A randomized head-to-head study of small-bowel imaging comparing MiroCam and EndoCapsule

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Background and study aims: The MiroCam is a new video capsule device offering a higher frame rate and a longer battery life-expectancy. We aimed to quantify its clinical impact and performed a randomized head-to-head comparison with the EndoCapsule device with respect to the rate of complete small-bowel examinations, diagnostic yield in the small bowel, and capsule transit time.

Patients and methods: Patients referred for video capsule endoscopy because of obscure gastrointestinal bleeding, chronic diarrhea, and anemia of unknown origin were randomly assigned to swallow either the MiroCam first, followed by the EndoCapsule 2 hours later, or vice versa. All videos were analyzed by two independent investigators.

Results: A total of 50 patients (median age 61, range 21–84) were included. Complete small-bowel examination was achieved in 48/50 patients using the MiroCam and 45/50 using the EndoCapsule (96% vs. 90%, odds ratio [OR] 2.67, 95% confidence interval [CI] 0.49–14.45; \(P=0.38\)). There was diagnostic yield in the small bowel for 25/50 patients using the MiroCam and 24/50 using the EndoCapsule (50% vs. 48%, OR 1.08, 95% CI 0.49–2.37; \(P>0.99\)). However, the findings were concordant in 68% only (kappa = 0.50). The combined diagnostic yield was 58%. Even solitary findings had a relevant clinical impact during a 6-month follow-up.

Conclusion: In this direct comparison the MiroCam and EndoCapsule devices were not statistically different with regard to their rates of complete small-bowel examinations or diagnostic yield. Their moderate concordance, mainly caused by missed pathological findings, which affected both devices, needs consideration in clinical practice.

Introduction

Over the past 10 years video capsule endoscopy (VCE) has become a valuable diagnostic instrument for the assessment of small-bowel pathology [1, 2]. Well established in the management of obscure gastrointestinal bleeding [3], it has also gained increasing importance in inflammatory bowel disease [4], unexplained iron deficiency anemia [5], polyposis syndromes [6], and celiac disease [7]. In general, VCE is safe, less invasive than conventional endoscopic methods, and well tolerated, even by children [8].

An important shortcoming of VCE is the high number of incomplete examinations, defined by the inability of the capsule to visualize the entire small bowel. This has been reported in about 20% of all VCE examinations [9]. Incomplete examinations carry a considerable risk of missing a pathological abnormality, which has significant implications for both a patient’s well-being and health-care costs. Patient-related risk factors for incomplete small-bowel examination include prior small-bowel surgery, poor bowel preparation [10], hospitalization [11], or type-2 diabetes [12].

Technical improvements in VCE devices have addressed this important drawback. MiroCam (IntroMedic Ltd., Seoul, Korea) is a new capsule device that was recently introduced into the market. It uses electric-field propagation instead of radio-frequency to transmit the video signal. Thereby, the human body serves as an electric conductor to transfer the pictures from the capsule to the body surface electrodes, which are connected to the data receiver. This technology consumes less energy and therefore saves battery life to allow longer video recording. The MiroCam device offers a higher frame rate of three frames per second and a broader angle of view of 150° (Table 1).

It has previously been evaluated in healthy subjects [13] and has been prospectively compared with the PillCam (Given Imaging Ltd., Yoqneam, Israel) in a small study [14].
Isreal), with which it gave a similar diagnostic yield [14,15]. EndoCapsule (Olympus Ltd, Tokyo, Japan) is another radiofrequency-based capsule device that is widely used in European centers [16]. This study was designed to compare the MiroCam and EndoCapsule devices with respect to their rate of complete small-bowel examinations and their diagnostic yield.

