PAPER

Wireless capsule endoscopy

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Gastroscopy, small bowel endoscopy, and colonoscopy are uncomfortable because they require comparatively large diameter flexible cables to be pushed into the bowel, which carry light by fibreoptic bundles, power, and video signals. Small bowel endoscopy is currently especially limited by problems of discomfort and failure to advance enteroscopes far into the small bowel. There is a clinical need for better methods to examine the small bowel especially in patients with recurrent gastrointestinal bleeding from this site.

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Visualisation of the whole stomach, upper small bowel, and colon became possible after the invention of fibreoptic endoscopy.[1] Miniaturisation of electronic components has allowed radical changes to the design of complex structures using electrical power. The invention of the transistor in the 1950s by Bardeen, Brattain and Shockley (awarded the Nobel Prize in 1956 for work announced in 1949) was probably the single most important advance responsible for the electronic revolution, which by miniaturising large electronic devices has permitted the development of portable computers, telephones, and personal stereo systems. The newly invented transistor was quickly exploited for medical purposes with the development of electronic radiotelemetry capsules, which were small enough to swallow for the study of gastrointestinal physiological parameters. These capsules permitted measurements of temperature,[2] pressure,[3 4] and pH.[3 4]

TECHNOLOGICAL DEVELOPMENTS

The development and testing is described of a new type of radiotelemetry capsule endoscope,[5 6] which is small enough to be swallowed (11×27 mm) and has no external wires, fibreoptic bundles, or cables.

The design of the video capsule was made possible because of progress in the design and performance of three technologies: complementary metal oxide silicon (CMOS) image sensors, application specific integrated circuit (ASIC) devices, and white light emitting diode (LED) illumination. In addition novel optical design and better energy management and overall system design were important in the capsule realisation.

During the past 10 years advances in CMOS technology lead to a substantial reduction of element size below 1 micron. This size reduction in turn made possible the inclusion of a buffer amplifier on each pixel of the CMOS image sensors thus reducing the output noise level that was initially associated with CMOS image sensors. As a result it is now possible to design and build a CMOS imager that is comparable in image quality to the charge coupled device (CCD) image sensors,[7] but of extremely small size, and requiring significantly lower power than CCD sensors.

Recent advances in ASIC design permitted the integration of a colour video transmitter of sufficient power output, efficiency, and bandwidth of very small size into the capsule.

Synchronous switching of the LED and the CMOS sensor was designed to minimise power consumption. By careful design of the optics and the transparent dome window it was possible to eliminate the stray light and reflections that are common problems when the illumination and imager are incorporated under the same dome.

The realisation of this technology has required the conjunction of a series of advances in image sensors, LED and ASIC design, the solution of taxing optical, power and size problems, as well as the development of successful airless methods of endoscopy.

Co-development

Two groups working independently on this project in Israel and London joined forces in 1997 to complete the technical development of the wireless capsule endoscope.[8] The London group published conceptual studies in 1994[9] and acquired the first live pictures from the stomach of a pig with a miniature wireless camera using CCD technology, and a microwave transmitter in 1997,[10] and performed the first feasibility studies on airless endoscopy.[11] Gavriel Iddan described a video system for wireless endoscopy with an innovative lens system in 1997[12] and the Israeli team were the first to realise the value of CMOS for this purpose and to make a device in dimensions that could be readily swallowed by a human. With ethical committee approval the first human volunteer study was performed in August 1999. The author was privileged to swallow the first two wireless capsule endoscopes on consecutive days. The capsule was easily swallowed and caused no discomfort. The capsule, propelled by peristalsis, successfully reached the caecum. The image window remained clear throughout the whole of the transmissions with transmission times of up to seven hours.

The wireless capsule endoscope has received a CE mark and FDA approval in August 2001 for use in patients.

