Wireless capsule endoscopy: a comparison with push enteroscopy in patients with gastroscopy and colonoscopy negative gastrointestinal bleeding

M Mylonaki, A Fritscher-Ravens, P Swain

**Background:** The development of wireless capsule endoscopy allows painless imaging of the small intestine. Its clinical use is not yet defined. The aim of this study was to compare the clinical efficacy and technical performance of capsule endoscopy and push enteroscopy in a series of 50 patients with colonoscopy and gastroscopy negative gastrointestinal bleeding.

**Methods:** A wireless capsule endoscope was used containing a CMOS colour video imager, transmitter, and batteries. Approximately 50 000 transmitted images are received by eight abdominal aerials and stored on a portable solid state recorder, which is carried on a belt. Push enteroscopy was performed using a 240 cm Olympus video enteroscope.

**Results:** Studies in 14 healthy volunteers gave information on normal anatomical appearances and preparation. In 50 patients with gastrointestinal bleeding and negative colonoscopy and gastroscopy, push enteroscopy was compared with capsule endoscopy. A bleeding source was discovered in the small intestine in 34 of 50 patients (68%). These included angiodysplasia (16), focal fresh bleeding (eight), aphthous ulceration suggestive of Crohn’s disease (three), tumour (two), Meckel’s diverticulum (two), ileal ulcer (one), jejunitis (one), and ulcer due to intussusception (one). One additional intestinal diagnosis was made by enteroscopy. The yield of push enteroscopy in evaluating obscure bleeding was 32% (16/50). The capsule identified significantly more small intestinal bleeding sources than push enteroscopy (p<0.05). Patients preferred capsule endoscopy to push enteroscopy (p<0.001).

**Conclusions:** In this study capsule endoscopy was superior to push enteroscopy in the diagnosis of recurrent bleeding in patients who had a negative gastroscopy and colonoscopy. It was safe and well tolerated.
A video SIF Q 140 Olympus (Keymed, Southend, UK) push enteroscope with 240 cm of working length was used for conventional enteroscopy.

The wireless capsule endoscopy was performed within two weeks prior to push enteroscopy. Wireless capsule and push enteroscopy examinations were performed and reported by different examiners who were unaware of the findings of the other examination. Two endoscopists (AFR and PS) carried out the push enteroscopy examinations. One physician (MM) administered the wireless capsule examinations and read the images. The endoscopist, who had not performed push enteroscopy and was unaware of the clinical details, subsequently reviewed the wireless capsule endoscopy images to reduce bias in interpretation, and to assess agreement in wireless capsule image interpretation.

The study was prospectively planned and ethics committee approval was granted for this study in 1999 and 2000. The human volunteer and clinical trial studies were considered and approved separately.

Volunteers and patients

Fourteen volunteers aged 21–58 years swallowed the capsule to provide information on image quality, transit, and normal appearance of wireless capsule endoscopy.

Fifty patients with gastroscopy and colonoscopy negative gastrointestinal bleeding and suspected small intestinal source were assessed in this study with both capsule and push enteroscopy. The median number of investigations apart from gastrointestinal bleeding agreed to 1.5–2 (table 1). These cysts were also seen in over half of all patients in our series. This appearance is probably a “normal” variation of no clinical significance. In volunteers as well as in patients, progressive darkening of the images was observed as the capsule passed to the distal small bowel. This appearance is probably due to concentration of bile but also to non-absorbed residual particulate food material. In the course of this study due to these dark images, the later seven volunteers were given a colonoscopy type preparation with sodium picolax. Five minute video segments taken at 10, 20, and 30 minutes after passage of the pylorus and at the same time intervals before crossing the ileocaecal valve were scored using a subjective visual analogue scale for brightness, absence of obscuring material, and image quality. The images from the lower small intestine were significantly brighter, contained less obscuring material, and had better image quality in volunteers who had received the preparation than in those who had not (p<0.05). Images in the upper small intestine were not significantly different between the two groups.

Fifty patients with gastroscopy and colonoscopy negative gastrointestinal bleeding and suspected small intestinal source were assessed in this study with both capsule and push enteroscopy. The median number of investigations apart from a gastrointestinal and colonoscopy carried out to localise the bleeding in this group of patients prior to this study was 8 (3–17) (table 1).

The wireless capsule examination identified a bleeding source in the small intestine in 34/50 patients (68%). These included angiodysplasia (fig 2), focal active bleeding (fig 3), small bowel tumour both located in the ileum (both carcinoid tumours), aphthous ulceration and skip lesions suggestive of

