

## TOPIC HIGHLIGHT

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# The future of wireless capsule endoscopy

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## Abstract

We outline probable and possible developments with wireless capsule endoscopy. It seems likely that capsule endoscopy will become increasingly effective in diagnostic gastrointestinal endoscopy. This will be attractive to patients especially for cancer or varices detection because capsule endoscopy is painless and is likely to have a higher take up rate compared to conventional colonoscopy and gastroscopy. Double imager capsules with increased frame rates have been used to image the esophagus for Barrett's and esophageal varices. The image quality is not bad but needs to be improved if it is to become a realistic substitute for flexible upper and lower gastrointestinal endoscopy. An increase in the frame rate, angle of view, depth of field, image numbers, duration of the procedure and improvements in illumination seem likely. Colonic, esophageal and gastric capsules will improve in quality, eroding the supremacy of flexible endoscopy, and become embedded into screening programs. Therapeutic capsules will emerge with brushing, cytology, fluid aspiration, biopsy and drug delivery capabilities. Electrocautery may also become possible. Diagnostic capsules will integrate physiological measurements with imaging and optical biopsy, and immunologic cancer recognition. Remote control movement will improve with the use of magnets and/or electrostimulation and perhaps electromechanical methods. External wireless commands will influence capsule diagnosis and therapy and will increasingly entail the use of real-time imaging. However, it should be noted that speculations about the future of technology in any detail are almost always wrong.

## INTRODUCTION

Wireless capsule is an incompletely developed technology, which may change endoscopy forever and has the capacity to replace a good deal of conventional endoscopy. Will capsule endoscopy replace much of conventional upper gastrointestinal endoscopy and colonoscopy? The answer is probably yes but the time frame is unclear. Will capsule endoscopy be able to deliver therapy? Again, the answer is probably yes.

There are major challenges to the expansion of capsule technology into a position where it can compete with conventional diagnostic gastroscopy and colonoscopy<sup>[1-5]</sup>. The first challenge is power management. At present the Pillcam capsule contains two small 3 volt hearing aid batteries which allow about 8 h of continuous imaging at 2 frames per second. The use of complementary oxide silicone (CMOS) technology for the video has the advantage of requiring extremely low power levels when compared with a charge coupled device (CCD). Slowing the video frame rate to two frames per second also increases the life span of the capsule. The esophageal capsule takes 14 frames a second and has a life span of about 20 min. Recent quite radical design changes have included the development of an esophageal capsule with 18 frames per second and small bowel and colon capsules, both with 4 frames per second, yet with an increase in capsule life to about 11 h. These changes have been accomplished

mainly by more efficient power management. More batteries or increased battery volume may be of help but would increase the size and weight of the capsule. The two small silver oxide batteries in current use are not the most efficient in terms of power to weight ratio, but were chosen because of their safety record. Lithium batteries could run the capsule for longer periods. There have been important "break-throughs" in battery design with the advent of carbon nanotubes and Buckytubes which have the intrinsic characteristics desired in the material used as electrodes in batteries and capacitors, two technologies of rapidly increasing importance. Buckytubes have a tremendously high surface area (approximate 1000 m<sup>2</sup>/g), good electrical conductivity, and their linear geometry makes the surfaces highly accessible to the electrolyte. It may be that better battery design and better power management will give the capsule the power required for additional performance and functions.

The development of external power transmission methods using electrical field induction, radio-frequency, microwaves or ultrasound technology could free the capsule from the requirement for batteries or at least prolong the functional lifespan. This would substantially lighten the capsule, allow space and power for other functions such as biopsy or drug delivery but above all allow the capsule to be powered for indefinite periods which would permit increase in the present rather low frame rate, and in particular make the problem of prolonged or implanted capsule endoscopy and remote controlled therapeutic capsule endosurgery much easier to solve.

The development of the capsule endoscopy was made possible by miniaturization of digital chip camera technology, especially CMOS chip technology. The continued reduction in size, increases in pixel numbers and improvements in imaging with the two rival technologies-CCD and CMOS is likely to change the nature of endoscopy. The current differences are becoming blurred and hybrids are emerging.

The main pressure is to reduce the component size, which will release space that could be used for other capsule functions such as biopsy, coagulation or therapy. New engineering methods for constructing tiny moving parts, miniature actuators and even motors into capsule endoscopes are being developed.

