Localisation in the Small Bowel of Lesions Found by Capsule Endoscopy for Obscure Gastrointestinal Bleeding

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Abstract

Aim: To precisely define and localise small bowel lesions causing obscure gastrointestinal bleeding, to aid in subsequent therapeutic intervention.

Methods: A pilot study was performed to compare surgical to capsule localisation of small bowel lesions. Subsequently, consecutive capsule endoscopies for obscure gastrointestinal bleeding were analysed to determine the type and location of individual lesions. Lesion location was recorded by dividing the small bowel transit time into quartiles.

Results:

Pilot study: Thirteen complete capsule examinations which proceeded to subsequent small bowel surgery were analysed. When comparing location of lesions at capsule endoscopy with surgical location: 7 of 13 were located in the same small bowel quartile, and the remaining 6 were found in the adjacent quartile.

Main study: From 190 studies performed for obscure gastrointestinal bleeding between 2004 and 2007, 135 were suitable for analysis. Fifty one percent of identified lesions were seen in the first quartile, 18% were in the second quartile, 13% in the third quartile and 18% in the fourth. Both angioectasias and red spots were found more commonly in the first small bowel quartile compared to other quartiles (p<0.0001). There was no significant difference between the quartiles for non vascular lesions.

Conclusions: Localisation of lesions to small bowel quartile by capsule endoscopy is acceptably accurate. In patients with obscure gastrointestinal bleeding, the majority of identified lesions are vascular and usually located in the proximal small bowel. These lesions are likely to be accessible for treatment with anterograde enteroscopy. Ulcers and tumours are more evenly distributed.

Introduction
Capsule endoscopy (CE) has developed an important role in the investigation of gastrointestinal bleeding. Subjects with either overt or occult gastrointestinal bleeding, and a non-diagnostic gastroscopy and colonoscopy, are termed as obscure gastrointestinal bleeding. In this group of patients, capsule endoscopy will often provide a diagnosis.

Whether CE alters patient management depends on the type of lesion identified. If tumours are visualised then prompt surgical or endoscopic resection is indicated. Similarly, the identification of small bowel ulceration at CE usually suggests either an NSAID-related condition or a diagnosis of Crohn’s disease. Conversely, a normal capsule examination reassures the patient, and usually reduces the need for further investigations.

The most common lesions found in the investigation of obscure GI bleeding are however, vascular ectatic lesions. Vascular lesions can occur throughout the small bowel and may be present in large numbers. The management of these lesions varies according to the clinical scenario, location (endoscopic accessibility), size and number. The most common modalities used to treat these vascular lesions are anterograde push enteroscopy or balloon enteroscopy combined with thermal ablation modalities such as argon plasma coagulation or bipolar electrocoagulation. Push enteroscopy is widely available and easy to perform, however the depth of insertion is variable and usually the procedure only examines the proximal jejunum. In contrast, in experienced hands, single and double balloon enteroscopy can potentially examine the entire small bowel however it is time consuming and currently availability is limited.

Although there is a growing body of literature concerning the types of small bowel lesions identified by CE for obscure GI bleeding there is limited available data concerning the location of identified lesions. Localisation of lesions by capsule endoscopy is difficult due to non-constant velocity of the capsule through the small bowel (SB) and particularly in cases where the caecum is not reached during the examination. Estimates of whether a lesion is within reach of push or balloon enteroscopy, and by anterograde or retrograde approach, are usually based on operator experience alone.

We and others have previously found that most subjects with obscure gastrointestinal bleeding with lesions identified by capsule endoscopy who had continued evidence of blood loss benefited from subsequent directed therapeutic push enteroscopy. In these subjects, therapeutic push enteroscopy (despite only accessing the proximal jejunum) reduces subsequent transfusion requirements, hospitalisations and further investigations.

We therefore hypothesised that the reason for this success is that most lesions identified by capsule endoscopy for obscure GI bleeding are in the proximal small bowel.

**Methods**

**Pilot Study**
The initial study determined the accuracy of capsule endoscopy in localising individual lesions in small bowel quartiles. We retrospectively analysed 13 capsule endoscopies that visualised the caecum and found a small bowel lesion which was subsequently resected at surgery. Studies were performed by two capsule endoscopists (SA, PC). Lesion localisation by CE was assessed as the time taken from the first duodenal image. The small bowel was then divided into four equal quartiles according to overall small bowel transit time (first duodenal image to first caecal image). Capsule localisation of the lesion was expressed by quartile. Thus if the time to the lesion was 80 mins and the time to the caecum was 200 mins, the lesion location would be Quartile 2. Surgical localisation of the lesion was determined from operating reports, and then converted to a quartile format according to small bowel length eg “proximal jejunum” as Quartile 1. The two methods of localisation were then compared.

