Motorized spiral enteroscopy: results of an international multicenter prospective observational clinical study in patients with normal and altered gastrointestinal anatomy

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ABSTRACT

Background Motorized spiral enteroscopy (MSE) has been shown to be safe and effective for deep enteroscopy in studies performed at expert centers with limited numbers of patients without previous abdominal surgery. This study aimed to investigate the safety, efficacy, and learning curve associated with MSE in a real-life scenario, with the inclusion of patients after abdominal surgery and with altered anatomy.

Methods Patients with indications for deep enteroscopy were enrolled in a prospective observational multicenter study. The primary objective was the serious adverse event (SAE) rate; secondary objectives were the diagnostic and therapeutic yield, procedural success, time, and insertion depth. Data analysis was subdivided into training and core (post-training) study phases at centers with different levels of MSE experience.

Results 298 patients (120 women; median age 68, range 19–92) were enrolled. In the post-training phase, 21.5 % (n = 54) had previous abdominal surgery, 10.0 % (n = 25) had surgically altered anatomy. Overall, SAEs occurred in 2.3 % (7/298; 95 %CI 0.9 %–4.8 %). The SAE rate was 2.0 % (5/251) in the core group and 4.3 % (2/47) in the training group, and was not increased after abdominal surgery (1.9 %). Total enteroscopy was achieved in half of the patients (n = 42)

undergoing planned total enteroscopy. In 295/337 procedures (87.5 %), the anatomical region of interest could be reached.

Conclusions This prospective multicenter study showed that MSE was feasible and safe in a large cohort of patients in a real-life setting, after a short learning curve. MSE was shown to be feasible in postsurgical patients, including those with altered anatomy, without an increase in the SAE rate.

Introduction

Device-assisted enteroscopy (DAE) allows for direct endoscopic access to the small bowel with the option for tissue acquisition and therapeutic procedures [1–5]. However, deep enteroscopy is a challenging and time-consuming procedure and, in particular, visualization of the entire small intestine is usually only achieved by experts in enteroscopy using DAE techniques [6–10].

Motorized spiral enteroscopy (MSE), using the novel PSF-1 PowerSpiral Enteroscope (Olympus Medical Systems Corporation, Tokyo, Japan), was recently introduced into clinical practice and represents a new technology, namely "self-propelling enteroscopy," that is a technical refinement of the principle of spiral enteroscopy [11]. An integrated electric motor is used to rotate a short spiral overtube at the distal part of the insertion section of the enteroscope. MSE was recently shown to be effective and safe for antegrade deep enteroscopy in terms of diagnostic success rates, procedural duration, and depth of maximum insertion (DMI) in an initial prospective pilot study [12]. In an additional prospective study involving the same two European centers, the novel technique achieved total enteroscopy using an antegrade or combined antegrade and retrograde approach in 70 % of the cases [13]. However, these results were achieved at two tertiary referral centers that already had vast experience in MSE after an initial learning period. Furthermore, patients who had undergone major abdominal surgery and with surgically altered anatomy were not included in these trials; these patients may be at higher risk of procedure-related adverse events [3, 14].

For these reasons, the current large multicenter study was designed with the primary objective of assessing the safety of the technique in a real-life setting, including appraisal of learning curve aspects and with investigations performed in patients after previous abdominal surgery, including with altered gastrointestinal (GI) anatomy.

Methods

Study design

This international multicenter prospective observational study (SAfety and performance of the MotorIzed Spiral Endoscope; SAMISEN) was conducted at ten European endoscopy tertiary referral centers. Data were collected from September 2019 until February 2021. The study protocol was approved by the institutional review board at each center prior to initiation of the study.

Study objectives

The aim of the study was to evaluate the safety, efficacy, and learning curve associated with MSE in a large cohort of patients with an indication for deep enteroscopy in a real-life setting. Antegrade, retrograde, and bidirectional procedures were included. To reflect the different levels of experience with MSE, the ten participating European reference centers/investigators were either already experienced in MSE, or experienced in DAE enteroscopy but newly starting to use MSE. Once enrollment into the study had reached the halfway point, the inclusion of patients who had undergone major abdominal surgery, including those with altered GI anatomy, was allowed.