Abbreviations: CMOS, complementary metal oxide silicon; ASIC, application specific intergrated circuit; LED, light emitting diode; CCD, charge coupled device

CURRENT TECHNOLOGY

A short focal length lens is used with a narrow aperture to increase the depth of field. Images are obtained as the optical window of the capsule sweeps past the gut wall, without requiring air inflation of the gut lumen. This optical arrangement allows the tissue to be in focus even if it is in contact with the optical dome window but also remain in focus over a few centimetres if the lumen is open with residual air or fluid. The capsule endoscope is propelled by peristalsis though the gastrointestinal tract and does not require a pushing force to propel it through the stomach, small bowel, or colon. Because the gut is a hollow tube it is comparatively unimportant whether the capsule points forwards or backwards as it passes through.

The video images are transmitted using radiotelemetry (operating in UHF at 432 megahertz) to an array of eight aerials attached to the body, which permitted image capture but which were also used to calculate and indicate the position of the capsule in the body. The images are stored on a small portable recorder carried on a belt. This aerial belt enables the continuous triangulation of the capsule location in the abdomen so that the whole trajectory can be shown on the work station monitor to help in locating abnormalities detected by the capsule imager. This method, which uses signal strength analysis of received signals from eight aerial antennae attached to the patient's abdomen, at present has an accuracy of about ±3 cm. The capsule transmits images at a rate of two frames per second for over seven hours permitting the acquisition of over 50 000 images. This system permits more than seven hours of continuous recording of images of the gastrointestinal tract. The patient need not be confined to a hospital or clinic environment during the examination and is free to continue their daily routine.

The images are subsequently downloaded from the portable recorder for analysis off line (software is also available for optional online viewing). Currently the time needed to evaluate the video sequence takes between 45 minutes to two hours and varies with on the experience and concentration of the examiner as well as the number of pathological abnormalities present. There is a learning curve even for experienced endoscopists as the images are different because of the airless nature of the endoscopy, which can make normal anatomy look strange and as abnormality may only be seen on a single frame. Physician time for evaluation may be the most costly part of the procedure and reimbursement for this new type of endoscopy will have to reflect the need for physician time as well as the capital costs of the equipment and the fact that the capsule endoscopes are disposable.

Software is available to view the findings in real time but the image quality is less good than after processing. Localisation software is available, which allows the position and path of the capsule to be tracked and recorded as the video stream is analysed. Blood recognition algorithms give a colour marker on the screen when the program analysing the image sequences suggests that blood is present in the lumen.

STUDIES IN HUMANS

After animals studies had demonstrated that capsule endoscopy was nearly as effective as push enteroscopy in identifying beads sewn into the small intestine of dogs and was able to image beads beyond reach of push enteroscopes[16] and successful testing in human volunteers,[6] the first four patients with recurrent gastrointestinal bleeding were examined in March 2000 at the Royal London Hospital.[13]

The wireless capsule endoscope has performed well in trials in patients with difficult gastrointestinal bleeding and in comparative studies with push enteroscopy.[17] A blinded comparison of capsule enteroscopy with push enteroscopy in 20 patients with recurrent bleeding and negative gastroscopy and colonoscopy found abnormalities to account for the bleeding in 55% with the capsule and 30% with push enteroscopy. The capsule found the only malignancy in this series and found a cause of bleeding beyond reach of the push enteroscope in 25%. There was good interobserver agreement between blind and unblinded observers. Wireless capsule endoscopy has been able to image abnormalities never seen before using flexible endoscopes. A report of the first endoscopic diagnosis of a Meckel's diverticulum made by wireless capsule has been reported.[18]

Several clinical studies presented during Digestive Disease Week 2002 that are published in abstract form have confirmed that wireless capsule endoscopy is significantly superior to push enteroscopy in its ability to find bleeding abnormalities in the small intestine and that the examination is invariably preferred by patients undergoing both procedures.[16–22] One study showed that wireless capsule endoscopy was significantly superior to barium studies if small intestinal pathology was suspected.[23]

The clinical indications for the use of wireless capsule endoscopy are becoming clearer in the light of recent studies. Several studies have demonstrated that this investigation is especially valuable in patients with difficult recurrent gastrointestinal bleeding when gastroscopy and colonoscopy are negative. It is likely to have a role in the further investigation of patients found to have small intestinal abnormalities on barium studies and may well become an adjunct to investigation of Crohn's disease patients,[24] or coeliac disease patients with weight loss. Its use in Crohn's disease is likely to be tempered by the fact that at present there is no non-surgical method for retrieval of capsules that become stuck in strictures in the small intestine and the problem that neither clinical history nor barium studies exclude the presence of a stricture.