**Main Study**
We retrospectively analysed consecutive capsule endoscopies performed by a single endoscopist (PC) between
January 2004 and July 2007 for obscure gastrointestinal bleeding. Obscure bleeding was classified as either being overt or occult bleeding. In the overt group, bleeding was either recent or ongoing at the time of the examination. Patients with occult bleeding had iron deficiency anaemia which was either persistent or recurred after a full course of iron replacement. Gastroscopy and colonoscopy were performed in all patients prior to referral for CE and were considered non-diagnostic.

Study exclusion criteria were: (1) poor bowel preparation; (2) failure of the capsule to reach the caecum (unless location of the lesion was identified at surgery); (3) previous small bowel therapy, either surgical or endoscopic or (4) repeat procedure in the same patient.

The Given Pillcam (Given Imaging Ltd, Yoqneam, Israel) was used from January 2004 to February 2006 (99 patients). The Olympus Endocapsule (Olympus Medical Systems Corporation, Shinjuku-ku, Japan) was used from February 2006 to July 2007 (91 patients). Twenty four hours before CE, patients were administered clear fluids orally and the evening prior to the examination two bottles of sodium picosulphate (45mls each) were administered. Patients were then fasted 8 hours prior to the study. On the morning of the examination, 15 mins prior to capsule ingestion, subjects were administered 10 mg oral metoclopramide to promote gastric passage of the capsule. The capsule was swallowed around 8 am with water mixed with 1 ml simethicone, unless endoscopic insertion into the proximal duodenum was required because of suspected oesophageal or gastric motility disturbance. Subjects were encouraged to ambulate during the examination, drinking clear fluids at 3 hours and eating 5 hours post capsule ingestion.

Images of all lesions were reviewed and classified as “red spot”, angioectasia, ulcer or tumour (Figure 1). A “red spot” was defined as a tiny (≤1mm), symmetrical, uniformly coloured vascular lesion. The time the lesion was seen during the procedure was noted, and its quartile location calculated as in the pilot study. Time of the first view of the second part of the duodenum was also recorded.

The distribution of identified lesions between various small bowel quartiles was compared using chi square test with $p < 0.05$ considered a significant difference in distribution.

**Results**

**Pilot Study**

The findings of the pilot study are described in Table 1 (see Capsule Videos and video still images 1-4). Of the 13 examinations requiring
surgery, 10 had histological confirmation of a neoplasm, 2 had a large cavernous haemangioma and 1 had pancreatic heterotopias (see figures 2-7). All 13 patients had small bowel localisation of lesions at surgery. Seven of the 13 had identical quartile localisation of the lesion by capsule and surgery. In the remaining 6 patients the difference in quartile location of lesion between capsule and surgery was only 1. Thus, no patients had a difference in capsule and surgical quartile localisation more than 1 quartile. The results suggested that the use of CE transit time to determine small bowel location by quartiles is an acceptable means of localising small bowel lesions.

Table 1. Histologic Results of the Pilot Study

<table>
<thead>
<tr>
<th>Patient</th>
<th>Histology</th>
<th>Capsule Endoscopy Quartile</th>
<th>Surgical Quartile</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Carcinoid</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>2</td>
<td>Adenocarcinoma</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>Adenocarcinoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>Gastrointestinal Stromal Tumour</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>Adenocarcinoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>Cavernous Haemangioma</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>Lymphoma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>Gastrointestinal Stromal Tumour</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>9</td>
<td>Adenocarcinoma</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>10</td>
<td>Gastrointestinal Stromal Tumour</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>11</td>
<td>Hyperplastic polyp</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>Cavernous Haemangioma</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>13</td>
<td>Ectopic Pancreas</td>
<td>3</td>
<td>2</td>
</tr>
</tbody>
</table>

Main Study: Demographics and Capsule study details

Overall 190 examinations were reviewed and 55 of these were excluded from analysis. Reasons for exclusion were poor small bowel preparation (10), failure of the capsule to reach the caecum during the study period (31), previous surgery or treatment of small bowel lesions (12) and repeat procedure (2). Capsule studies from 135 subjects were therefore included for analysis. The average age of the cohort was 65 (range 21-90) and 64% were female. The indications for capsule endoscopy in this group were recurrent or persistent iron deficient anaemia in 75% (101), recent overt bleeding in 16% (21) or, recent overt bleeding and iron deficiency in 9% (13).

The mean small bowel transit time for the cohort was 254 minutes (median 246, range 73-543 minutes, standard deviation 97). The mean transit time for each small bowel quartile was therefore 63.5 minutes. The mean time between the initial image of the first part of the duodenum to the initial image of the second part of the duodenum was 1.5 minutes (range 0-74 minutes, standard deviation 7).

