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Enhancing Endoscopy With Optical Filters

Source: Iridian Spectral Technologies

In 2012, stomach cancer was responsible for 723,000 deaths, making it the third-leading cause of cancer-related deaths globally, according to the World Health Organization (WHO). The ability to visualize and identify early cancerous lesions is critical in improving patient outcomes through early and accurate detection and diagnosis. Endoscopic examination is a key technique used in diagnosis of the early stage neoplastic lesions associated with stomach and other gastrointestinal cancers.

Endoscopic diagnostic techniques have been around since the invention of flexible fiber optic endoscope in the late 1950s. This innovation allowed physicians direct visual access to the gastrointestinal, urinary, and bronchial tracts in a minimally invasive manner. White-light reflectance (WLR) imaging, in which the area of investigation is illuminated by a broadband visible white light source, became the standard means for *in vivo* diagnosis using "conventional endoscopy." While conventional endoscopy has greatly helped in detecting and diagnosing cancers, images obtained through WLR are evaluated using human vision only[1], and are thus subject to the interpretation of the examiner conducting the endoscopy.

However, structural and morphological details of neoplastic lesions can be endoscopically indistinguishable from surrounding benign tissue. This lack of sensitivity can lead to under-diagnosis of potentially harmful cancers in an early state, reducing the positive patient outcomes possible though early treatment. Lack of specificity (resulting in false-positives) can lead to unnecessary treatments, such as endoscopic biopsy, creating a physical, physiological, and financial burden on the patient and the medical system.

Alternatives or supplements to WLR endoscopic imaging include three techniques leveraging the wavelength selectivity provided by optical filters, each in different ways: narrow-band imaging (NBI), auto-fluorescence imaging (AFI), and endoscopic Raman spectroscopy.

Narrow-Band Imaging (NBI) And Auto-Fluorescence Imaging (AFI)

Both NBI and AFI provide improved visualization and increased sensitivity, compared to WLR endoscopy, by inserting optical filters at the instrumentation (proximal) end of the system to select either the illumination or excitation wavelengths desired. In the case of AFI, the emission wavelength corresponds to the auto-fluorescence of the tissues of interest.

Lesion and microvasculature features can be more visible in different wavelength regions due to wavelength-selective scattering. With NBI, the examiner can select the wavelength of interest to investigate and identify these different types of structures, typically using blue (around 415 nm) and green (around 540 nm) bandpass filters in front of the light source feeding into the endoscope. These different colours of illumination allow for "virtual chromoendoscopy" without the need for dye sprays.

This technique has been shown to improve diagnosis in colonoscopy, bronchoscopic imaging, and gastrointestinal endoscopy. Specifically, H. Machida et al[2] found improved visualization of colorectal mucosal lesions using NBI, compared with conventional colonoscopy, due to the difference in hue afforded by the filtered illumination source (using three 30 nm wide bandpass filters) in NBI. Additionally, information on the surface of the tumours is not obscured using NBI, in contrast to conventional chromoendoscopy, which requires an indigo carmine dye spray.

Also, dysplastic and neoplastic lesions often exhibit auto-fluorescence, and this property can be leveraged in discriminating them from benign tissues. An additional advantage of AFI is that it is a "zero background" technique — in the absence of auto-fluorescing tissues there is no background fluorescence, which greatly improves the signal-to-noise, and thus sensitivity.

AFI systems can implement a filter wheel with narrow visible bandpass filters to select specific excitation wavelengths to be transmitted, via the endoscope, to the tissues of interest. Different fluorescence emission bands can be analyzed with the use of separate bandpass filters [typically green (480-520 nm) and red (625 nm)] at the instrument to block unwanted light, including the excitation light or other undesirable emission bands[1]. Some AFI systems implement a near-infrared (NIR) notch filter at the proximal end of the head, rejecting excitation light while allowing both longer wavelength NIR fluorescence emission light and shorter wavelength visible light (used for WLR or NBI) to be transmitted to the detector or imaging system.

Endoscopic Raman Spectroscopy

While NBI and AFI improve on the visualization and sensitivity of conventional endoscopy, they still have limited specificity, as they do not provide biomolecular information about the tissues under investigation. In particular, inflamed tissue can sometimes be difficult to distinguish from cancerous tissues when using AFI, resulting in potential for false-positive diagnosis. In contrast, endoscopic Raman spectroscopy leverages the interactions of light with vibrational modes of molecules to deliver the unique molecular fingerprints of the tissues under examination without requiring any preparation of the tissues of interest[3,4,5].

