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Authors

Kukreti, S
Cerussi, AE
Tanamai, VW
[et al.](#)

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Intrinsic near-infrared spectroscopic biomarkers applied for evaluation of final pathological response to neoadjuvant chemotherapy.

Kukreti S, Cerussi AE, Tanamai VW, Tromberg BJ, Rita M, David H, Gratton E. University of California, Irvine, CA; University of Illinois, Urbana-Champaign, IL

Background: Near-infrared (NIR) optical methods provide a noninvasive view of tissue based on compositional and functional characterization. In the wavelength region of 650-1000nm, NIR light is sensitive to the four major absorbing components in breast tissue, namely, oxyhemoglobin, deoxyhemoglobin, bulk lipid and water. We have already shown that cancer tissue and cancer tissue undergoing neoadjuvant chemotherapy display changes in these functional parameters. However, it is debatable whether these are specific “markers” of cancer. Recently it was shown that double-differential analysis of breast tissue absorption spectra from cancer-containing tissue reveals specific tumor components (STC) present only in tumor tissue. The STC absorption signature is an intrinsic biomarker characterized by specific NIR absorption bands. Here we apply the double-differential analysis to tissue after chemotherapy. In this pilot study we ask the following question: Can the STC biomarker be used to non-invasively evaluate the final pathological response in cancer tissue after administration of neoadjuvant chemotherapy?

Materials and Methods: A Diffuse Optical Spectroscopy (DOS) instrument was used to recover non-invasively the absorption and scattering spectra from 650-1000 nm in the breast tissues of patients pre and post-chemotherapy. 7 patients total with complete pathological responses, ages 32-53 years, with stage 2 or 3 cancers obtained the following neoadjuvant chemotherapy regimen: 2-4 cycles of doxorubicin-cyclophosphamide (AC), followed by 2-4 cycles of carboplatin-taxol/abraxane-avastin (nabTC). We used the double-differential method to analyze the NIR absorption spectra of breast tissues. Briefly, this is a self-referencing method to reveal only the spectral differences between normal and tumor tissue. We quantify the spectral changes by characterizing the spectral features in an index called the Specific Tumor Component (STC) index.

Results: STC spectral signatures were present in all tumor-containing regions in the pre-chemotherapy measurements. Spectral signatures obtained pre- and post- chemotherapy were different, correlating pathology results. The STC Index results in 100% sensitivity and specificity for the presence of residual disease. The STC Index values were significantly different ($p=0.003$).

Discussion: Here we present a pilot study suggesting NIR optical methods can potentially be used to non-invasively evaluate tumor specific changes in physiological and metabolic states to chemotherapy. Furthermore, NIR optical methods can be used to identify the presence of residual disease. Future work will determine the prognostic utility of the STC biomarker for the separation of partial from complete responders, as well as investigate other therapy regimens.