Although semi-conductor lasers that are small enough to swallow are available, the nature of lasers which have typical inefficiencies of 100-1000 percent makes the idea of a remote laser in a capsule capable of stopping bleeding or cutting out a tumour seems to be something of a pipe dream at present, because of power requirements. The construction of an electrosurgical generator small enough to swallow and powered by small batteries is conceivable but currently difficult because of the limitations imposed by the internal resistance of the batteries. It may be possible to store power in small capacitors for endosurgical use, and the size to capacity ratio of some capacitors has

recently been reduced by the use of tantalum. Small motors are currently available to move components such as biopsy devices but need radio-controlled activators. One limitation to therapeutic capsule endoscopy is the low mass of the capsule endoscope (3.7 g). A force exerted on tissue for example by biopsy forceps may push the capsule away from the tissue. Opening small biopsy forceps to grasp tissue and pull it free will require different solutions to those used at flexible endoscopy-the push force exerted during conventional biopsy is typically about 100 g and the force to pull tissue free is about 400 g.

Future diagnostic developments are likely to include capsule gastroscopy, attachment to the gut wall, ultrasound imaging, biopsy and cytology, propulsion methods and therapy including tissue coagulation. Narrow band imaging and immunologically or chemically targeted optical recognition of malignancy are currently being explored by two different groups supported by the European Union as FP6 projects: -the VECTOR and NEMO projects. These acronyms stand for: VECTOR = Versatile Endoscopic Capsule for gastrointestinal Tumour Recognition and therapy<sup>[6]</sup> and NEMO = Nano-based capsule-Endoscopy with Molecular Imaging and Optical biopsy.

Both projects also include the development of remote manipulation methods.

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## CHALLENGE TO USING CAPSULE ENDOSCOPY FOR COLONOSCOPY

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There are challenges to using wireless capsule endoscopy for colonoscopy but most of these have been solved. Currently the capsule acquires images for 8 h and usually reaches the right side of the colon before the battery expires. The capsule may have to run for 24-48 h in order to perform a complete examination of the colon unless we can speed up the total gut transit. The power problem can be addressed in several ways including the use of more batteries, batteries with a delay mode which are switched on when the capsule reaches the distal small intestine, external power transmission and methods to move the capsule faster in the colon. A very effective timed colon cleaning will be necessary. Deletion of identical frames would make it easier to examine the images since the capsule in the colon may remain stationary for prolonged periods. Currently, wireless capsule colonoscopy has generated images from all areas of the colon and has imaged pathology especially in the right side of the colon, but also in the rectum. Initial clinical studies have provided promising results.

Autonomous wireless capsule laparoscopy is technically feasible and has been tried *in vivo* but needs to develop further and offer advantages over conventional laparoscopy. The obvious advantages might be that port numbers can be reduced for selected laparoscopic operations. It can be used to improve visualization during NOTES, and may allow multiple camera angles

during surgery, and views of structures that are difficult to see with conventional rigid laparoscopes such as the retroesophageal space or the pouch of Douglas. Wireless imaging of cardiac or vascular structures is conceivable, but would require substantial development and control strategies.

Wireless laparoscopy is a desirable extension of wireless capsule endoscopy. This may allow deconstruction of laparoscopes or NOTES platforms, separating the imager from the surgical effectors, thus reducing the outer diameter of trocars, and making surgery less invasive.

The manufacture of an autonomous video capsule the size of a red blood cell as described in Isaac Asimov's "The Fantastic Voyage" and made into a movie in 1966 by Richard Fleischer with Stephen Boyd, Raquel Welsh and Donald Pleasance is some way in the future. Reduction in size by up to an order of magnitude is currently conceivable with available components. It would be relatively easy to reduce by one-half the current dimensions of the capsule.

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## ATTACHMENT OF CAPSULE ENDOSCOPES TO THE GI TRACT

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It may become possible to stitch or clip the capsule to the wall of the stomach so that prolonged examination of bleeding ulcers or varices becomes possible. An on/off radio-controlled command may be helpful to conserve power. Long-term endoscopy with wireless endoscopes attached to the wall of the gut seems an obvious way to improve the management of gastrointestinal bleeding and other disorders.

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## TISSUE INTERACTIVE DIAGNOSTIC METHODS SUCH AS BIOPSY

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At present, the capsule cannot obtain biopsies, aspirate fluid or brush lesions for cytology. These common endoscopic manoeuvres may become possible during capsule endoscopy. 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. Biopsy using a spring loaded Crosby capsule-like device with an evacuated chamber is feasible with existing capsule technology. In preliminary studies, patients were almost always able to retrieve the capsules from the stools using a net and a magnet. Experimental brush, biopsy and radio-controlled release mechanisms which can be used in autonomous capsules have been tested in "in vivo" studies. It may become possible to combine capsule technology with "optical biopsy" such as narrow band imaging or pathology-targeted enhanced tissue markers.

