Capsule endoscopy: Future horizons

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Abstract
Capsule endoscopy (CE) was launched at the beginning of this millennium and has since become a well established methodology for evaluating the entire small bowel for manifold pathologies. CE far exceeded early expectations by providing a tool for establishing the correct diagnosis for elusive gastrointestinal (GI) conditions such as obscure GI bleeding, Crohn’s disease, polyposis syndrome and others. Contemporary CE, like radiology, gives results that can only be read, unlike conventional endoscopic procedures which enable concomitant biopsy when indicated. This is one of the major limitations of the technique. The ideal CE should improve the quality of the image and have a faster frame rate than the currently available one. There should be a therapeutic capsule capable of performing a biopsy, aspirating fluid, delivering drugs as well as measuring the motility of the small bowel wall. Another major leap forward would be the capability of remote control of the capsule’s movement in order to navigate it to reach designated anatomical areas for carrying out a variety of therapeutic options. Technology for improving the capability of the future generation capsule is almost within grasp and it would not be surprising to witness the realization of these giant steps within the coming decade.

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INTRODUCTION
Capsule endoscopy (CE) had been proven to be a safe and painless procedure that is superior to several other imaging modalities for diagnosing small bowel pathologies such as small bowel follow-through X-ray, colonoscopy with ileoscopy, computerized tomographic enterography, magnetic resonance enteroclysis and push-enteroscopy.[1,2]

Since the emergence of CE, more than 1000000 capsules have been swallowed worldwide and nearly 1000 peer-reviewed publications have appeared in the literature. The ideal CE of the gastroenterologist’s imagination should be capable of performing an ordinary biopsy as well as carry out an online analysis (an “optical” biopsy) and “stop” bleeding by an adrenaline injection, a heat probe, argon plasma coagulation, etc. The ultimate capsule would include special detectors for white blood cells and be capable of checking oncological markers (e.g. CEA, CA 19-9), perform serology tests (e.g. anti-endomysial, IgE) and measure various cytokines, pH, temperature and pressure, in addition to delivering drugs. The capsule’s motility feature in the small bowel may open a window to study the pathophysiology of relatively elusive medical entities such as irritable bowel syndrome.[3-5]. Finally, the optimal capsule
needs to contain a computerized system for automatic detection of pathologies such as the design of a Holter electrocardiographic recording in order to overcome the drawback of time-consuming viewing the video.

**IDEAL CAPSULE ENDOSCOPY**

Solutions of fundamental problems in CE technology have not been forthcoming since its promising entrance into GI diagnostics. Has a technological plateau been reached? Probably not. Until the next breakthrough, however, CE remains a diagnostic tool that has yet to realize its potential. A look at the history of GI endoscopy reminds us that the first step had been limited to no more than viewing the organ. Only later did it develop into a tool for biopsy and then a conduit through which to perform therapeutic procedures such as polypectomy, sphincterotomy and others. Will the capsule of the future replace single or double balloon enteroscopy? According to a number of authors, the answer is probably yes[6].

What, then, would be the ideal capsule of the gastroenterologist’s wildest imagination? Would we prefer a single capsule that, in one “shot”, can give us the entire view from the oral cavity to the anal canal, or are we hoping that some day there will be an “intelligent” capsule that specializes in each section of the GI tract? Unfortunately, the anatomical and physiological differences in the GI tract make it impossible to use the same capsule for both purposes. Small bowel, esophageal and colonoscopy capsules are now commercially available. The latter two are equipped with miniature cameras on both ends of two video cameras.

How would we love to be able to pinpoint drug deliveries in specific diseases such as Crohn's disease! The problem is that it would have to be done daily over a long period and this would be time consuming and costly. A pre-programmed non-viewing (i.e. no camera) capsule for drug delivery would be much cheaper and one can imagine a combination of viewing and non-viewing capsules that can be used to make this treatment efficient and cost-effective. This possibility of drug delivery would open enormous windows of opportunity to pharmaceutical companies. For clinicians, the capsule’s motility feature in the small bowel would open a window to study the pathophysiology of relatively elusive medical entities such as irritable bowel syndrome. Malagelada et al[9] were the first to publish their findings on CE motility in the clinical setting and they found that CE was useful in diagnosing patients with irritable bowel syndrome.