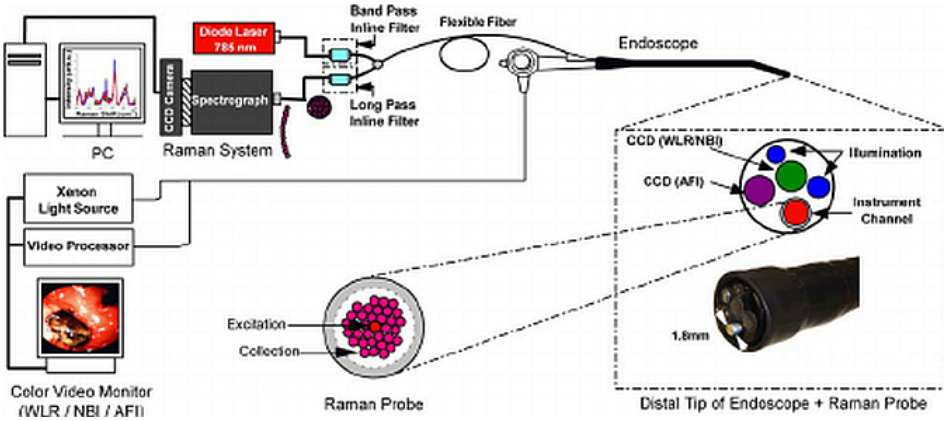

Image courtesy of Zhiwei Huang

The challenge has been to take the existing Raman technology, used in handheld analytical instruments for years, and achieve both the miniaturization and speed needed to make it a viable in vivo examination technique. Huang et al have developed endoscopic Raman spectroscopy with the speed needed for in vivo analysis (<0.5 sec per scan) and the accuracy (sensitivity and specificity >90 percent) for use in gastric or oesophageal cancers and pre-cancerous lesions[3].

In contrast to NBI and AFI systems, endoscopic Raman spectroscopy can use filters at both the proximal end and the distal tip of the endoscopic probe, creating special demands on the performance and durability of the optical coatings required.

The proximal filters are standard Raman band-pass (BP) and long-pass (LP) filters, typically used in bench-top or handheld Raman systems. The Raman BPF serves to suppress laser noise and other unwanted sources of light, such as fluorescence, from entering the illumination fiber on the endoscope. Key filter characteristics are high transmission and broad blocking away from the excitation laser line (typically 785 nm). The Raman LPF is positioned between the collection fibers and the spectrometer, blocking any unwanted Rayleigh scattered laser light from reaching the detector. This is critical due to the small ratio (1:1000000) photons that are Raman scattered. These filters need deep blocking (optical densities of 6 or greater) at the laser line to maintain good signal-to-noise at the spectrometer.

The distal filtering provides similar functionality as the proximal filters, but has the added challenge of being coated on the ends of the endoscope (coated fibers or lenses). Additional BP filtering can be provided at the distal tip to remove any contributions due to fluorescence in the endoscopic fiber. The distal LPF provides the first removal of more powerful Rayleigh scattered laser light, preventing it from entering the collection fibers and creating more noise from the fiber itself.

AFI and Raman endoscopy can be combined to leverage the strengths of each in detecting changes in molecular structure indicative of early or pre-cancerous lesions in the lung. AFI provides higher sensitivity to allow for rapid identification of potentially malignant regions, but can suffer from high numbers of false positives (up to 40 percent). Using AFI to identify regions of interest, followed by Raman analysis (and its increased specificity) of the tissues in these regions of interest, greatly increases the efficiency of the inspection procedure[1,6]. Similarly, NBI and Raman have been combined for gastro-intestinal analysis where NBI serves to pre-select regions of interest.

Conclusion

All of these techniques serve as an “optical biopsy,” replacing the need for physical tissue biopsies and subsequent *ex vivo* examination[6]. This reduces the time needed for diagnosis, reduces patient discomfort (and possibility for infection), and facilitates “real-time” diagnostic biopsy, allowing the physician to identify and remove potentially problematic tissue, and to optically verify that a complete resection has been successful.

About The Authors

Iridian has long been a leader in wavelength selective optical filters for Raman and other bio-analytical instruments. Iridian has recently manufactured optical filters for several endoscopic applications, including visible and NIR band-pass, long-pass, and notch filters used both on the instrument and in the endoscope itself.

Resources:

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2. H. Machida et al, *Narrow-band Imaging in the Diagnosis of Colorectal Mucosal Lesions: A Pilot Study*
3. Zhiwei Huang et al, *Integrated Raman spectroscopy and trimodal wide-field imaging techniques for real-time in vivo tissue Raman measurements at endoscopy*, Optics Letters, Vol.34, No.6, March 15, 2009
4. Hyung Hun Kim, *Endoscopic Raman Spectroscopy for Molecular Fingerprinting of Gastric Cancer: Principle to Implementation*, Biomed Res. Int., May 27, 2015
5. Mads Sylvest Bergholt et al, *Raman Endoscopy for Objective Diagnosis of Early Cancer in the Gastrointestinal System*, Journal of Gastrointestinal & Digestive System, 2013
6. Paras N. Prasad, *Introduction to Biophotonics*, Wiley-InterScience, 2003