Main Study: Description of lesions

The major pathology found in the 135 patients at capsule endoscopy is summarised in Table 2. Consistent with previous series, the most
common final diagnosis was small bowel vascular lesions - either angioectasiae (56%) or red spots (24%)\(^1\). Small bowel ulcers or erosions were found in 4% of cases, and small bowel tumours in 5%. Likely contributing causes of bleeding identified outside the small bowel included gastric erosions, gastric vascular lesions and caecal angioectasiae (3% of patients). Multiple pathologies were found in 32% of patients (eg tumour and angioectasia) however the final diagnosis was determined from the lesion considered to be the most likely cause of gastrointestinal bleeding.

A total of 995 lesions were identified in the 135 subjects. **Figure 8** shows the proportion of all lesions identified by type. Vascular pathology accounted for 92% of the small bowel lesions seen at capsule endoscopy, 59% (591) angioectasiae and 33% (325) red spots. Small bowel ulcers 7% (69) and tumours 1% (10) accounted for the remaining identified lesions.

### Main Study: Location of lesions

When analysed by lesion location, 51% (509) of all lesions were found within the first quartile of small bowel transit time. In contrast, 18% (174) of all lesions were found in the second, 13% (131) in the third and 18% (181) in the fourth quartiles (**Figure 9**).

Analysis of the location of individual types of lesions revealed that vascular lesions were more often located in the first quartile, while non-vascular lesions appeared more evenly distributed throughout the small bowel (**Figure 10**). Angioectasiae were more proximally distributed with 324 lesions in the first quartile, 105 lesions in the second, 58 in the third and 104 in the fourth quartiles (p<0.0001). That is, 55% of all angioectatic lesions occurred in the first quartile. Similarly, red spot lesions were found more often in the first quartile compared to the more distal small bowel quartiles (p<0.0001). Ulcers however, were more evenly distributed with 16, 10, 15 and 28 in the first to fourth small bowel quartiles respectively (NS). Similarly, tumours were evenly distributed throughout the small bowel with 5, 2, 1 and 2 tumours found in the first to fourth quartiles respectively (NS)**(Figure 10)**.

### Discussion

The principal aim of the current study was to examine the distribution of small bowel lesions found in subjects undergoing capsule endoscopy for obscure gastrointestinal bleeding. When capsule transit in the small bowel was assessed by quartile, two important and novel findings were observed. Firstly, over half of all identified vascular lesions were identified in the first quartile; with a decline in the number of vascular lesions identified in the remaining quartiles. Secondly, in contrast to vascular lesions, non vascular lesions (ulcers and

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**Table 2: Major pathology found at capsule endoscopy**

<table>
<thead>
<tr>
<th>Pathology</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vascular Lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angioectasiae</td>
<td>76</td>
<td>56.3</td>
</tr>
<tr>
<td>Red spots</td>
<td>33</td>
<td>24.4</td>
</tr>
<tr>
<td>Ulcer or Erosions</td>
<td>6</td>
<td>4.4</td>
</tr>
<tr>
<td>Tumour</td>
<td>7</td>
<td>5.2</td>
</tr>
<tr>
<td>Non Small Bowel Diagnoses:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caecal angioectasiae</td>
<td>2</td>
<td>1.5</td>
</tr>
<tr>
<td>Gastric erosions</td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td>Normal</td>
<td>10</td>
<td>7.5</td>
</tr>
</tbody>
</table>

1. The lesions identified at CE thought most likely to be responsible for gastrointestinal bleeding; some patients had multiple pathologies.
2. Three additional patients had submucosal tumour identified that were unlikely responsible for the bleeding.

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**Figure 8:** All small bowel lesions identified in 135 capsule endoscopy examinations by type.

**Figure 9:** Proportion of all lesions identified at capsule endoscopy by small bowel quartile.

**Figure 10:** Small bowel location by quartile of individual lesions identified at capsule endoscopy. Angioectatic lesions and red spots were more commonly found in the first quartile compared to the remaining quartiles (p<0.0001 for each).
tumours) tend to be more evenly distributed throughout the small bowel.

The concept of dividing the small bowel into quartiles for analysis has previously been described. Gay et al devised a capsule localisation index based on the time from capsule ingestion to arrival at the lesion divided by time from capsule ingestion to arrival at the caecum\(^\text{10}\). An index >0.75 was highly accurate in predicting accessibility of lesions by retrograde double balloon enteroscopy. Thus, prediction of lesion location in the 4th quartile, based on small bowel transit time by capsule predicted a distal small bowel position, and influenced the method of endoscopic intervention. Additionally, in recent scoring systems of small bowel inflammatory change, the small bowel has been divided into tertiles based on transit time\(^\text{11, 12}\). These methods of dividing the small bowel into segments have come about because of the appreciation that the small bowel is not affected uniformly by disease. Indeed the distribution of lesions identified at capsule endoscopy is important as it can help with diagnosis (NSAIDs vs Crohn’s ulceration), assessment of severity (terminal ileal vs. extensive small bowel Crohn’s) and influence subsequent management (route of enteroscopy).

