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Can optical biopsies accurately diagnose prostate cancer? First-in-human clinical trial data

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Introduction & Objective: We conducted a clinical trial during July-December, 2012 to determine the efficacy of a 14G optical biopsy needle adjunct with fluorescence spectroscopy (FS) for diagnosis of prostate cancer (PCa). The optical properties of biological tissues are determined by their molecular composition and cellular morphology. The fluorescence emissions from natural fluorophores (e.g., tryptophan) in prostate tissue are altered by the presence of carcinoma. Thus, changes in FS can be used to identify PCa. Current TRUS-guided prostate biopsies taken randomly are subjected to sampling errors and often fail to diagnose PCa. Hence, optical biopsies could potentially minimize sampling errors and improve diagnosis of clinically important PCa by targeting areas positive for cancer.

Materials & Methods: Optical sensor uses 8x100µm fibers for excitation and 1x200µm fiber to collect FS data. Custom made fluorometers with 2 light-emitting diodes at 290 and 340nm and a spectrometer were used to measure FS of prostate tissue. User interface for fluorometer operation and data collection was developed using LabView software. Each spectral data acquisition takes ~250 milliseconds. The *in vivo* biopsies were performed during radical prostatectomy surgery on the exposed prostate with blood flow to the gland intact. A tissue biopsy core was obtained from each biopsy site after acquisition of FS data. Above procedure was repeated *ex vivo* after surgical excision of the prostate. Biopsy cores were histopathologically classified as benign or malignant and correlated with corresponding FS data. Spectra with signal-to-noise ratio ≤6 were discarded. Partial Least Square (PLS) analysis of the FS data was performed to determine PLS components at each excitation wavelength. Using linear support vector machine (SVM) and leave-one-out cross validation method, PLS components were tested for their ability to classify benign vs. malignant prostatic tissue.

Results: Thirteen patents were consented. A total of 208 *in vivo* biopsies (29 malignant) and 224 *ex vivo* biopsies (51 malignant) were studied. SVM analysis based on selected PLS components provided 84% sensitivity (SE), 90% specificity (SP), 60% positive predictive value (PPV), and 97% negative predictive value (NPV) for *in vivo* and 81% SE, 95% SP, 79% PPV and 96% NPV for *ex vivo* benign *vs.* malignant prostatic tissue.

Conclusions: Our optical biopsy needle has sufficient SE, SP, and NPV for diagnosis of PCa by targeting areas positive for cancer within the prostate gland. Systematic use of TRUS-guided optical biopsies may permit customized patient care based on accurate histologic grade and stage of the disease. Limitations of our study are small sample size. Further studies are warranted to confirm these findings and to develop a prostate tissue classification algorithm.

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