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Authors
Chung, SH
Cerussi, AE
Hsiang, D
et al.

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Non-Invasive Measurement of Pathological Heterogeneity of Cancer Tissues Using Water State Information from Diffuse Optical Spectroscopic Imaging.

S. Chung, S. Chung, A. Cerussi, D. Hsiang, B. Tromberg, B. Tromberg, and B. Tromberg

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Abstract

Background: In our previous work, we have shown that biochemical tissue water state correlates with histopathological scores of breast cancer (R=-0.96). Based on the result, we extended our research to test whether the tissue water measurement can differentiate heterogeneous pathological structures of cancer tissues of different grades. Diffuse Optical Spectroscopic Imaging (DOSI) measures water molecular vibrational states associated with macro-molecular complexes in tissues such as proteins in a non-invasive way without compression of the breast. For DOSI measurements, a large region over breast tumors is scanned using a hand-held probe and spectral information on each point is spatially mapped to generate an image. Subjects and Methods: DOSI was employed to measure 19 primary cancers (18 IDC and 1 ILC). The spectral features of tissue water absorption from 935 nm to 998nm were compared to those of a pure water spectrum measured at body temperature in order to acquire the Bound Water Index (BWI: the residual between tissue and pure water spectra). In the spectroscopic images, the average and standard deviation of the pixels less than 20% of the range of the BWI in the image were calculated based on our previous finding that carcinoma tissues have lower BWI (more free water). The same parameters were calculated on normal tissues from the same patients in order to compare the tissue heterogeneity. The standard deviation was divided by the average value of each tissue type, and this value is communicated as a Heterogeneity Index (HI).

Results: In our in vivo clinical studies, the cancer tissues showed 51% higher heterogeneity than the normal tissues (cancer HI: 0.046±0.018, normal HI: 0.024±0.018, p<0.001). Furthermore, the low (N=4), medium (N=9) and high grade (N=6) tumors, defined by the Nottingham Bloom-Richardson histopathological scores (3-5: low, 6-7: med and 8-9: high), demonstrated increasing heterogeneity in the water disposition with the tumor grade. The medium and high grade tumors had 10.5 and 28% more heterogeneity than the low grade tumors in average (low grade HI: 0.041±0.015, med: 0.045±0.02 and high: 0.052±0.017). Discussion: The tissue water measurement using DOSI showed its ability to measure increased pathological heterogeneity in more invasive cancer tissues. This result supports our earlier finding that the BWI can report on histopathological grades of cancer tissues. These pathological properties were acquired in a completely non-invasive way with non-ionizing low power light. The results of this study suggest that the water state measurement using DOSI may be used as a non-invasive optical biopsy with high specificity.

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