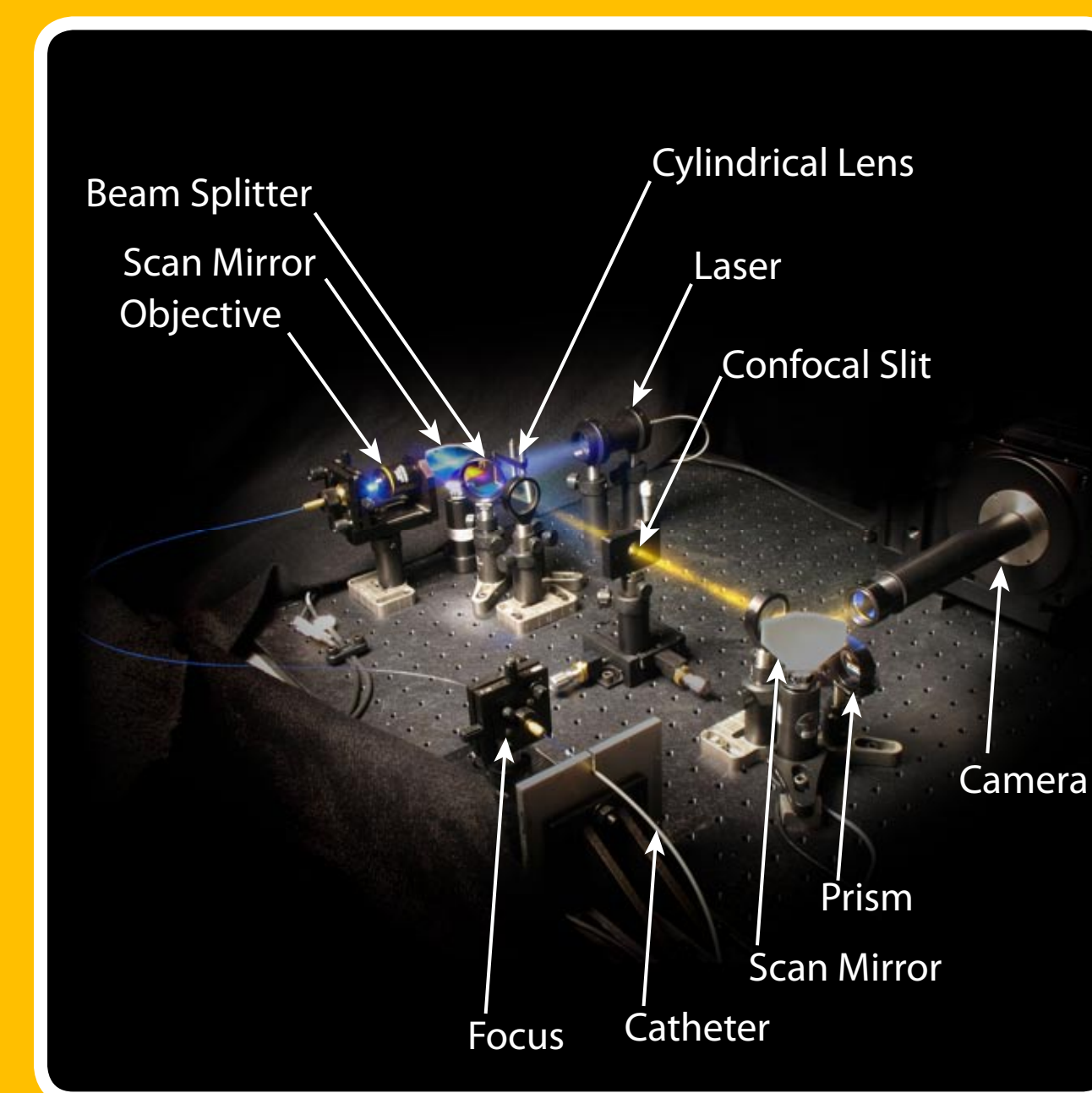


# THE MULTI-SPECTRAL CONFOCAL MICRO-ENDOSCOPE

# OPTICAL BIOPSY

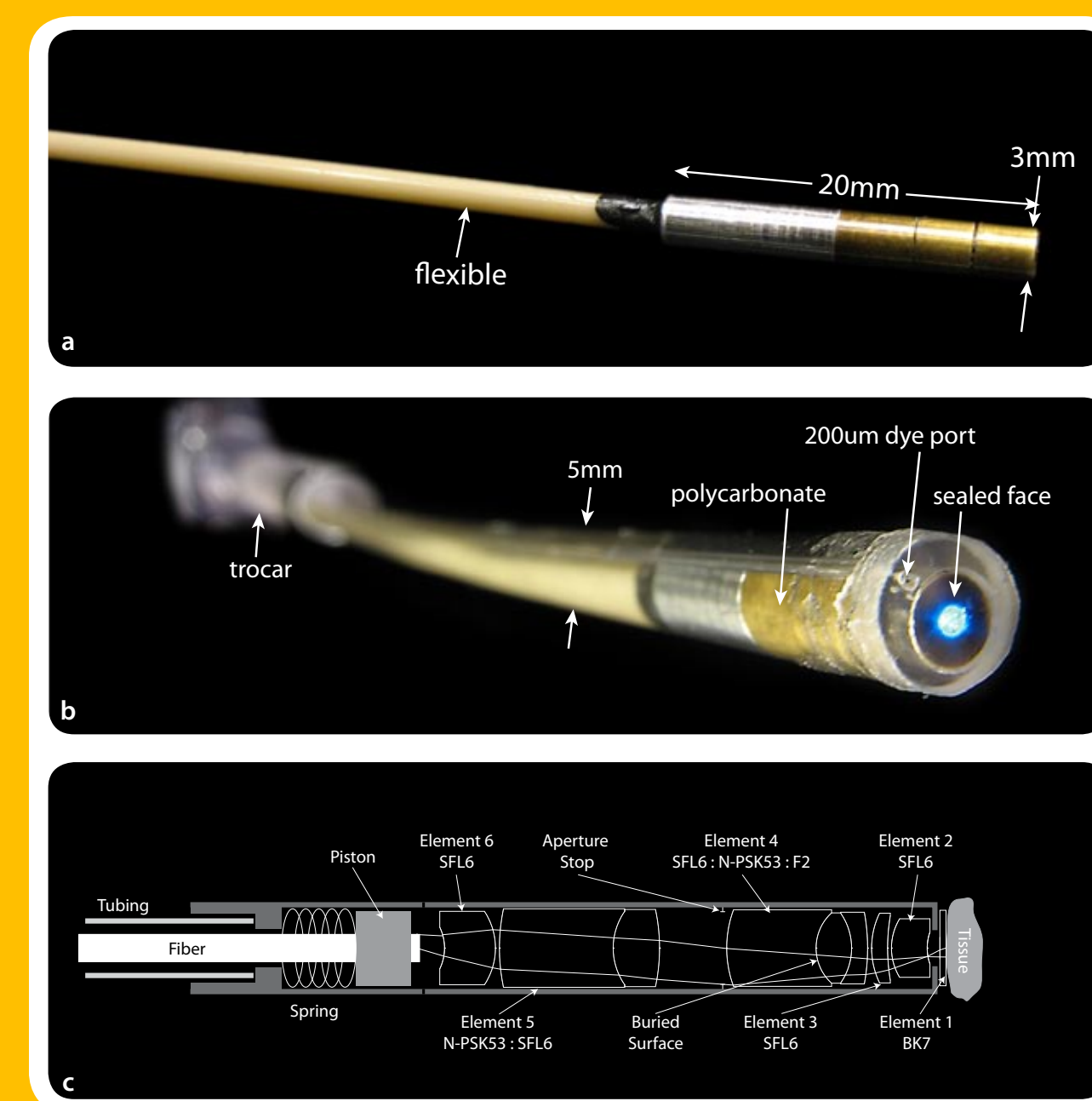
## SYSTEM

An anamorphic optical system scans a line of 488nm laser illumination on the proximal face of the imaging fiber bundle. The fiber bundle relays this profile to the distal end where a miniature objective and focusing mechanism scan the tissue. Exogenous tissue fluorescence is collected by the same catheter, de-scanned, and separated from the reflected illumination by a dichroic beam splitter. This fluorescence signal is optically sectioned by a confocal slit aperture and rescanned onto the image detector array. For multi-spectral acquisitions, the fluorescence signal is diverted through a prism dispersing the chromatic information across the image detector array. The full spatial and spectral information is recorded through a series of images.



