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Optical Coherence Tomography for Gastrointestinal Endoscopy

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33.1 Brief Review of Gastroenterology and Endoscopy

Gastroenterology, the study of the physiology and pathophysiology of the organs responsible for digestion, together with the treatment of patients with digestive disorders, has been shaped extensively by technology. As a clinical specialty, gastroenterology relies substantially on visual examination of internal organs with an optical device, i.e., endoscopy. Adolf Kussmaul (1822–1902) is credited with the first endoscopy in 1868, for which he used a long, rigid instrument [1]. Although such instruments became “semi-flexible” by the 1930s, they were challenging to use and therefore impractical. It was the development of the coherent fiberoptic bundle and its incorporation into an endoscope in 1957 that made endoscopy safe and widely applicable. Using the fiberoptic endoscope, in 1969, a method for removal of precancerous polyps from the colon was developed, the first of many endoscopic therapeutic procedures [2]. Although the fiberoptic endoscope evolved to a high level of technical sophistication, the coherent optical fiber bundle was largely supplanted after 1980 by the charge-coupled device (CCD).

Since the advent of colonoscopic polypectomy, therapeutic endoscopy has continued to evolve. Conversely, the development of diagnostic endoscopy, with the exception of endoscopic ultrasonography (EUS), has remained largely static. Since 1886, the endoscopic diagnosis of pathologic disorders has been based essentially on visual inspection. Consequently, endoscopic diagnosis is relatively inaccurate; its precision actually derives from the ability to obtain biopsies, and many such samples acquired because of suspected disease prove to be superfluous to clinical care, except that negative or non-contributory findings, even though necessary, increase costs.

Most disorders of the gastrointestinal (GI) tract, cancer in particular, arise within its innermost layer, i.e., the mucosa. An ability to interrogate the status of the mucosa at endoscopy would be highly desirable. Endoscopic biopsy interpretation is based on visual assessment, using a microscope, of the morphology of a small sample of mucosa. Potentially, a duplication, even a
facsimile, of this capability in “real time” at endoscopy could greatly enhance diagnosis. It might reduce the frequency of unnecessary biopsies; perhaps even eliminate the need for biopsies in some cases.

The many efforts to improve endoscopic diagnosis, to move beyond reliance on visual inspection alone, have taken numerous directions. These include EUS, magnification endoscopy, chromoendoscopy (application of chemical dyes to enhance mucosal detail), and a range of methods based on the various light-tissue interactions. Of these, only EUS has become established as a clinical modality, with applications in tumor staging and detection of small tumors (e.g., in the pancreas). However, the resolution of echoendoscopes is insufficient for investigation of many mucosal disorders.

The gut mucosa consists of three distinct layers: an innermost layer or layers of cells (epithelium), a middle layer of connective tissue (lamina propria), and a layer of muscle cells (muscularis mucosae). Deep to the mucosa is the submucosa with various components, including fat cells, neural and lymphatic tissue, and inflammatory cells. Proceeding outward from the gut lumen, the next layer is the muscular coat (muscularis propria). Last is the serosa, which consists of a single layer of cells (mesothelial cells) together with fibrous and fatty tissue.

All the tubular structures comprising the gut (e.g., esophagus, colon, pancreatic duct, bile duct) have an epithelial lining. Most pathologic processes involve or arise in the epithelium. Of these, cancer will be the focus of this discussion.

Cancerous transformation of the gut epithelium is a methodical sequence of events. As a gross simplification, the initial step may be genetic mutation(s), perhaps preexisting and/or in response to an external stimulus, followed by the appearance of abnormalities within the epithelial cells and evidence of deviant behavior of these cells, the latter attributes being readily evident by standard light microscopy. Opinions vary as to the extent and number of criteria required for a diagnosis of cancer. However, there is frequently a precancerous stage in which groups of cells are clearly abnormal, but not sufficiently so for the changes to be termed cancer. In such cases, the descriptive term dysplasia is applied. In general, this term signifies that the cells are precancerous with the implication that frank cancer will develop if the dysplastic cells are not eliminated. Dysplasia is usually subclassified as low grade or high grade; if especially severe but noninvasive, it may be labeled cancer (carcinoma) in situ. The microscopic diagnosis of dysplasia is subjective; essentially the opinion of a pathologist. Because of this it is always advisable that biopsies be interpreted by one or more expert pathologists when the conclusions influence clinical decisions, especially where alternatives impose risks of morbidity and mortality.

Eventually, the abnormal (dysplastic) cells escape the normal confines of the epithelium, in which case the lesion is termed invasive and is conclusively cancerous. The muscularis mucosae is an especially important boundary with respect to invasiveness. Because lymphatic channels are not present in the