Von Willebrand's disease is the one condition for which British National Health Service funding has been found. These patients with a bleeding diathesis may use tens or hundreds of thousands of euros worth of blood products in the course of a single bleed. The cost of establishing an anatomical diagnosis, which may help plan treatment with a wireless capsule is comparatively small in comparison.

The disposability of the wireless capsule may have some advantages in the investigation of some patients with graft versus host disease especially in the setting of small intestinal transplantation,[25] HIV+ enteropathy, or parasitic enteropathies. In one study the capsule sometimes gave useful views of right colon when colonoscopy was incomplete.[26] Although the capsule is not yet released for use in children it is likely that it will have some role in the investigation of children especially in those with failure to thrive, anaemia, or difficult abdominal pain.[27]

The clinical value of wireless capsule endoscopy in non-bleeding patients is less clear. The physiological studies in human volunteers and patients shows that the non-invasive nature of wireless capsule endoscopy lends itself well to observation and measurements of the response of the gastrointestinal tract to a variety of stimuli or stresses.[28] Studies of transit have provided information on normal and abnormal motility.[29–31]

CONTRAINDICATIONS AND COMPLICATIONS

The main complication associated with capsule use is that is can become stuck in strictures[25] or diverticulae[26] that are inaccessible to flexible endoscopic retrieval. The incidence seems to be about 1% in published series. Oddly usual capsule impaction seems to cause no symptoms. It may be sensible to consider performing abdominal radiography in patients who do not observe passage of the capsule into the toilet and whose imaging result does not indicate that the capsule enters the caecum. This process may be helpful to surgeons in localising strictures but it would be preferable if solutions could be developed to deal with this, short of surgical removal (surgical/endoscopic removal has come to be called "non-natural excretion" in current capsule euphemistic jargon). Methods, which need to be developed and tested, include the test passage of a capsule sized and shaped biofragmentable capsule and the occasional use of a capsule on a thread, which would allow the capsule to be pulled out if it got stuck. There is no secure way at present to predict which patients may have strictures, barium studies are poor at detecting strictures especially in early Crohn's disease.

Although the commercially available M2A device lists the presence of pacemakers and use in children as contraindications to its use some groups including our own have used the capsule in patients in both of these settings.

PATIENT PERSPECTIVES

The perception of the indications for wireless capsule endoscopy is different among patients who have heard about this examination. Many patients who are reasonably anxious about conventional endoscopy wonder if wireless capsule endoscopy may not be a painless alternative. One study suggests that this investigation might also prove valuable in a small subset of patients with difficult abdominal pain syndromes.[27] The problem is how to select such patients so that the costs and time spent on negative investigations are not too great. We have received letters from advocacy groups and societies wanting to improve the lot of patients with the irritable bowel syndrome as well as from many people who probably have this condition. It is probable that a wireless capsule endoscopy will be negative in such patients. There is a question of whether such patients would receive more reassurance from a negative wireless capsule endoscopy than from a colonoscopy, which is perhaps the commonest current investigation in patients with this condition. A colonoscopy is certainly more painful and probably more dangerous than a wireless capsule examination.

For many patients the capsule brings the hope that the pain and discomfort of endoscopy and colonoscopy will no longer be necessary. Substantial progress has been made but this hope has yet to be realised.

CURRENT STATUS

To date, the wireless capsule endoscope has been used in about 4000 patients.

There has been continued development and improvement of wireless capsule endoscopy. A blood sensing algorithm that uses colour pattern recognition has been added to the software to ease detection of blood in the lumen.[33] In experimental studies electrostimulation has been used to move capsule endoscopes suggesting that remote robotic control is feasible[34] and for the first time wireless images of the gastrointestinal tract have been transmitted from a robotically propelled endoscope.[35]

Conflicts of interest: the author is a consultant on the medical advisory body of Coran Imaging.

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