Inclusion and exclusion criteria

Patients with suspected small-bowel disease with either a positive or suggestive finding on prior small-bowel imaging (video capsule endoscopy [VCE], radiology) or another clinical indication for deep enteroscopy were enrolled, after informed consent had been obtained. The indications for deep enteroscopy and the study exclusion criteria are presented in ▶ **Table 1**.

Recruitment of patients

All consecutive patients with an indication for deep enteroscopy were registered at 10 European reference centers and screened for enrolment. Patients who did not meet the inclusion criteria or refused to sign the informed consent form were excluded from the study.

Data management and statistical analysis

All consecutive patients at the study centers fulfilling the inclusion criteria were registered and enrolled after informed consent had been obtained. A PostgreSQLdatabase was created using an XClinical platform (Munich, Germany) with an electronic case report form (eCRF). Data entry was done by trained study nurses at each study center and was verified by a physician.

Statistical analyses were carried out by a professional statistician (SCO:SSiS, Berlin, Germany) using SAS, version 9.4 (SAS Institute Inc., Cary, North Carolina, USA). Continuous measures are summarized with sample size, mean, median, SD, minimum and maximum, and interquartile range (IQR). Categorical measures are presented with the counts and percentages of subjects in each category, with 95 % Clopper–Pearson confidence intervals where reasonable. Fisher's exact test was used to compare categorical variables. *P* values less than 0.05 were considered statistically significant. All authors had access to the study data, and reviewed and approved the final manuscript.

▶ **Table 1** The indications for deep enteroscopy using motorized spiral enteroscopy (MSE), and the study exclusion criteria and secondary end points.

Indications for deep enteroscopy[1]
▪ Gastrointestinal bleeding
▪ Inflammatory bowel disease, i. e. Crohn's disease
▪ Abdominal pain or chronic diarrhea
▪ Large polyps (> 10–15 mm) in the jejunum and ileum in patients with Peutz–Jeghers syndrome
▪ Nonresponsive or refractory coeliac disease
▪ Results and hints from other preliminary investigations (i. e. small-bowel video capsule endoscopy, small-bowel imaging examinations) that warranted further work-up with direct enteroscopy
Exclusion criteria
▪ Patients under the age of 18 years
▪ Pregnancy
▪ Any contraindication to standard enteroscopy (e. g. severe coagulopathy or known coagulation disorder, bowel obstruction/stenosis, stents or other instruments implanted in the intestinal tract, suspected gastrointestinal perforation, esophageal or gastric varices, eosinophilic esophagitis) as judged by the investigator after careful individual risk assessment
▪ Concurrent participation in another competing clinical study
▪ Absence of informed consent
Secondary end points
▪ Adverse events during and early after the procedure
▪ Procedural success rate (per patient and per procedure): number of patients/procedures in which the anatomical region of interest could be reached using MSE
▪ Total enteroscopy rate (per patient and per procedure): complete evaluation of the small bowel either with a single antegrade or retrograde approach, or in a combined bidirectional approach
▪ Time to depth of maximum insertion: the time from oral (anal) insertion until reaching the deepest point of insertion
▪ Total procedure time: the time from oral (anal) insertion until complete withdrawal of the device out of the patient
▪ Diagnostic yield: percentage of procedures that either confirmed a diagnosis from previous studies, or established a new definitive diagnosis at the anatomical location identified in previous studies, or findings that could explain the clinical symptoms
▪ Therapeutic yield: percentage of patients with any endoscopic intervention/therapy during any MSE procedure in the study, with the exception of biopsies
▪ Total therapeutic intervention time: procedure time dedicated to therapeutic maneuvers (biopsies were not considered here)
▪ User feedback and assessment of handling characteristics: number and rate of procedures, subjectively assessed by the endoscopist who performed the procedure, as worse, similar, or better than balloon-assisted enteroscopy in the following categories: (a) handling; (b) insertion; (c) positioning; (d) procedural time needed; and (e) staff and resources needed