### Patients and methods

This prospective randomized, clinical, head-to-head study was conducted at a single University-based center between April 2010 and March 2011. The study protocol was approved by the internal review board of the Medical University of Vienna and registered at clinicaltrials.org (NCT01090843). Patients who were referred for VCE were included in this study if they met at least one of the following criteria: (i) obscure gastrointestinal bleeding (defined as bleeding from the gastrointestinal tract, occult or overt, of unknown origin that had persisted or recurred after an initial negative upper and lower gastrointestinal endoscopic evaluation); (ii) chronic diarrhea (defined as three or more liquid stools per day for more than 4 weeks); or (iii) anemia of unknown origin (defined by a hemoglobin level <12g/dL for women and <13g/dL for men that had persisted or recurred despite medical treatment, such as iron replacement therapy).

It was obligatory for all three indications that at least one prior gastroscopy and colonoscopy had been performed. For chronic diarrhea and anemia of unknown origin, it was required that these endoscopies had included serial biopsy sampling. Patients aged outside the range 18–85 years or with any contraindication to VCE, such as small-bowel strictures, were excluded. After patients had given informed consent, they were randomly assigned to swallow either the MiroCam first, followed by the EndoCapsule, or vice versa. The randomization codes were computer generated and kept away from the investigational site.

### Capsule procedure

Bowel cleansing was achieved by ingestion of 2L of polyethylene glycol washout solution on the evening prior to the capsule procedure and 70mg of simethicone directly before intake of the first capsule. On the day of the VCE, all study patients were fitted with both the MiroCam and the EndoCapsule sensors using single-electrode patches. In order to avoid visual interference, the second capsule was swallowed after an interval of 2 hours. Patients were allowed to drink or eat 2 and 4 hours after intake of the second capsule, respectively. The capsule sensors were detached 12 hours after the second capsule had been swallowed, provided that both data recorders were indicating no further data transmission.

### Video analysis

All videos were analyzed by two experienced investigators (W.D. and A.P.) who were blinded to the patient’s identification, the randomization assignment, and the results of the corresponding VCE. The first set of 30 MiroCam videos was read first by W.D., while the EndoCapsule videos were read first by A.P. The second set of 20 videos was assigned in the opposite order. The corresponding videos were analyzed in a random order after a time period of at least 4 weeks. The frame rate during video examination was individually chosen. Pathological abnormalities were reported according to the “Capsule Endoscopy Structured Terminology (CEST)” [17]. In cases of disagreement between the two investigators, the respective video was reviewed together in order to reach consensus on the final diagnosis. Re-analysis was also performed in all discordant capsule pairs.

### Study endpoints

The primary endpoint of this study was the rate of complete small-bowel examinations, defined by the ability of the capsule to visualize the whole small intestine from the duodenum to the terminal ileum, including the transition of the capsule into the cecum. Secondary endpoints were the diagnostic yield in the small bowel, gastric and small-bowel transit times, and the total video length.

### Follow-up

As the diagnostic yield of VCE does not necessarily result in clinically meaningful diagnosis [18], we assessed the clinical impact of the VCE findings during a 6-month follow-up period. The result of the capsule endoscopy was assumed to have had a relevant clinical impact if it led to the establishment of a new clinical diagnosis (either directly or after performance of further investigations for clarification of the capsule-derived findings) that indicated the need for a therapeutic change or performance of an invasive treatment.

### Statistical assessment

The sample size was calculated for the primary endpoint in the context of a superiority trial design with a statistical power of 0.80 and a P value of 0.05, based on expected rates of complete small-bowel examination of 80% and 99% for the EndoCapsule and the MiroCam, respectively [13,19]. For the statistical assessment of the primary endpoint and the diagnostic yield, the McNemar chi-squared test was used. Transit times were compared with the paired-samples t test. Interobserver agreement between the two investigators and intra-individual agreement between the two capsule devices were calculated using kappa statistics. All statistical analyses were done with SPSS version 17.0. A P value <0.05 was considered significant.

