The multi-spectral confocal imaging system for optical biopsy in surgery

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Introduction

We have developed a real-time multi-spectral confocal microendoscope imaging system (MCME) providing surgical teams instant optical biopsies for early cancer detection via a laparoscope or daughter endoscope. Optical biopsy delivers instant in-vivo cellular images, comparable to those provided by histology, through a minimally invasive procedure. For the surgeon, this means that more tissue can be explored and abnormalities can potentially be dealt with during the same procedure with less harm to the patient. Currently, surgeons must extract tissue and wait for frozen section processing and pathology analysis to determine if the tissue is abnormal.

Interchangeable catheters connected to a mobile high-speed slit scanning confocal system (Figure 1) provide both flexible endoscopic and rigid laparoscopic abilities for compatibility in a variety of common procedures (Figure 2). The confocal nature of the system optically sections the tissue and enables real-time display and collection of high-resolution grayscale video of tissue. The MCME's ability to image at the cellular level can help diagnose the subtle morphological changes that take place during the early stages of cancer development (Figure 3). The MCME can also collect high-resolution multi-spectral images (Figure 4). These images have enhanced contrast and provide additional information about the tissue including targeted contrast agent concentrations, pH levels, and ion concentrations.

Using Apple hardware and Mac OS X technologies, we have developed a mobile system that is reliable, fast, and easy to use. Leveraging the Unix foundation of OS X we have been able to integrate scientific libraries and existing code with OpenGL, HDF, Python, and PyObjC to control our hardware and develop a user interface in Cocoa suitable for the surgical suite.

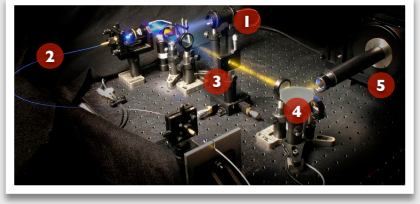

Figure 1: The high-speed slit scanning confocal system
Our mobile system consists of a 488nm laser source (1) that excites tissue fluorescence through a catheter containing a 30k fiber bundle (2) and micro objective. The same fiber bundle collects the fluorescent signal, which is directed through a confocal slit (3) to reject defocused light. An image is collected by sweeping a second scan mirror (4) across the image detector (5).

System Characteristics

Field of View: 450um
Transverse resolution: 3um
Axial resolution: 20um
Spectral resolution: 5nm
Greyscale imaging: 30 fps
Multipsectral imaging: 0.2 fps
Catheters: endoscope, laparoscope

Operating system: Mac OS X
Languages used: Objective C, Python
Application Environment: Cocoa
Frameworks & Libraries: Accelerate (vImage, vDsp), OpenGL, HDF, PyPlot, PyObjC.

Confocal Imaging

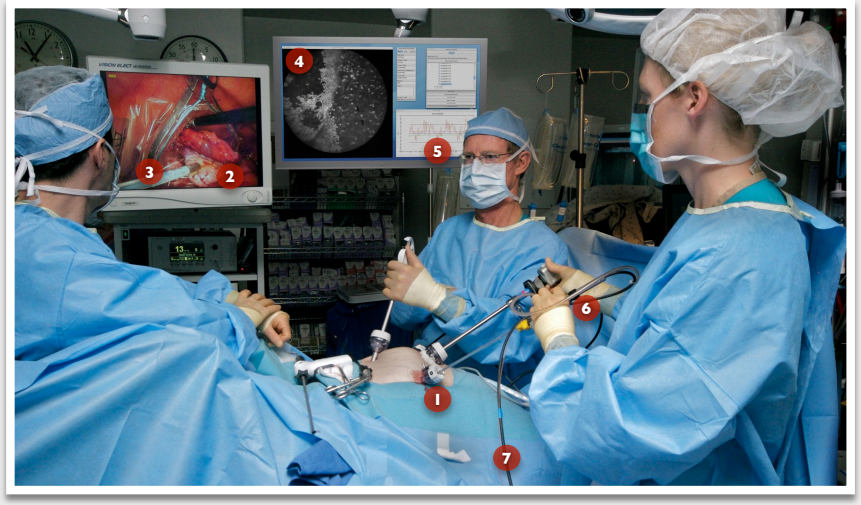

Figure 2: Live cellular imaging of ovaries in surgery
Dr. Kenneth Hatch directs a laparoscopic surgery in which a female patient's right ovary with an abnormality is "optically biopsied" during a clinical trial of our system. The assisting surgeon images the ovary with our 5mm confocal laparoscope entering the foremost trocar (1) and contacting the ovary (2) from the lower left (3). The integrated contrast agent delivery system meters 1ul of fluorescent dye to the field of view resulting in a fluorescent video of the epithelial cells (4) in real-time. To the right of the live video feed, image feature analysis results (5) are displayed to aid in the detection of abnormal tissue. Adjustment of the depth selector knob (6) allows the surgeon to image below the tissue surface. The images are carried back to the slit scanning confocal system through the protected 20' fiber bundle (7).

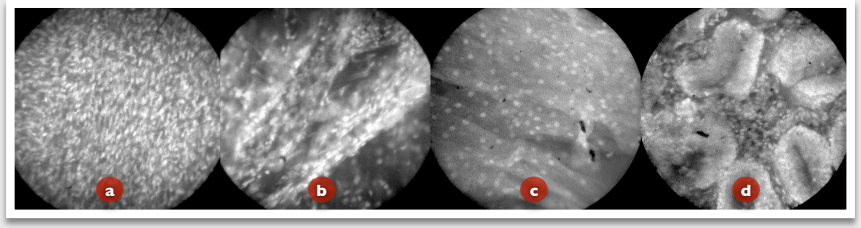

Figure 3: Images of human tissue
Example images of in-vitro human tissue illustrate our system's ability to discriminate between normal and abnormal tissues. Normal human ovary (a) with strong heterogeneity is clearly discriminated from abnormalities (b) which introduce striations in the cellular structure. Normal human esophagus (c) has evenly dispersed bright nuclei but morphological changes take place once Barrett's Esophagus envelopes and gastric mucosa dominate (d).

Multi-Spectral Imaging

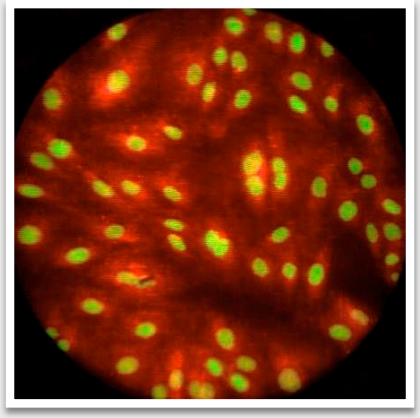

Figure 4: Multi-spectral cellular image
During multi-spectral acquisition mode multiple dyes can be used to enhance cellular structure such as nuclear contrast with MitoTracker Deep Red and SYTO 16 in a culture of rat smooth muscle cells. Spatially localized spectra can then be extracted with a 5nm resolution to further characterize fluorophores.

Applications

The initial applications of the system include diagnosing diseases of the female reproductive system and the gastro-intestinal tract. Our current research involves endoscopically imaging the esophagus and laparoscopically imaging the ovaries. For individuals with Barrett's esophagus, the instrument will help the surgical team pinpoint and localize regions of dysplasia. Clinical trials are currently underway for women at high risk of ovarian cancer where the instrument will ultimately be used to screen for early onset of this disease.

References & Acknowledgments

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