activation in the presence of parenchymal abnormalities

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Functional MRI (fMRI) is an important tool for pre-surgical localization of eloquent cortex prior to resection of brain lesions. To increase the inherently low activation signal to noise ratio, fMRI pre-processing steps often include spatial smoothing. However, the effects of smoothing in the presence of brain lesions have not been studied. We have adapted the widely used method of Gaussian spatial filtering to include an "edge stopping" function. This method, termed bilateral filtering, minimizes blurring of apparent brain activity across anatomic boundaries and into regions of non-activation. fMRI data were acquired in a patient with a known low grade glioma during a blocked finger-tapping paradigm. Simulated activity was superimposed on baseline images of non-activated brain using the same paradigm, with additive signal equal to 1, 3, and 5% of the mean physiologic background. Comparison of Gaussian and bilateral filtering suggests that the modified technique more accurately locates brain activation and increases the significance of activation bordering sharp transitions. Thus, spatial pre-processing with a bilateral filter may be particularly useful in the pre-operative assessment of brain lesions.
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Introduction

The ability of functional MRI (fMRI) to localize sensorimotor or eloquent brain cortex and define its relationship to brain tumors has brought this technique into greater clinical use. Eloquent cortex was previously and still is localized by anatomic landmarks; however, brain lesions often distort or obscure normal sulcal anatomy. Although the effect of lesions on blood–oxygen-level-dependent (BOLD) fMRI contrast is not well understood, previous studies using the BOLD technique have identified distortions of motor or speech cortex in the presence of pathology and, in some cases, migration of function to undamaged brain cortex in either the ipsilateral or contralateral hemisphere (Latchaw et al., 2005; Batjer and Loftus, 2003). Quantifying the distance between the lesion and functional cortex is critical for assessing the risks of neurological deficit following surgery. Motor deficits may be identified after tumor resection in patients who have less than 2 cm between lesion margin and sensorimotor cortex. Speech deficits have occurred with less than 2 cm from lesion margin to language cortex (Yetkin et al., 1998; Berger and Ojemann, 1992).

Typically, fMRI data are pre-processed to increase activation signal to noise ratio. For fMRI research applications, significant effort has been placed on avoiding type I errors (false positive voxels) at a cost of increased type II errors (decreased sensitivity). This is usually achieved by increasing the significance threshold for activated brain (Huettel et al., 2004). To maximize sensitivity, spatial smoothing is introduced as part of the data pre-processing, most commonly employing a Gaussian filter. Spatial smoothing increases sensitivity by substantially decreasing noise, while at the same time spreading out the activation signal and decreasing its overall amplitude. Parrish et al. has shown that smoothing significantly improves the sensitivity for detecting activated brain, especially near lesions and regions sensitive to motion. The trade-off for this increased sensitivity is loss of specificity, particularly at the margin of activation (Parrish et al., 2000). Other filters have attempted to improve on the Gaussian method by altering filter shapes depending on the structures within the raw image (Friman et al., 2003; Rydell et al., 2006).

With the goal of improving the specificity of spatial filtering in regions near a brain lesion, we have modified the standard Gaussian method, taking advantage of a priori knowledge that activation is a localized phenomenon, typically within cortex (Logothetis et al., 2001). Viewing Gaussian spatial smoothing as a random process similar to heat diffusion, we introduce a stopping function that does not allow signal to diffuse across sharp signal intensity boundaries. This has been termed bilateral filtering and has mainly been applied in the field of digital photography (Durand and Dorsey, 2002; Barash, 2002). The stopping function reduces the width of the spatial filter at interfaces between gray

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and white matter, edema, tumor, and activated brain. Away from these interfaces, the Gaussian filter is unaffected and allows for increased activation signal to noise ratio. Our hypothesis was that compared to Gaussian filtering, bilateral filtering would decrease the "blurring" of activation signal across lesion boundaries resulting in increased sensitivity and specificity of detection of brain activation in the presence of a brain neoplasm.

Materials and methods

Acquisition and paradigm

In vivo and simulated data analysis was performed on functional MR images from a patient with a known low grade glioma in the right frontal–parietal lobe. MR images were acquired using standard quadrature head coil on a 1.5 T MR system (Magnetom VISION; Siemens AG, Iselin, NJ). A total of 120 gradient-echo echo-planar imaging (EPI) data sets were collected using the following parameters: TE 50 ms, TR 2500 ms, 64×64 mm^2 matrix, 240×240 mm^2 FOV, 20 axial 5 mm slices, 1 mm gap, angled parallel to the planum sphenoidale. These parameters resulted in a voxel size of $3.8\times3.8\times5$ mm^3. We used a simple block design finger tapping task paradigm consisting of 6 cycles, 20 volumes per cycle.