### Results

In total, 76 patients were screened, of whom 50 patients were eventually included in the study (23 men, 27 women; median age 61, range 21–84; Fig. 1). All study patients had undergone at least one upper gastrointestinal endoscopy and one colonoscopy prior to VCE. All study capsules were swallowed without complication. No capsule-related adverse events were observed.
Video findings

The rate of complete small-bowel examinations was 48/50 using the MiroCam and 45/50 using the EndoCapsule (96% vs. 90%, odds ratio [OR]=2.67, 95% confidence interval [CI] 0.49–14.45; \( P=0.038 \)). The diagnostic yield in the small bowel was 25/50 using the MiroCam (a total of 35 different pathological abnormalities being detected) and 24/50 using the EndoCapsule (a total of 29 pathological abnormalities being detected); 50% vs. 48%, OR =1.08, 95% CI 0.49–2.37; \( P=0.99 \); Fig. 2, Table 2 and Table 3.

The combined diagnostic yield of the MiroCam and EndoCapsule was 29/50 (a total of 41 different pathological abnormalities; 58%). There was no obvious difference between the diagnostic yields for the three different indications. The combined diagnostic yield according to indication was 54% for obscure gastrointestinal bleeding (n=31), 60% for chronic diarrhea (n=10), and 66% for anemia of unknown origin (n=18). However, a difference was detected between the obscure gastrointestinal bleeding subgroups: the obscure-overt bleeding group showed a far higher combined diagnostic yield than the obscure-occult bleeding group (88% vs. 43%; \( P=0.045 \)). The degree of bowel cleansing did not differ between the two devices. There were no significant differences in the mean gastric transit times (MiroCam 46 ± 50 minutes vs. EndoCapsule 47 ± 56 minutes; \( P=0.98 \)) or small-bowel transit times (MiroCam 319 ± 113 minutes vs. EndoCapsule 316 ± 100 minutes; \( P=0.83 \)). The total video length was on average 2 hours longer with the MiroCam (704 ± 56 minutes vs. 578 ± 53 minutes; \( P<0.01 \)). No relevant visual interference between the two capsules was observed. Additional pathologic findings in the stomach and cecum were observed in 15/50 patients (30%), in 8/50 patients (16%) these findings had been missed by prior endoscopic workup.

Interobserver agreement

Interobserver agreement was excellent regarding the rate of complete small-bowel examinations (concordant assessment of the gastroduodenal and ileocecal junction in 100 of 100 capsule videos, 100%; kappa =1.0) and very good regarding the diagnostic yield in the small bowel (concordant diagnoses in 93 of 100 capsule videos, 93%; kappa =0.88).

Agreement between MiroCam and EndoCapsule

Intra-individual agreement between the corresponding capsule pairs with regard to the diagnostic yield in the small bowel was observed in 34 of 50 patients (68%; kappa =0.50; Table 4). In the 16 patients with discordant results, nine were classified as normal using one device but had one or more pathological abnormalities shown using the other device (Fig. 3). For seven patients, the number or types of abnormalities identified differed using the two different capsule devices. For one of these patients, the pathologic finding was an erosion located in the terminal ileum that was not reached by the EndoCapsule (patient #4, Table 3 [available online only]). There were 15 other pathological abnormalities that were not identified by both devices, all of which were located within the reach of both devices but were simply not visualized by one of them. No difference was observed in missed pathologies related to capsule type or capsule order. In addition, the location of the pathological abnormalities had no impact on the probability of their detection. Abnormalities composed of several lesions were more often detected by both capsules than those that presented with only a solitary finding (Table 3). Re-analysis of the 16 discordant capsule pairs by the two investigators did not reveal additional pathological abnormalities.

Clinical impact

During the 6-month follow-up period, a relevant clinical impact, as defined above, was detected in 15 of the 20 patients who had a pathological result detected by both capsules, in 7/9 patients who had a pathological result detected by only one of the capsules, and in 4/21 patients where both capsules showed normal results.

