Spectral analysis of hemodynamic response delays in brain tumor patients

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Purpose/Introduction
Functional magnetic resonance imaging (fMRI), using the blood oxygenation level dependent (BOLD) contrast, can be used to map motor or language areas in the brain as an explorative step in pre-surgical planning of tumor patients. An important assumption in the analysis method, the general linear model (GLM), is that following a neural event, the image intensity in an activated voxel increases in about 6 seconds closely following a predefined hemodynamic response curve, and that the shape and delay of this response is the same for all voxels and all subjects. This assumption could be wrong, especially near tumor tissue where the shape of the hemodynamic response may be entirely different due to an altered interaction between regional blood volume, blood flow and oxygen consumption.
In this study, we look at activation of left and right hand fingertapping tasks, and delay of the hemodynamic response, in tumors patients with spectral analysis (SA) of fMRI time series. With SA, there is no assumption on the delay time or shape of the response curve; the only condition is that a block design is used. With SA, apart from activation, the delay time can also be calculated. We compare the delay time between the healthy hemisphere and the 'diseased' hemisphere in tumor patients.

Subjects and Methods
We retrospectively analyzed a dataset of 22 brain tumor patients. Patients were scanned on a Philips 3.0 T Intera scanner using a block design paradigm (unilateral finger tapping of the right and the left hand). All of the patients had no paresis at the time of examination. Functional T2*-weighted images were obtained with an echoplanar imaging (EPI) sequence. We motion corrected and smoothed our data with a 6 mm FWHM kernel using the FSL package. For each voxel, we subsequently calculated the Fourier transform of its time series, which yielded values for magnitude and phase (offset) for each spectral component. From these spectra, we used the magnitude and phase at the frequency of the block design for further analysis. The magnitude is an indicator of activation and, after a slice-timing correction, the phase can be converted into a delay time. We used this analysis on the motor cortices in the diseased and healthy hemispheres. In each hemisphere, we selected active voxels by applying a threshold on the magnitude. From the phase of the active voxels, we calculated the mean delay time.

Results
Figure 1, left panel, shows delay times between healthy hemisphere and diseased hemisphere for all tumor patients. These times differ greatly across subjects, but are about the same for both hemispheres in the same subject except for a few exceptions, as shown in the histogram. For one such exception, patient 19, we show the GLM and SA activation maps of the left-hand finger-tapping task. GLM and SA both show that activation has shifted from the contralateral side to the ipsilateral side. Furthermore, the SA shows activation within the tumor, which is missed by the GLM. For one such voxel, the time series is plotted and shows a 'shifted' BOLD response, by (in this case) 10.2 seconds.

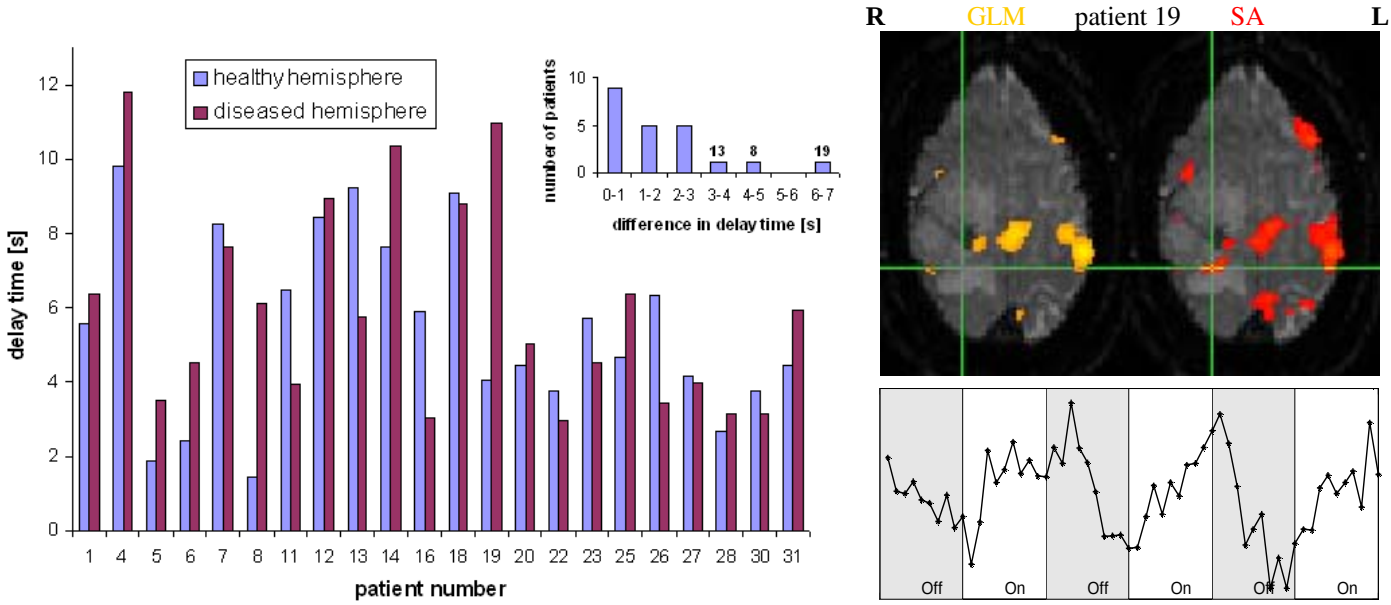

Figure 1. Left: delay times for healthy and diseased hemispheres for all tumor patients. Inset: histogram of the difference in delay times. Right: For subject 19 the time series of an 'undiscovered' voxel is plotted. Delay time for this voxel is 10.2 seconds, whereas the average delay time for the motor area at the ipsilateral side is 6.0 ± 0.5 seconds.

Conclusion
Delay times can increase drastically when a tumor is near the site of activation. Consequently the standard GLM approach can 'miss'activations near a tumor. Spectral analysis overcomes this drawback, reducing the number of false negative responses and can be used for quantifying the delay times.