Simulated 3D data set

A physiologic "baseline" data set was created by concatenating the blocks of non-activated time-series data over the entire brain volume. The resting periods during the block experiment were concatenated together over time, duplicated, and subsequently concatenated again. To simulate activation, a hemodynamic response function (Purdon et al., 2001) was convolved with the block design, scaled to either a 1%, 2%, 3% or 5% signal change based on the mean of the time series, and then added to the time series. A single voxel activation was placed at and away from the border of the glioma, as well as multiple voxel activations placed at the border of the glioma.

Image analysis

Images were motion-corrected using SPM 99 and then analyzed using an in-house application written in IDL (Interactive Data Language, RSI, Inc., Boulder, CO). After motion correction, either a standard spatial Gaussian filter or bilateral filter was applied (8 mm full-width-half-maximum (FWHM)) prior to statistical analysis using a Student's t test. A threshold level of activation was set at $p\leq10^{-6}$ (approximate Bonferroni correction for total number of voxels). In addition, a second more liberal threshold level was estimated to be $p\leq10^{-5}$ for the Gaussian filter using random field theory, as calculated in SPM.

Bilateral filter

Fig. 1 shows that 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, $f(p-s)$ is the Gaussian convolution kernel, and k_s is a normalization factor. p represents a summation over the region affected by the filter, while s is the coordinate of a given point within the image (Barash, 2002). The bilateral filter modifies this approach by adding an "edge-stopping" function which decreases the weight of the filter at voxels that have intensities significantly different from their neighbors (e.g. voxels at the edge of the brain). This results in a function:

$$J_s = \frac{1}{k_s}\sum_{p\in\Omega} f(p-s)g(I_p-I_s)I_p$$

where g is an edge stopping function such as Gauss, Tukey, or Lorentz. For this study a Gaussian edge-stopping function of

$$g_\sigma(x) = e^{-\frac{x^2}{2\sigma^2}}$$

was used, where x represents the difference in intensity of I_p and I_s, with σ calculated as the standard deviation of the voxels within the kernel window (termed adaptive bilateral filtering) or assigned a value representative of the noise in the image data set (termed bilateral filtering). In our case, the 2D kernel window was defined as twice the FWHM of our filter (i.e. 16×16 mm^2). The bilateral filter smoothes voxels that are both near each other and similar in intensity, but avoids smoothing across tissue boundaries and in regions of sharp interfaces. The effect is similar to anisotropic diffusion but is non-iterative and simple in design (Durand and Dorsey, 2002).

Simulated 1D data set

A synthetic 1-D data set was also created to more closely evaluate the effect of filtering on sensitivity at the gray and white

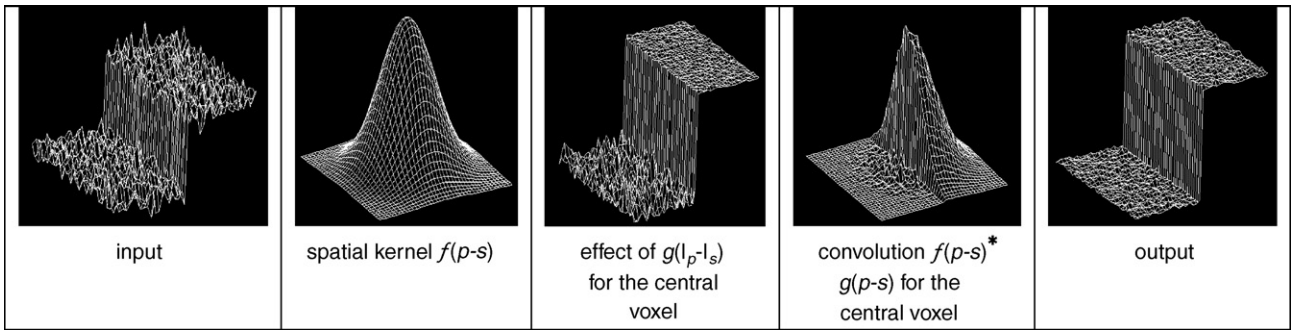

Fig. 1. Input consists of random noise superimposed on an "edge". $f(p-s)$ represents the standard Gaussian spatial smoothing filter. The function $g(I_p-I_s)$ acts in the intensity domain. The value at a voxels is influenced mainly by voxels that are spatially nearby and similar in intensity.

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