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## CAPSULE COAGULATION

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A prototype coagulation capsule has been built and tested which employs an exothermic chemical reaction to

generate heat using the interaction of calcium oxide and water. It seems possible that other thermal therapeutic applications will be added in the future.

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## ELECTRO-STIMULATION FOR PROPELLING CAPSULE ENDOSCOPE

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One way to manipulate a wireless capsule endoscope autonomously in the gastrointestinal tract is to use electro-stimulation to propel the device, for example with a pair of bipolar electrodes at either end of the capsule. This technology has been tested in humans. Electrodes attached to a PILLCAM capsule have been used to propel the device in the porcine esophagus and small intestine, as well as in the human small intestine. A dumb-bell shaped capsule allows the imaging capsule to view the traction capsule. A radio-controlled electro-stimulation capsule has been developed. Radio-commands can be sent from a transmitter to the receiving traction capsule causing it to propel the video capsule forwards or backwards in the human gastrointestinal tract.

Water-jet propulsion has also been used to propel very light weight (3.7 g) capsules in the gastrointestinal tract. The light weight of the capsule compared with the 1.5 kg of a colonoscope makes it possible to think in terms of developing new types of very light weight colonoscopes, which can be passed on a wire through the anus, and would require much less force on the wall of the colon to reach the cecum.

Olympus in a news release (November 30, 2004) announced the following developments in capsule endoscopy: wireless power supply system, capsule guidance system, drug delivery system, body fluid sampling technology, self-propelled capsule and ultrasound capsule. Competition is likely to stimulate new technical developments which may make capsule endoscopy cheaper. Olympus is using CCD technology in their small bowel capsule that was released recently in Europe and USA, with FDA approval and a CE mark. A Chinese wireless small intestinal capsule (OMOM) has gone through 3 technical design changes, with improving image quality, and currently costs less than the other systems. A Korean small intestinal capsule (MIRO) includes some novel technological features including two external electrodes and a single skin electrode to facilitate transmission of image data using the body as an electrical conductor, thus eliminating the need for radiofrequency (wireless) data transmission, and as a result saving power. Recent technical improvements in the Given Imaging capsules (SB2, ESO2, COLON1) include adaptive light control i.e. if a frame is too dark the light emitting diodes will emit more light in subsequent frames. The frame rates of commercially available Given capsules have increased from 2 to 4 frames per second, for prolonged image transmission of up to 11 h and from 14-18 frames per second for rapid esophageal double imager viewing. Additional lenses have been added to the

redesigned optics to increase the depth of focus and widen the angle of view from 140 to 156 degrees which can more than double the surface area of the mucosa examined. The software continues to improve in order to manage the technical advances. Rapid 5, is the most recent version, indicating that the software has been revised 5 times. Real-time viewing has improved and will be increasingly important for new diagnostic and therapeutic options. At the time of writing (May 2008) more than 750 000 wireless capsule endoscopes have been sold since they were first launched in 2001.

## CONCLUSION

Capsule video-enteroscopy has opened up a new world of diagnostic and other possibilities for the gastroenterologist. It is remarkable to see images of small intestinal abnormalities such as an ulcerated Meckel's diverticulum or active bleeding from a tumour in the middle of the small intestine, which was not possible until recently. The development of wireless capsule endoscopy has changed video endoscopy of the small intestine into a much less invasive and more complete examination. The increasing use of these resources and the comfort and ease with which some of these examinations can be performed makes it likely that wireless capsule video imaging will have a substantial impact on the management of small intestinal disease as well as other parts of the body.

It is usually a mistake to try to predict the future

because the chances of error are very high. "It is impossible to predict the future, and all attempts to do so in any detail look ludicrous within a very few years." These are the opening words of "The Profiles of the Future" by Arthur C. Clarke, who wrote an amusing account of eminent scientists predicting that electric light, human flight and space travel were impossible at the same time as Edison perfected the light bulb, the Wright brothers made their first motor powered flight and Yuri Gagarin circled the earth in a sputnik. Einstein who probably knew more than most about the potential impact of physics on the future of mankind was goaded during an interview in 1929 on board the *Belgoland* into saying "I never think about the future; it comes soon enough".

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