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Authors
Xu, Shanshan
Cerussi, Albert
Gratton, Enrico

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Self-Referencing Differential Spectroscopy Analysis in Breast Translational Research

Shanshan Xu, Albert Cerussi, Enrico Gratton.
University of California, Irvine, Irvine, CA, USA.

A self-referencing differential spectroscopy analysis approach has been developed for broadband near-infrared (NIR 650-1000 nm) absorption spectra to reveal intrinsic optical breast cancer biomarkers. Through the application of this method that accounts for inter-patient variability using the normal tissue as an internal control, we have characterized the metabolic differences between malignant and normal tissues that result from subtle alterations in molecular disposition.

From a pilot study of 15 cancer patients performed in 2007, absorption signatures, not arising from the individual abundance in the four major chromophores (lipid, oxy-hemoglobin, deoxy-hemoglobin and water), have been demonstrated to successfully differentiate the normal and malignant tissues. Based on the data acquired from a NIR Diffuse Optical Spectroscopy Imaging instrument, specific spectral signatures containing specific NIR absorption bands are located in regions at about 760, 930, and 980 nm indicative of lipid biomarkers or water in abnormal state. The shape of the fingerprint spectra, namely specific tumor component (STC) spectra, is highly reproducible and exhibits consistent and particular wavelength-dependent characteristics. STC index algorithm was set up to quantitatively computing the residual due to components that are unaccounted for by the basis spectra.

A 61 subject retrospective study aiming to distinguish between benign and malignant breast tumors was carried out in 2008 on top of previous findings. By converting the observed molecular dispositions into a simple index (malignancy index) derived from a weighted wavelength analysis to maximize the differences between the benign and malignant tumors, two types of tumors were stratified with 95% sensitivity, 89% specificity, 91% positive predictive value, and 94% negative predictive value. The observation of pathology specific spectral signatures provides a potentially substantial method for differential diagnosis and monitoring response to neoadjuvant chemotherapy or hormonal therapy.

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