### Table 1 Volunteer and patients characteristics, and outcome

<table>
<thead>
<tr>
<th></th>
<th>Volunteers</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>14</td>
<td>50</td>
</tr>
<tr>
<td>Age (y) [median (range)]</td>
<td>45 [28–58]</td>
<td>50.3 (17–80)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>8/6</td>
<td>21/29</td>
</tr>
<tr>
<td>No of investigations</td>
<td>0.2 (0–2)</td>
<td>8 (3–17)</td>
</tr>
<tr>
<td>Overt/occult bleeding</td>
<td>11/39</td>
<td></td>
</tr>
<tr>
<td>Duration of bleeding (y) [median (range)]</td>
<td>4.2 (0.5–20)</td>
<td></td>
</tr>
<tr>
<td>Transfusion units (units) [median (range)]</td>
<td>35.5 (0–400)</td>
<td></td>
</tr>
<tr>
<td>No of bleeding causes found with capsule</td>
<td>68%</td>
<td></td>
</tr>
<tr>
<td>No of bleeding causes found with enteroscopy</td>
<td>32%</td>
<td></td>
</tr>
<tr>
<td>No of pathologies found with capsule</td>
<td>38%</td>
<td>88%</td>
</tr>
<tr>
<td>No of non-small intestinal sources found with capsule/enteroscopy</td>
<td>4/3 (8%/6%)</td>
<td></td>
</tr>
</tbody>
</table>
Crohn’s disease (fig 4), Meckel’s diverticulum, ulcerating proximal jejunitis, ileal ulcer, and ulcer due to intussusception. The wireless capsule also made some diagnoses outside the small intestine: Cameron erosions in a large hiatus hernia, small gastric angiodysplasia (associated with small intestinal angiodysplasia) in two patients, a gastric ulcer, a caecal polyp, and a caecal angiodysplasia. All gastric abnormalities were confirmed at subsequent push enteroscopy; the colonic abnormalities were confirmed and treated at subsequent colonoscopy. Capsule endoscopy however failed to detect a Cameron lesion in one patient. This was detected at push enteroscopy. The total diagnostic yield of wireless capsule endoscopy was 38/50 (76%).

Push enteroscopy detected angiodysplasia in 10 patients, focal active bleeding in five, and ulcerating jejunitis in one. The diagnostic yield of push enteroscopy to diagnose a bleeding source in the small bowel was 16/50 (32%). No additional small bowel diagnoses were made by enteroscopy at first attempt. Following a further bleed, on a second enteroscopy an active bleeding from a small angiodysplasia on a fold 10 cm distal to the papilla was detected in a patient with von Willebrand’s disease. As the capsule endoscopy did not detect it and although enteroscopy identified it only on a second occasion, this was considered to be a false negative result of capsule endoscopy. If the additional extraintestinal diagnoses found at push enteroscopy are included, the total diagnostic yield was 19/50 (38%). The time taken for push enteroscopy was a mean of 22 minutes. An overtube or X ray was not used.
in the course of this examination. Sedation used was a mean dose of 50 mg of pethidine and 6.5 mg of midazolam.

Wireless capsule endoscopy was significantly superior to push enteroscopy in the identification of bleeding sources in the small intestine (34/50 v 16/50; p<0.05, χ² test). The wireless capsule was also significantly superior to push enteroscopy when the total diagnostic yield was analysed (38/50 v 19/50; p<0.05).

Wireless capsule endoscopy led to alteration in therapy in 25/38 patients. Seven patients had surgery—six of these had no further bleeding after discharge (Meckel (two), intussusception (one), ileal carcinoma (two), and isolated large jejunal angiodysplasia (one)). One patient with extensive proximal jejunal angiodysplasia had a marked reduction in transfusion requirement. Twelve patients with proximal jejunal angiodysplasia had endoscopic therapy (with bipolar, argon plasma, or heater probe through a push enteroscope). Three patients with probable Crohn's disease were treated with mesalazine and steroids (two subsequent biopsies at colonoscopy showed granulomas and inflammation). Three had other alterations in drug therapy (stopping occult aspirin therapy, reducing warfarin dosage, or starting/increasing proton pump inhibitor treatment).

At a follow up interview two weeks or more after the examination, patients were asked to compare wireless capsule investigation with push enteroscopy and to indicate whether either examination was painful. A total of 49/50 said that they found wireless capsule endoscopy preferable to push enteroscopy; 2/50 found wireless capsule endoscopy uncomfortable but only at the time of swallowing the capsule; and 34/50 found push enteroscopy painful (p<0.05).

The technical problems encountered were as follows. One capsule remained in the oesophagus for seven hours in a patient with undiagnosed achalasia. This capsule was pushed into the stomach using a flexible endoscope and passed through the patient. Subsequently, another capsule was inserted using a hydraulic delivery device into the duodenum and demonstrated the presence of bleeding jejunal angiodysplasia. Temporary electrical disconnection at the aerial recorder interface was associated with some image loss in three patients. In one patient the battery power ran out at two hours and only a short period of small intestinal imaging was acquired (22 minutes). In seven patients the capsule passed into the pylorus and then returned to the stomach before passing on down the small intestine at least once. In one patient this occurred seven times. The capsule never got stuck in the small intestine or colon. No other serious complications occurred.

The capsule battery expired before reaching the caecum in 16/50 patients (28%). In the other patients the capsule delivered images from the right colon for 0–4.5 hours (median 2.20 hours).

The time taken to examine the wireless capsule images was a median of 75 minutes (range 40–120 minutes). With its 22 minutes of examination time, push enteroscopy was significantly quicker in achieving a diagnosis (p<0.05).