Discussion

This is the first head-to-head comparison of the MiroCam and EndoCapsule devices in patients with obscure gastrointestinal bleeding, chronic diarrhea, or anemia of unknown origin. There was no significant difference between the MiroCam and EndoCapsule devices with regard to the rate of complete small-bowel examinations or the diagnostic yield, despite a video recording time that was 2 hours longer with the MiroCam capsule. The moderate level of diagnostic concordance between the devices was mainly due to missed pathological findings, which questions the generally accepted high negative predictive value of VCE. The number of missed pathological abnormalities may be clinically relevant for patients with persistent clinical symptoms despite an uneventful VCE.

Other strategies to improve the rate of complete small-bowel examinations have been previously evaluated. Prokinetic agents such as erythromycin, for example, have been shown to accelerate the transpyloric passage of the capsule in some studies. However, their benefit in terms of the rate of complete small-bowel examinations has not yet been proven [20, 21]. Additionally, it has been reported that accelerated capsule movement in the small bowel could even lead to a lower diagnostic yield [22]. Recently, externally controllable magnetic capsule devices have been developed. Preclinical studies and in vivo case series have shown promising results for external influence on capsule movement in the stomach [23, 24]. Further studies may investigate the benefit of this technology for transpyloric passage and the rate of complete small-bowel examinations.
Fig. 2  Representative images of various pathological abnormalities detected using the MiroCam (left) and EndoCapsule devices (right): a angiodysplasia; b polyp; c erosion; d aphthous lesion;  
Continuation see following page
Table 2  Numbers of each type of pathological abnormality identified by the two different capsules among 50 patients with obscure gastrointestinal bleeding, chronic diarrhea, or anemia of unknown origin.

<table>
<thead>
<tr>
<th>Pathological Abnormality</th>
<th>MiroCam</th>
<th>EndoCapsule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiodysplasia</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>Polyp</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Erosion</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Aphthous lesion</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Ulcer</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Active bleeding</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Atrophic villi</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 4  The intra-individual agreement between the capsule pairs as shown by the number of different pathological abnormalities identified in each patient using the MiroCam device compared with the number of abnormalities identified using the EndoCapsule device (concordant results are shown in bold).

<table>
<thead>
<tr>
<th>MiroCam</th>
<th>None</th>
<th>One</th>
<th>Two</th>
<th>Three</th>
</tr>
</thead>
<tbody>
<tr>
<td>EndoCapsule</td>
<td>None</td>
<td>21</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>One</td>
<td>11</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Two</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Three</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Although in one patient a single pathological abnormality was identified by each of the devices, the type of abnormality detected differed.

Dolak W et al. Head-to-head study of smallowel imaging devices... Endoscopy 2012; 44: 1012–1018
In our study, the crossover results showed excellent interobserver agreement between the two examiners. Simultaneous examination with two different capsule devices seems to be safe, as has also been demonstrated in previous studies [15, 25]. In contrast to prior comparative trials of capsule devices, there was no relevant visual interference between the two capsule devices used in this study, which indicated that a time interval of 2 hours between swallowing of the capsules gives the first capsule time to be sufficiently ahead of the second. Mean gastric transit times of 46 ± 50 minutes and 47 ± 56 minutes further support this conclusion.

The most unexpected finding in this study was that there was only moderate agreement between the two devices, with a kappa of 0.50. This is even lower than the previously reported levels of agreement between the MiroCam and PillCam devices (kappa values of 0.74 and 0.66) [14, 15] and comparable with the results of a prospective comparison of the EndoCapsule and PillCam devices (kappa value of 0.48) [26]. In our present study, 15 diagnoses within reach of both capsules were missed by one of the capsules. These were not related to the capsule brand, capsule position, or location of the abnormality. In patients with obscure gastrointestinal bleeding, the time between onset of bleeding and performance of VCE impacts on the diagnostic yield because submucosal lesions may vanish or heal after a certain period, active bleeding that was detected using the MiroCam device only (patient #15). Angiodysplasia that was detected using the EndoCapsule device only (patient #34).

Competing interests: None.

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