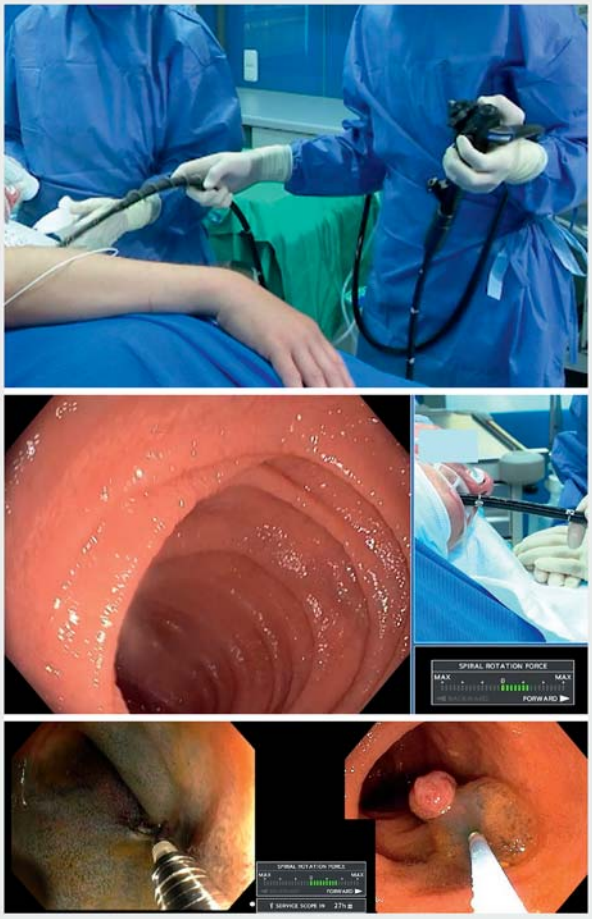
[1] Indications were not limited to this list.

Study device

The novel motorized spiral enteroscope PSF-1 was approved in Europe with a CE mark during the entire study period (▶ **Fig. 1**). The MSE system and procedural steps have been described in detail in previous publications [11–13, 15] (Appendix 1 s, see online-only Supplementary material).

Study investigators and endoscopist requirements

All procedures were performed by one or two accredited endoscopists at each study site. Each study endoscopist had vast experience in deep enteroscopy using a standard device-assisted technique (double-balloon enteroscopy, single-balloon enteroscopy, and/or manual spiral enteroscopy) and had successfully passed a dedicated theoretical and practical hands-on training module on MSE prior to accreditation (Appendix 2 s). The first five cases for each individual endoscopist were considered to be learning curve cases and were allocated to the training phase of the study protocol. This was not applicable for study endoscopists who had performed more than 20 documented cases of MSE outside the study protocol prior to initiation. For these endoscopists, all MSE procedures performed within the study were allocated to the core phase of the study protocol.



▶ **Fig. 1** Images of motorized spiral enteroscopy being performed using the PSF-1 PowerSpiral enteroscope (Olympus Medical Systems Corporation, Tokyo, Japan), which is 1680 mm in length, with an outer diameter of 11.3 mm at the insertion portion, and has an integrated electric motor that is used to rotate a short disposable spiral overtube (240 mm in length, 31.1 mm outer diameter of the soft spiral fins) that is attached to a rotation coupler located 40 cm proximal to the endoscope's tip. For antegrade MSE, the study device is inserted through the mouth and advanced with the assistance of motorized clockwise spiral rotation. Marking of the deepest point (depth of maximum insertion) was done using ink dye injection and/or clipping. Therapeutic interventions were usually performed during the withdrawal phase.

Motorized spiral enteroscopy and periprocedural management

The MSE procedure was performed as an antegrade, retrograde, or combined bidirectional procedure. The selection was made on the basis of the pre-investigational results of VCE or other imaging methods. For patients in whom an indication for total enteroscopy was present, a second MSE could be performed from the opposite direction (in the same session or on another day), if the first approach remained incomplete.

Post-procedural measures

In this observational study, clinical investigations and blood sample analyses were performed according to the local policies at each center. The final study visit was completed before each patient was discharged from the hospital.