In 2/38 patients there was disagreement on interpretation as to the source of bleeding. In both cases this related to the presence or absence of angiodysplasia seen as “red spots” on the images. In one, push enteroscopy confirmed the presence of angiodysplasia. Both reviewers were correct about the site of bleeding in the patients who had subsequent surgery. Both worsened thought that an appearance, which at surgical pathology was an intussuscepted Meckel's diverticulum, was an intestinal polyp.

**DISCUSSION**

Despite careful examination of the upper and lower gastrointestinal tract with flexible endoscopy, the reason and location of occult gastrointestinal bleeding remains unexplained in 30–50% of patients. Studies of non-endoscopic imaging techniques in patients with obscure bleeding give generally disappointing results. Development of a wireless endoscopy capsule, which can travel through the whole gut and is moved by the patient's own peristalsis, offers the prospect of painless imaging of the whole of the small intestine. A study by Lewis and Swan comparing push enteroscopy and capsule endoscopy for occult gastrointestinal bleeding in patients with negative endoscopy and colonoscopy was performed to obtain American Federal Drug Administration approval for the capsule. In 21 patients with gastroscopy and colonoscopy negative obscure bleeding, capsule endoscopy detected a bleeding site in 11 and enteroscopy in six (55%/30%).

In our study with 52 patients, the wireless capsule endoscopy performed similarly well in the investigation of selected patients. It was significantly superior (68%/32%) to push enteroscopy in the identification of bleeding abnormalities in the small intestine. In addition to findings in the small bowel, both methods detected pathologies that had been missed at gastroscopy and/or colonoscopy. Several reported series of push enteroscopy show that in patients with recurrent bleeding a source within reach of a gastroscopy can be found in 10–25% of cases. The commonest missed lesions are Cameron erosions in a large hiatus hernia, peptic ulcers, Dieulafoy ulcer, and watermelon stomach, and the miss rate at colonoscopy both of polyps and cancers has also been documented. In this study, the wireless capsule and enteroscopy also made some diagnoses outside the small intestine: Cameron erosions in a large hiatus hernia, small gastric angiodysplasia, a gastric ulcer, a caecal polyp, and a caecal angiodysplasia. All gastric abnormalities were confirmed at push enteroscopy. The miss rate at wireless capsule endoscopy is uncertain at present but is not zero. In one case of recurrent bleeding, an angiodysplasia in the fourth part of the duodenum was missed with the capsule. It was also missed with an initial push enteroscopy but identified and treated on a second approach. It is also true that the number of angiodysplasia identified at push enteroscopy was frequently larger than the number seen during the capsule examination but in patients where the cause of bleeding is uncertain the number of angiodysplasia is less important.

There are some limitations to wireless capsule endoscopy, which is at present a relatively immature technology. The picture quality is not as good as the best quality flexible video
endoscopy (fig 5). The frame rate with the capsule is lower (2 v 25 frames per second), the light intensity cannot yet respond to altering requirements, lesions cannot be washed or repeatedly examined, and the optics are not yet as good. There is a sense in which comparison with push enteroscopy is unfair. The push enteroscope cannot reach the lower small intestine. The wireless capsule can make diagnoses beyond the reach of push enteroscopy. There may have been a tendency to overestimate the length of the small intestine examined by push enteroscopy when this was the only available endoscopic method. Patient studies in this series are highly selected, troublesome to manage, expensive, and not very common. Our unit acts as a referral centre for patients with obscure gastrointestinal bleeding and performs 2–3 push enteroscopy examinations each week. Wireless capsule endoscopy is currently the only non-operative method to examine the whole of the small intestine beyond the reach of the push enteroscope as Sonde type enteroscopy has been largely abandoned.

Another limitation of capsule endoscopy at present is the lack of funding as only a few National Health Service Trusts or private insurance companies have as yet agreed to pay for this examination. The disposable capsule currently costs £350 with a capital cost for the work station, recorder, and aerial belts of £20 000. The medical time required to analyse the images is another cost.

It is too early to be dogmatic about algorithms for investigating patients with gastroscopy and colonoscopy negative gastrointestinal bleeding. This study suggests that capsule endoscopy is likely to find more bleeding sources than push enteroscopy. These results are supported by other studies published in abstract form.推 stomach enteroscope has therapeutic potential unlike the capsule and is currently somewhat more widely available than capsule endoscopy and so perhaps should be considered first at the present time. Repeat gastroscopy and colonoscopy by an experienced operator may well be worth undertaking before investigating the small intestine. Careful history taking, access to all previous imaging information, and good clinical judgement remain important in managing this difficult subgroup of patients with gastrointestinal bleeding.

Although wireless capsule endoscopy has limitations, it is the only imaging method that can provide optical colour images of the lower small intestine painlessly without surgery and has opened a new perspective in the investigation of the causes of bleeding in patients with suspected small intestinal abnormalities. It is as yet an immature technology. Technical improvements need to be encouraged.

CONCLUSIONS

This study shows that capsule endoscopy can provide small intestinal imaging comparable with push enteroscopy and can diagnose intestinal bleeding sources at sites beyond the reach of push enteroscopes. It was safe, painless, and well tolerated.

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