Principal Component Analysis Enhanced Dynamic Electron Paramagnetic Resonance Imaging of Cycling Hypoxia In Vivo

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Introduction: Low oxygen concentration (hypoxia) in tumors strongly affects their malignant state and their resistance to therapy. The effects of hypoxia may be more deleterious in regions undergoing cycling hypoxia. Electron paramagnetic resonance imaging (EPRI) has provided a non-invasive, quantitative imaging modality to investigate static pO_2 in vivo. However, in order to image cycling hypoxia, EPRI images with better temporal resolution may be required. The tradeoff between temporal resolution and signal-to-noise ratio (SNR) results in lower SNR for EPRI images with imaging time necessary to resolve cycling hypoxia.

Methods: To allow for accelerated image acquisition with acceptable SNR, principal component analysis (PCA) is presented as a method for filtering out noise in the projection data prior to image reconstruction. PCA is a method for defining, from an n-D data set, a new space based on the covariance of the data, such that the first few basis vectors, or principal components, form a q-D space ($q < n$) containing the relevant, highly-correlated features, while the space spanned by the other components contains mostly uncorrelated noise. Therefore, PCA provides a means for low-order approximation of the data by projection onto the subspace spanned by the first q principal components. This low-order approximation acts as a spatiotemporal noise filter for a high-dimensional set of data from a dynamic EPRI study by separating correlated features from uncorrelated noise and only retaining these correlated features. PCA filtering produces reduced noise projections and, subsequently, images with higher SNR.

Results: Simulated and experimental studies show that PCA approximation as a method for filtering EPRI projection data increases SNR, enabling an order of magnitude increase in temporal resolution with minimal deterioration in spatial resolution or image quality. Figure 1 shows the results of applying PCA filtering to an EPRI experiment with a live tumor bearing mouse undergoing forced FiO_2 fluctuations of a known temporal pattern. The PCA filtered images clearly show the expected physiologic response to the fluctuating FiO_2, which was not clear in the unfiltered images. Figure 2 depicts the results of applying PCA filtering to an EPRI experiment with a live tumor bearing mouse breathing air. In this preliminary study, PCA filtering helps elucidate what appears to be a spontaneous sinusoidal temporal pO_2 fluctuation that could be due to cycling hypoxia.

Conclusion: The SNR necessary for dynamic EPRI studies with temporal resolution required to non-invasively investigate cycling hypoxia and its physiological implications in vivo is enabled by PCA filtering.

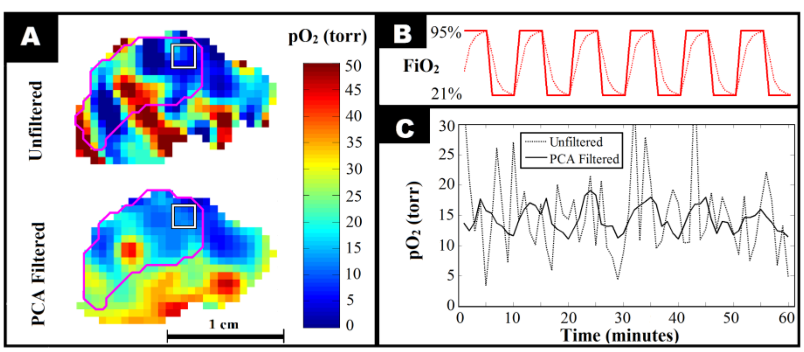

Figure 1: PCA filtered EPRI study with tumor bearing mouse breathing alternating normoxic and hyperoxic gases. (a) PCA Filtered and unfiltered images with the tumor outlined in magenta and the 27 voxel ROI outlined in white. (b) Diagram of breathing gas changing with time (forced FiO_2 fluctuations). The bold line shows breathing gas changes and the dotted line shows expected response of the tissue pO_2 assuming physiologic latencies. (c) Observed temporal pO_2 fluctuations within the ROI. Unfiltered data correlation with expected response: r = 0.13. PCA filtered data correlation with expected response: r = 0.84.

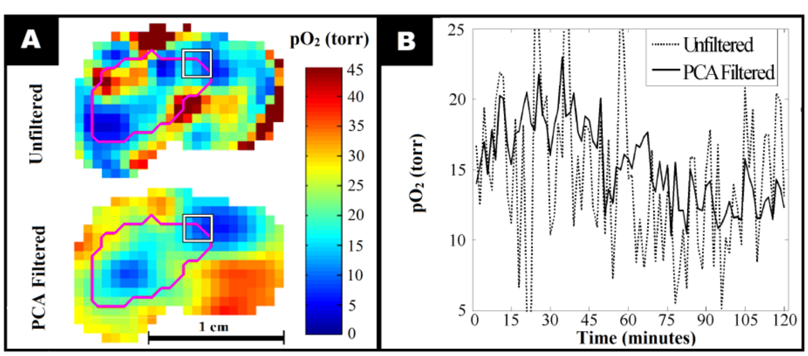

Figure 2: PCA filtered EPRI study of spontaneous pO_2 fluctuations in a murine tumor. (a) PCA Filtered and unfiltered images with the tumor outlined in magenta and the 27 voxel ROI outlined in white. (b) Observed temporal pO_2 fluctuations within the ROI on the periphery of the tumor. PCA filtering elucidates apparent sinusoidal pO_2 fluctuations that may be biologically relevant cycling or acute hypoxia.