Our pilot study demonstrates that a quartile system to describe lesion location is acceptably accurate. Dividing the small bowel into quartiles according to transit time appears a useful tool to estimate lesion localisation and to aid subsequent therapeutic interventions. However it is important to further validate this approach by comparing small bowel lesion location at CE with endoscopic, radiological and surgical localisation of lesions. The reason for the proximal distribution of vascular lesions in the small bowel is unclear. This finding however supports our previous observation that patients with evidence of ongoing obscure bleeding from vascular lesions after capsule endoscopy strongly benefit from thermal ablation of these lesions using standard anterograde push enteroscopy\(^\text{8}\). This approach has been shown to result in reduced subsequent transfusion requirements for these patients. Thus, this data collectively supports our belief that many vascular lesions found at capsule endoscopy are often amenable to anterograde balloon or push enteroscopic therapy. Our second observation that ulcers and tumours tend to be more evenly distributed in the small bowel however, emphasises the importance of ensuring complete examination of the small bowel in obscure gastrointestinal bleeding by either capsule endoscopy or enteroscopy\(^\text{13}\).

Consistent with previous series, another major finding in the present study was that vascular lesions, either angioectasias or red spots, were by far the most common cause of obscure gastrointestinal bleeding detected by CE. Other important causes for small bowel bleeding, small bowel ulceration (4%) and tumours (5%), were identified less often. In the present series the yield of capsule endoscopy was 92.5%. This is higher than other reported series that quote yields of 42 to 85%\(^\text{1, 14}\). The greatest difference is in the number of vascular lesions reported. We found angioectatic lesions in 56% of our patients and red spots in 24%. Thus, our overall yield for vascular lesions was 80%. We elected to divide vascular lesions into two groups, angioectasias and red spots, as has been described by others\(^\text{9, 15}\). Leighton et al designated angioectasias as being, “definite or probable” causes of obscure gastrointestinal bleeding, and red spots or red dots as, “possible or unlikely causes of obscure gastrointestinal bleeding”. However, while we accept that red spots may often not be clinically important, these lesions can bleed, and may be relevant in patients in whom no other cause for obscure gastrointestinal bleeding has been identified\(^\text{9, 15}\). The inclusion of red spots in our series is therefore, in part, responsible for the high number of vascular lesions identified. Our yield for angioectasias (56%) is also high compared to a recent meta-analysis of lesions identified for obscure gastrointestinal bleeding reporting 36%\(^\text{16}\), although some series reported yields for vascular lesions of up to 60%\(^\text{17, 18}\). The strict entry criteria for inclusion in this study of either overt bleeding or refractory or persistent iron deficiency anaemia may have contributed to the high positive capsule lesion detection rate. Finally, exclusion of patients assessed as having a poor bowel preparation and those with incomplete examinations is also likely to be responsible for the overall high yield. Even if red spot lesions are excluded, the majority of angioectasias are still found in the first quartile.
In capsule endoscopy, there is an inherent tendency to underestimate the number of distal small bowel lesions identified. This relates to either failure of the capsule to reach the caecum before the battery expires or because in general, faecal fluid is encountered more often in the distal ileum thereby partially obscuring the lumen. In the present study however, all patients were given bowel preparation, and those assessed as having inadequate mucosal views in any part of the small bowel were excluded from analysis. We are therefore confident that the distal small bowel was adequately examined in the studied patients.

A possible limitation in this study relates to assumptions of small bowel motility. Dividing small bowel transit time into four equal quartiles and correlating transit time with small bowel location, assumes constant small bowel capsule velocity. Although an understanding of the transit of small bowel contents is increasing, it is still relatively poorly described. In the fasting state, either migrating motor complexes or giant migrating complexes begin in the gastric body or the proximal small bowel, these may have either propulsive or retropulsive components. Thus there are many influences on small bowel transit which clearly cannot always be considered linear.

In conclusion, the majority of identified lesions in patients with obscure gastrointestinal bleeding are vascular and located in the proximal small bowel. Vascular lesions are therefore often amenable to treatment with anterograde enteroscopy. Non vascular lesions such as tumours and ulcers however appear more evenly distributed throughout the small bowel.

References


endoscopy versus push enteroscopy for evaluation of obscure gastrointestinal bleeding with 1-year outcomes. 