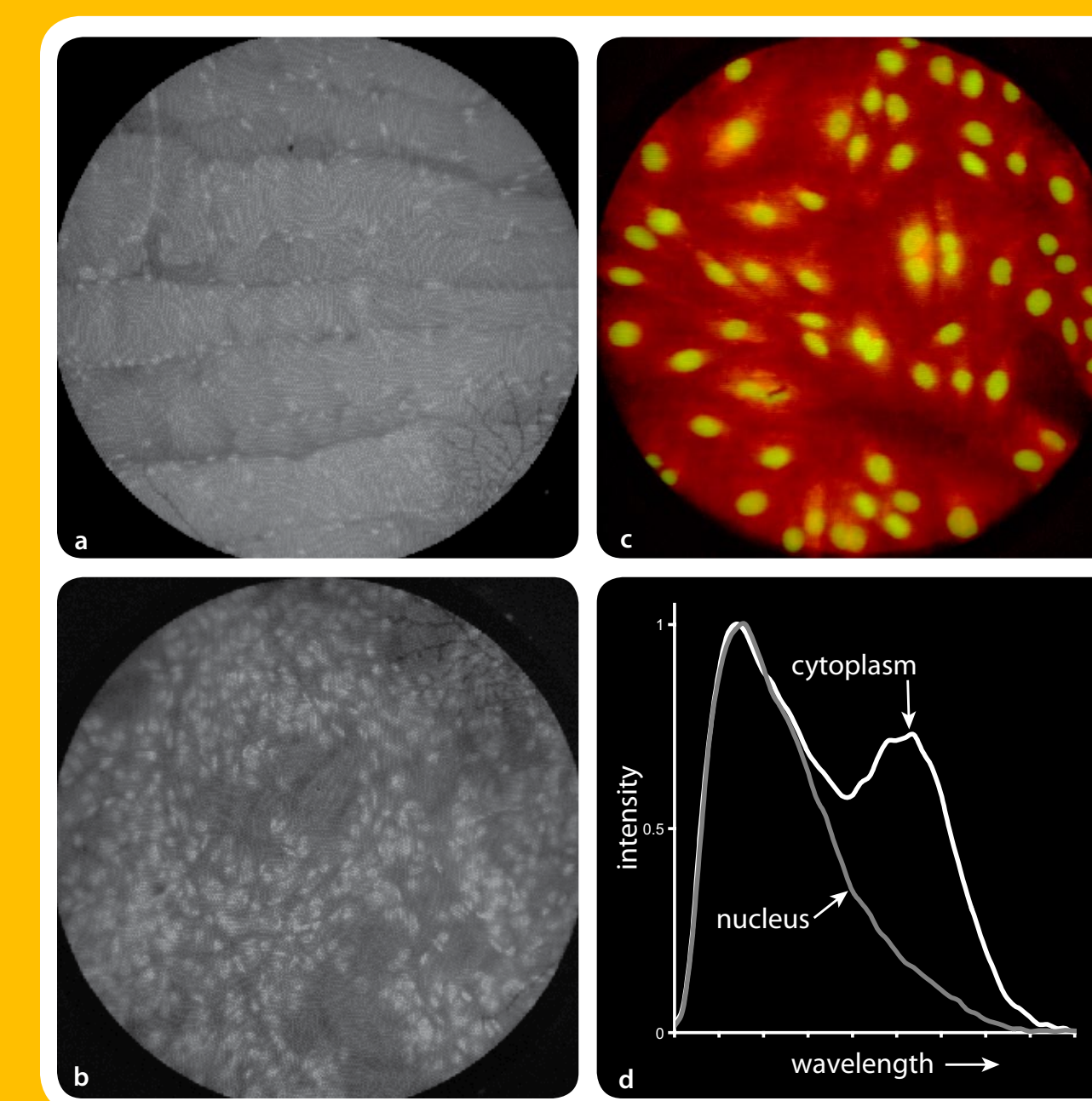
## CATHETERS

The primary MCME catheter (a) is 3mm in diameter and flexible with computer controlled focusing. This catheter can interrogate tissue independently or work as a daughter scope through the therapeutic channel of an endoscope. Procedures requiring a rigid imaging device utilize the (b) laparoscopic catheter. This catheter encapsulates the flexible catheter in a sterilizable polycarbonate housing with a 5mm outer diameter. The housing contains an integrated contrast agent delivery channel and a sealed face eliminating the need to sterilize the flexible catheter. In both cases the images are collected with a (c) 3mm diameter polychromatic, large numerical aperture micro-objective with integrated focusing. The nearly diffraction limited micro-objective consists of 6 elements with 13 optical surfaces and provides a 1.6x magnification.