Next in our dream of CE are zooming or magnification capabilities. Why not? Think of chromo-endoscopy, narrow band imaging, ultrasound imaging and the delivering of therapy including tissue coagulation and immunologically or chemically targeted optical recognition of malignancy as it exists in endoscopy, capable of spraying fluid (methylene blue, Lugol solution, etc.) in specific areas of the small bowel. At present, the capsule cannot obtain biopsies, aspirate fluid or brush lesions for cytology. These techniques require real-time viewing as well as radio-controlled triggering and remote controlled capsule manipulation if they are to be used with precision. However, optical biopsy seems feasible[8]. We can easily visualize our capsule eventually becoming a complete miniature laboratory with the functions of bio-sensing luminal contents and biopsy (probably by optical technologies) as well.

**ENERGY SUPPLY**

Technological advances, particularly in reducing the size of components and improving power management, will be needed before the next generation of capsule endoscopy devices can be developed. The quality of current CE images is inferior to that of conventional endoscopes and the solution awaits advances in microelectronics that will lead to image sensors with a smaller pixel size that enable higher resolution. In addition, current CE systems use image data compression which causes blurring at the edges of objects and leads to lower image quality, a major limitation of CE. In particular, depletion of the two silver oxide batteries used in current devices may prevent complete imaging of the small intestine if the pill remains in the stomach for too long. The problem becomes most apparent by the inability to view the cecum (the marker of a complete examination) in 10%-15% of CE examinations of the small bowel[1,2]. This will eventually be overcome by using power transfer methods from outside the body. In the short term, this problem can partly be solved by using more efficient power management algorithms that enable an 11 h recording time. There have been important “breakthroughs” in battery design with the advent of carbon nanotubes (Buckytubes) which have the intrinsic characteristics desired in the material used as electrodes in batteries and capacitors. Buckytubes have an enormous surface area (approximately 1000 m²/g) and good electrical conductivity. Their linear geometry makes the surfaces highly accessible to the electrolyte. It may be that their application will lead to enhanced battery design and better power management to give the capsule the power required for additional performance and functions for improving the quality of the image[7].

Other methods that are under consideration for development for solving imaging issues include control units that vary the frame rate. One example is the OMOM capsule, developed at Chongqing Jinshan Science and Technology Group (Chongqing, China), which can switch from 0.5 frames per second (fps) inside the stomach to 2 fps after entering the pylorus[3]. In a well-conducted randomized prospective study of 50 patients in China, the cecum was visualized in the 25 subjects who ingested the capsule in the switching frame rate mode compared with 18 of 25 in whom the pill functioned at a steady frame rate of 2 fps[10].

The benefit from size reduction and power efficiency is best exemplified by MiroCam by Intromedic (Seoul, South Korea). This is the first endoscopic capsule that uses the human body instead of radiofrequency to trans-
mit data, reducing power consumption. In the first clinical trial on 45 patients in South Korea, MiroCam captured images from the whole small intestine as far as the cecum in all the subjects. Because the device does not use image compression, the bowel mucosa was viewed without blurring or distortion in over 90% of patients[11]. This system also uses fewer components for remote transmission, thus saving space for the possible addition of modules for biopsy or locomotive guidance[11].

All in all, the technical shortcomings are quite straightforward and so we have every reason to believe that CE will be able to exploit the energy and enthusiasm of modern technology to deal with them. It is only a matter of time.

PROPELLING THE CAPSULE

We eagerly look forward to the day that we will be able to “control and steer” the CE as endoscopists are able to do in standard endoscopy. This would give us control in maintaining the capsule steady in a selected area and hold the view in order to have more time to examine the opposite wall of the bowel. Miniaturization of capsule components and power consumption are also pivotal to tackling the biggest challenge of all, that of active capsule locomotion. Two research projects supported by the European Union are currently pursuing this goal. One is VECTOR (Versatile Endoscopic Capsule for gastrointestinal TumOr Recognition and therapy) and the other is NEMO (Nano-based capsule-Endoscopy with Molecular Imaging to develop a self-propelled miniaturized robotic pill for microelectronics will produce image sensors with smaller pixel sizes and resultant higher resolution to considerably enhance the image quality versus standard tests in influencing management of obscure digestive bleeding: results from a German multicenter trial. Am J Gastroenterol 2005; 100: 1736-1742.

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CONCLUSION

Technological advances together with improving power management will be needed before the next generation of CE devices can be developed. Advances in microelectronics will produce image sensors with smaller pixel sizes and resultant higher resolution to considerably enhance the image quality provided by CE which is currently inferior to that of conventional endoscopes. Future gastroenterologists will have a number of types of capsules from which to choose according to whether the purpose of the evaluation is diagnostic and/or therapeutic. We are confident that our expectations of CE will soon become a reality and that CE will enrich the gastroenterologist’s armamentarium, providing “Star Wars” patient care in which almost all things are possible.

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