

"Multimodality Microendoscope for the Detection of Metastatic Ovarian Cancer"

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Ovarian epithelial cancer is the fifth leading cause of cancer death among women in the US, and has the highest fatality-to-case ratio of all gynecological cancers. Ovarian cancer is especially dangerous due to its propensity to rapidly metastasize, as the disease invades tissues throughout the abdomen by exfoliating from the original tumor. 90% of all ovarian cancer fatalities arise from this occult metastatic disease, which often is composed of a multitude of micrometastases that are exceedingly difficult to detect. While white-light and fluorescence endoscopy have been used, their selectivity and sensitivity have been too limited to accurately detect the microscopic, deadly metastases without high false-positive and false-negative rates. Without the ability to detect this sub-clinical disease state, many women miss a critical period where alternative chemotherapy or radiation treatment might be lifesaving. It is the long-term goal of this project to improve the dismal survival rates (<30%) of ovarian cancer by building, testing, and deploying a sensitive new paradigm for micrometastases detection. This proposal combines the visualization of suspect tumors *in situ* by fluorescence with the structural optical coherence tomography (OCT) imaging technology to provide a selective, sensitive, and fully quantitative microscopic imaging probe for ovarian cancer diagnostics. By utilizing fluorescence detection for rapid examination and OCT for 3D structural imaging, this *in situ* probe will not only visualize a tumor, but also render its size, underlying tissue structure, and vasculature. In the first aim, a novel imaging probe will be built utilizing an image fiber composed of tens of thousands of individual image elements. Each image element is serially scanned one-at-a-time on the near (proximal) end, ensuring a small distal form factor for minimally invasive imaging. OCT depth scans from each image core will be combined to visualize the full three-dimensional tissue structure for quantitative imaging. In order to selectively visualize ovarian cancer tumors and metastases, a confocal fluorescence detection system will be combined with the OCT system. Fluorescent markers, which are engineered to selectively bind or concentrate to cancerous tissue, are injected into the intraperitoneal space to allow for rapid and sensitive tumor identification. Fluorescence illumination will be delivered collinearly with the OCT laser beam, which will enable simultaneous, automatically co-registered, structural and molecular imaging of suspect tissue sites *in situ*. In the second specific aim, the multimodal contrast of the microendoscope will be extensively characterized using both *in vitro* models and *ex vivo* tissues. Three-dimensional tumor models of ovarian cancer will be used for *in vitro* characterization, where the tumor cells self-assemble into acinar structures that resemble the tumor nodules found in metastatic ovarian cancer. *Ex vivo* characterization will utilize tissue obtained from a murine model of ovarian carcinomatosis. Both healthy and diseased tissues will be used for extensive characterization and cataloging so that the multimodal contrast can be used for *in situ* diagnosis of occult metastatic disease. Ultimately, this research seeks to vastly improve the detection and subsequent treatment of ovarian cancer to save the lives of women with this disease.