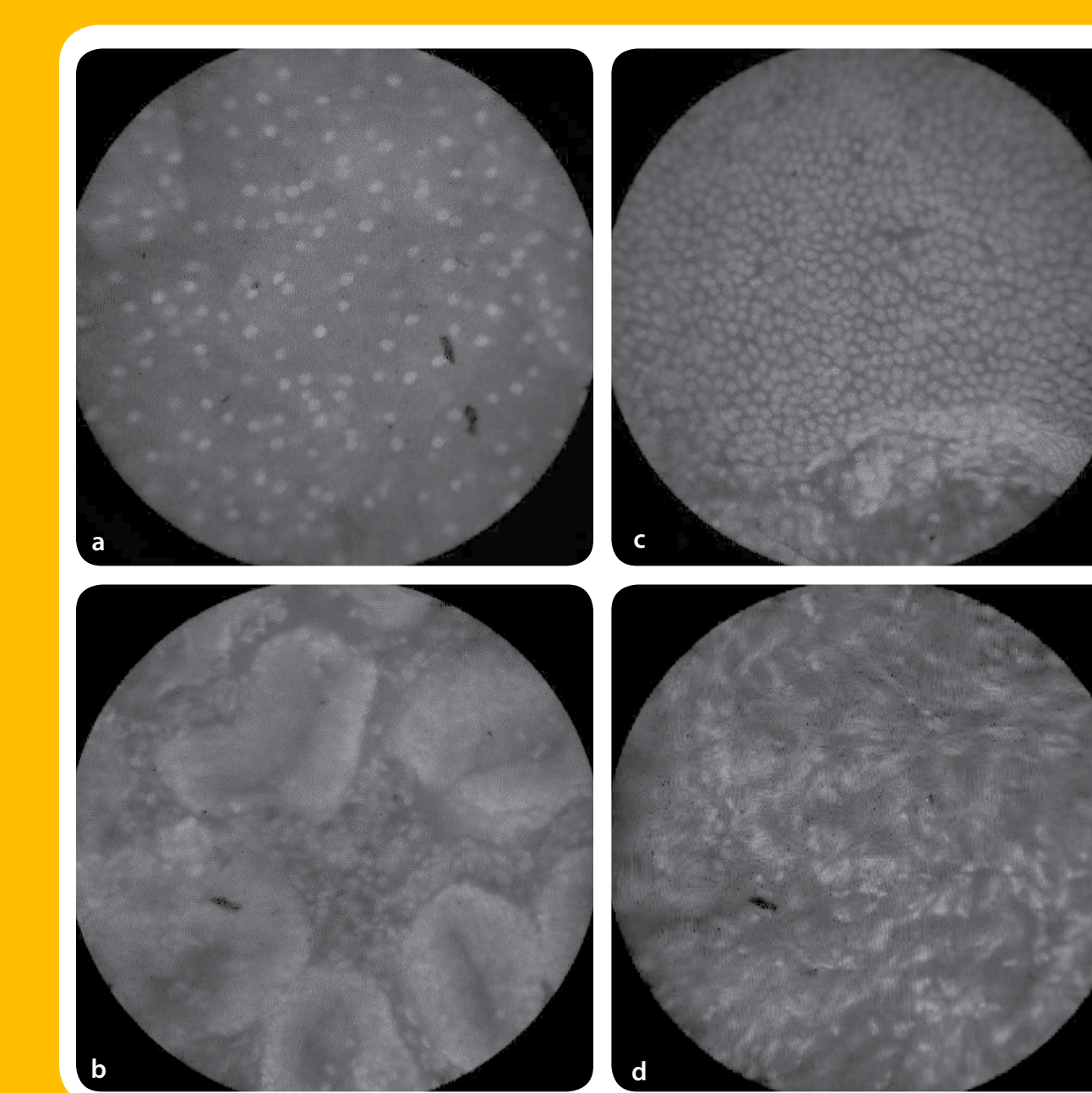
## DATA

Initial testing of the MCME was performed on a mouse that was sacrificed immediately prior to the experiment. Data were acquired in-vivo after topical application of 330µM acridine orange (AO). The experiment illustrates the MCME's ability to differentiate tissue types such as (a) peritoneal wall and (b) kidney. In Multi-spectral acquisition mode multiple dyes can be used to enhance cellular structure such as (c) nuclear contrast with MitoTracker Deep Red and SYTO 16 in a culture of rat smooth muscle cells. Spatially localized spectra can be extracted to further characterize fluorophores such as (d) the cytoplasmic red shift of acridine orange in the human esophagus.



## HUMAN TRIALS

Clinical studies are underway to determine the sensitivity and specificity of the MCME in detecting carcinoma in the human esophagus and ovaries. Patients with Barrett's esophagus exhibit a change in normal squamous mucosa to columnar mucosa with associated intestinal metaplasia. A patient's risk of developing esophageal cancer increases 30 to 50 times with the presence of Barrett's. Initial work with the MCME is currently underway to discriminate (a) squamous mucosa from (b) columnar mucosa and subsequent dysplasia. The MCME will soon undergo a clinical trial to evaluate it as a screening tool for the early detection of ovarian cancer. This disease has a high mortality rate due to late diagnosis. Ovaries will be imaged in-vivo prior to laparoscopic oophorectomy. Initial testing on ex-vivo samples has shown that the MCME can distinguish (c) normal



## REAL-TIME IN-VIVO CELLULAR IMAGING

## MCME

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The early diagnosis of cancer is critical for the successful treatment of patients. The **Multi-spectral Confocal Micro-Endoscope** enables early detection via optical biopsy. 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.

## Interchangeable catheters

on the MCME provide both flexible endoscopic and rigid laparoscopic capabilities for compatibility in a variety of common procedures. The confocal system images a thin section of tissue at a selected depth. Collection of high-resolution grayscale images occurs in real-time. The MCME's ability to resolve at the cellular level can

