**Project Title**: Feasibility of Diffuse Optical Tomography in Prostate Cancer Detection and Risk Assessment

**Background**: Prostate cancer (PC) is the most common cancer and the second most common cause of cancer deaths in American men, but not all who are diagnosed with the disease need treatment. This is compounded by the fact that therapies for localized PC are morbid. Who to treat is thus a significant and ongoing clinical question, managed with predictive nomograms and models. However, these tools depend on the Gleason score from prostate biopsies, which are subject to sampling error, with risks of missing clinically significant lesions and upstaging or upgrading of the disease. Current imaging modalities have limited sensitivities and specificities and can be costly and inconvenient.

Diffuse optical tomography (DOT) is an emerging technology that analyzes the absorption and scattering of near infrared light as it passes through tissue and generates three-dimensional maps of oxyhemoglobin [HbO], deoxyhemoglobin [Hb], water [$H_2O$], fat, and light scattering coefficient ($\mu_s$). These parameters serve as surrogates for tissue vascularity and architecture, both of which are associated with risk of PC recurrence and mortality. DOT is fast, inexpensive, and does not require intravenous contrast or ionizing radiation and can thus be used simultaneously with transrectal ultrasound (TRUS) imaging in the office or operating room. DOT has been evaluated in PC but these studies use prostate biopsy specimens, which may be subject to sampling error. Others used phantom or non-human models that do not represent real world situations.

**Specific Aims/Hypothesis**: We propose a pilot study to evaluate three specific aims:
Aim 1: To evaluate the feasibility of concurrent TRUS/DOT imaging defined as successfully imaging and generating usable DOT data in 60% of subjects.
Aim 2: To determine the difference in DOT parameters between benign and malignant prostate tissue. As PC is more vascular and has a less organized cellular architecture compared to benign tissue, we hypothesize that PC will have higher DOT-measured [HbO] and [Hb] and a higher $\mu_s$ compared to benign prostate tissue.
Aim 3: To determine the correlation between $\mu_s$ and Gleason score, and the correlation between [HbO], [Hb], [$H_2O$], and fat and microvessel density (MVD). We hypothesize that the $\mu_s$ will positively correlate with Gleason score and that [HbO] and [Hb] will positively correlate with tumor MVD.

**Study Design**: We will recruit 25-40 men with stage T2 or greater PC scheduled to undergo radical prostatectomy. After sedation and prior to surgery, the combined TRUS/DOT probe will be inserted into the rectum. Gain settings for the DOT device will be calibrated for the patient's prostate. DOT data will then be collected. During the optical measurement, light from three laser diodes (wavelengths 765-905nm) will be sequentially coupled into 16 collocated fibers that serve both as light sources and detectors. Reflected light intensities will be collected by 16 detection fibers coupled to individual silicon photodiodes, which record the light intensities. Using ultrasound images obtained simultaneously with DOT data, a hierarchical clustering method will be used to reconstruct the prostate and divide it into progressively finer geometric clusters to search for anomalies. Using this method, in combination with the multi-wavelength image reconstruction code previously developed by our group, sequential cross sectional maps of [HbO], [Hb], [$H_2O$], fat, and light scattering ($\mu_s$) will be generated for each prostate that will then be combined to generate 3D maps. Feasibility will be determined on an ongoing basis after every 5 subjects. If fewer than 3 subjects in each 5-subject group are successfully imaged, adjustments will be made on reconstruction algorithms, adding light source/detector pairs, adding wavelengths of light, and using an injectable contrast agent. Prostatectomy specimens will be analyzed independently of the DOT data for location and size of the tumor. We will compare the DOT parameters between benign and malignant areas. Gleason score and microvessel density of tumor sections will be determined and correlated to DOT parameters.

**Impact/Future Directions**: Concurrent TRUS/DOT imaging of the prostate could change the way PC is diagnosed and managed. Accurate diagnosis of an indolent or aggressive PC would reduce the number of men being over-treated for PC, and improve the cost/benefit ratio of men undergoing definitive therapy for PC. With an estimated accrual rate of 3-4 patients per month we anticipate completing the study within 7-9 months, allowing time for data analysis and manuscript preparation. With these preliminary data we would further develop and validate this technology. Funding would be sought through multiple mechanisms including the Prostate Cancer Foundation Young Investigator Award, the Conquer Cancer Foundation and American Cancer Society Career Development Awards, the Department of Defense Prostate Cancer Research Program Training Award, as well as an NIH K23 Mentored Patient Oriented Research Career Development Award.