Study end points, outcome measures, and definitions

The primary end point of the study was the number of serious adverse events (SAEs; the number of patients with at least one SAE) caused by MSE during or after the procedure. As a secondary safety end point, the overall frequency of adverse events was registered. All adverse events were defined and classified using the most recent version of MedDRA (Medical Dictionary for Regulatory Activities; www.meddra.org). All adverse events were stratified by severity (mild, moderate, severe) [16] and by relation to the study treatment and/or the study device. All AEs were systematically registered in the eCRF. Additionally, all SAEs were promptly reported via a paper form (fax). The secondary end points are detailed in ▶ **Table 1**.

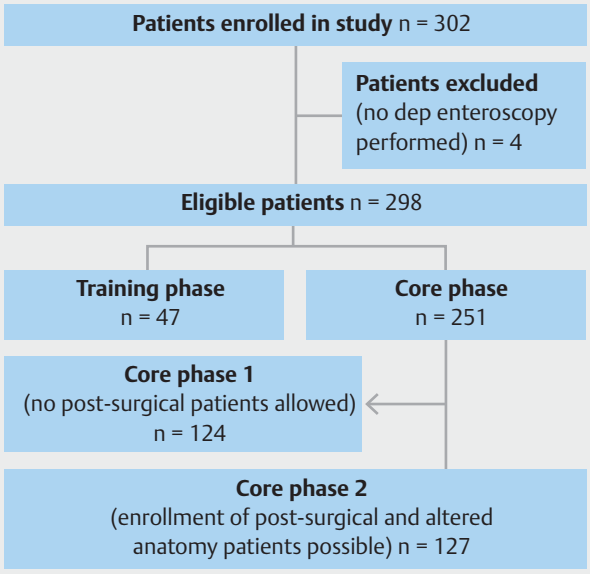
Definition of analysis populations and subgroup analyses

The study enrolment was subdivided into two phases: training phase (as previously defined) and core phase (all cases that were not training phase cases). To further address the learning curve and reflect the increase in complexity, the core phase was further subdivided according to the enrolment plan into: core phase 1 (CP1; first half of the core phase population, which included only patients without previous major abdominal surgery) and core phase 2 (CP2; second half of core phase population, which also included patients who had undergone major abdominal surgery, including those with altered GI anatomy).

Further information was prospectively registered and subsequent subgroup analyses were performed, where reasonable, including subgroups of patients treated at experienced MSE centers (previous experience of > 20 MSE cases) and new MSE centers (experience of < 20 MSE cases, who therefore enrolled patients in the training phase population), undergoing diagnostic and interventional procedures, who had undergone previous abdominal surgery or had altered anatomy, with Crohn's disease, who were taking aspirin during the study (80–100 mg daily), and who underwent MSE with or without general anesthesia.

Data management, statistical analysis, and sample size calculation

The primary aim of this observational study was to evaluate the safety of MSE. The SAE rate was used as a surrogate parameter. A technical review by the European Society of Gastrointestinal Endoscopy (ESGE) reported SAE rates of up to 8 % or higher associated with interventional DAE procedures, and up to 0.8 % for purely diagnostic procedures [3]. In order to guarantee a reasonable number of subjects that needed to be enrolled in the current study, a viable case number calculation was initially done to demonstrate that the SAE rate was below an 8 % threshold as the upper limit. Therefore, a minimum of 245 subjects



▶ **Fig. 2** Patient enrollment and allocation to study groups. Four patients had to be excluded from the analysis, because no deep enteroscopy was performed: training phase (n = 1), core phase 1 (n = 3).

for the core phase of the study was considered necessary for statistical analysis. The precision of the SAE rate was estimated based on at least 245 patients (width of the 95 %CI): n = 5, SAEs 2 % (0.7 %–4.7 %); n = 10, 4.1 % (2.0 %–7.4 %); n = 15, 6.1 % (3.5 %–9.9 %); n = 20, 8.2 % (5.1 %–12.3 %). Taking into account an expected dropout rate of 5 %, a total of 260 subjects was determined to be the minimum total sample size required.

