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APPLICATION ON CLINICAL DATA OF ROBUST ESTIMATION OF PPIX IN MULTISPECTRAL EXCITED FLUORESCENCE SPECTROSCOPY

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Introduction

Diffuse gliomas account for more than fifty percents of primitive brain tumors and are challenging to remove because tumor margins are not distinguishable from healthy tissues for the naked eye. To help neurosurgeon in localizing tumoral areas, 5-ALA induced fluorescence of protoporphyrin IX (PpIX) is currently used through surgical microscopes. To overcome sensitivity issues, some works [1] focused on the extraction of biomarkers from the signal resulting from a single excitation wavelength at 405 nm using priors on the link between the biomarkers and the microenvironment of PpIX. A recent study showed that the absorption spectrum of each form of PpIX has a distinct maximum absorption wavelength [2]. This has inspired new methods based on multiple excitation wavelengths, aiming at improving the expert-based estimation models for classification of the tumoral areas.

Method and Experiments

The fluorescence emission spectrum used in this study relies on multiple excitation wavelengths. At each excitation wavelength, the fluorescence emission spectrum is a linear combination of emission spectra attached with fluorophores of interest and a baseline $b(\lambda)$ which represents endogenous fluorophore emission spectra. To estimate the linear combination factors, we compared a state-of-the-art Gaussian Baseline Model (GB) where $b(\lambda)$ has a Gaussian shape [2] and Estimated Baseline Model (EB) where $b(\lambda)$ is also estimated [3]. Using a digital phantom calibrated with clinical and experimental data, we demonstrated that our method is more robust than state-of-the-art methods for classifying pathological status, particularly when applied to images of simulated clinical gliomas.[3] To account for the high variability in the baseline, we examined various scenarios. Our method maintains the ability to distinguish between healthy and tumor tissue with an accuracy of up to 87%, while the ability of existing methods drops near 0% in cases where the baseline emits close to PpIX.

We now want to extend this study to real clinical data. Thus, we used clinical data of fluorescence spectroscopy acquired at two excitation wavelengths. The original dataset contains a total of 236 samples including 25 samples that are related to multiple anatomopathological categories.

After normalization by endogenous fluorescence, each spectrum was processed separately by each post-processing model. In order to ease the comparison of the

proposed model with those issued from the literature, we considered only the most performing state-of-the-art Gaussian Baseline Model (GB). Once all the spectra have been processed, we compare the fit residuals of each model.

Results and Discussion

When the whole dataset is processed, the mean value and standard error of fit residuals for all models are given by category in Table 1. One notice that the fit residuals are lower of at least one order of magnitude for the EB model than for the GB model. The relative reduction of the fit residual with the EB model compared to the GB model is at least 95%.

	GB Model		EB Model	
	Mean	Std. error	Mean	Std. error
Core	1199.1615	316.2153	4.9088	3.3626
Dense Margin	250.2348	125.0935	0.1617	0.0557
Sparse Margin	39.5764	21.0655	0.2950	0.2477
Healthy	0.5028	0.1375	0.0155	0.0075

Table 1: Mean value and standard error of fit residuals for each model in all High-Grade samples

This study strengthens that the EB model is more robust than references models of this article[3] to unmix emission spectra of the fluorophores of interest and a baseline $b(\lambda)$ from the measurements. This is particularly interesting for the Sparses Margins and Healthy categories; because according to Alston et al.'s article [2], these categories are close in the space of estimated α parameters. This reduction in the fit residual could have positive consequences for the classification and separability of these two categories. Thus, further work would focus on the consequences of the fit residual reduction on the final classification.

Bibliography

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