help diagnose the subtle morphological changes that take place during the early stages of cancer development.

The MCME can also collect high-resolution **multi-spectral** images. Multi-spectral images have enhanced contrast and provide additional information about the tissue including targeted contrast agent concentrations, pH levels, and ion concentrations. Multi-spectral collection allows multiple spectrally overlapping fluorophores to be simultaneously recorded and then decomposed into specific fluorophore concentrations.

The initial applications of the MCME include **diagnosing diseases** of the gastro-intestinal tract and the female reproductive system. We are currently using the MCME in humans to endoscopically image the esophagus and laparoscopically image the ovaries. For individuals with Barrett's esophagus, the MCME will help the surgical team pinpoint and localize regions of dysplasia. For women at high risk of ovarian cancer, the MCME will ultimately be used to screen for the early onset of this disease.

## OPTICAL SPECIFICATIONS

- TRANSVERSE RESOLUTION:** 3µm
- AXIAL RESOLUTION:** 20µm
- MAXIMUM DEPTH:** 200µm
- MOBILE:** compact and robust
- FLOUORESCENT:** exogenous dyes
- CONFOCAL:** slit-scanning with dual synchronized single-axes scan mirrors
- GRAYSCALE:** 30 frames per second acquisition
- MULTI-SPECTRAL:** Spectral bandwidth of 450nm to 750nm with 5nm resolution. A 512x512 spatial by 130 spectral data set is collected in 5.5 seconds.

**For More Information:** Additional details and publications concerning the MCME and other research activities can be found at the Biomedical Imaging Lab at <http://bil.arizona.edu>.

## CATHETER SPECIFICATIONS

- EXCHANGEABLE:** standardized connection
- FIELD OF VIEW:** 450µm in tissue
- STERILIZABLE:** ETO compatible
- NUMERICAL APERTURE:** 0.46 in tissue
- FOCUS:** computer automated
- FIBER-OPTIC:** 30,000 element flexible imaging bundle
- ENDOSCOPE:** flexible 3mm diameter
- LAPAROSCOPE:** rigid 5mm diameter with integrated dye delivery

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