Shortly, after study initiation, a new joint guideline by the ESGE and United European Gastroenterology (UEG) for the first time proposed upper limits for SAE rates of 1 % and 5 % for diagnostic and therapeutic DAE procedures, respectively [14]. However, this recommendation was only based on moderate quality evidence and also suggested that higher complication rates can be expected after previous abdominal surgery and in patients with altered anatomy.

Results

Patient characteristics and procedural details

Between September 2019 and February 2021, 302 patients were enrolled in the study ▶ **Fig. 2**. Four patients had to be excluded because no deep enteroscopy had been performed. A total of 298 patients (120 women; median age 68 years, range 19–92) were eligible for analysis, with 47 patients allocated to the training phase and 251 allocated to the core study phase.

Overall, 80.9 % of the patients had positive findings on previous VCE (n = 151; 50.7 %) or in other imaging modalities (n = 90; 30.2 %). There were 116 patients (38.9 %) who were enrolled at two experienced MSE centers and 182 (61.1 %) who were enrolled at new centers. Among the 298 patients, 337 MSE procedures were performed: (antegrade, 241; retrograde, 75; combined [single session], 21). Among the core phase patients, 54 (21.5 %) had had previous abdominal surgery, resulting in surgically altered GI anatomy in 25 patients (10 %). Also in the core phase group, one-third of the patients were initially planned for total enteroscopy (81/251; 32.3 %) (▶ **Table 2**).

▶ **Table 2** Characteristics of the 298 patients entered into the study who underwent deep enteroscopy using motorized spiral enteroscopy (MSE).

Patients in training phase/core phase, n	47/251
Sex, male/female, n	178/120
Age, mean/median (range), years	68/64.4 (19–92)
Body mass index mean/median (IQR), kg/m2	26.1/25.2 (22.8–29.0)
ASA classification, n (%)	
▪ I	33 (11.1 %)
▪ II	124 (41.6 %)
▪ II	129 (43.3 %)
▪ IV	12 (4.0 %)
Previous abdominal surgery, n (% of core phase group)	54 (21.5 %)
Surgically altered gastrointestinal anatomy n (% of core phase group)	25 (10.0 %)
▪ Esophagectomy with gastric sleeve	1
▪ Gastrectomy (Billroth I or II)	3
▪ Roux-en-Y gastric bypass (bariatric)	8
▪ Duodenopancreatectomy (Roux-en-Y)	3
▪ Bilioenteric anastomosis (hepaticojejunostomy)	2
▪ Ileocecal resection	1
▪ Total/hemi colectomy	6
▪ Other	1
Previous positive imaging as indication for MSE, n (%)	241 (80.9 %)
▪ Video capsule endoscopy	151 (50.7 %)
▪ Other modalities	90 (30.2 %)
Patients planned for total enteroscopy, n (%)	
▪ Overall group	98 (32.9 %)
▪ Core group	81 (32.3 %)

IQR, interquartile range; ASA, American Society of Anesthesiologists.

Safety analysis

The population for safety analysis was comprised of all 298 patients (including the 47 training patients). Eight SAEs were reported in seven patients. Therefore, the overall SAE rate per patient was 2.3 % (95 %CI 0.9 %–4.8 %). The upper limit of the 95 %CI was below the predefined threshold of 8 % and also below the 5 % threshold suggested by the latest European guideline for therapeutic procedures [14]. In the core safety popula-

▶ **Table 3** Details of the motorized spiral enteroscopy (MSE) procedures performed.

	Overall group	Core group	
Number of patients	298	251	
MSE approach (per patient), n (%)			
▪ Antegrade first	229 (76.8 %)	200 (79.7 %)	
▪ + retrograde second	27 (9.1 %)	22 (8.8 %)	
▪ Retrograde first	48 (16.1 %)	36 (14.3 %)	
▪ + antegrade second	12 (4.0 %)	11 (4.4 %)	
▪ Combined antegrade and retrograde in single session first	21 (7.0 %)	15 (6.0 %)	
Total number of procedures performed	337	284	
MSE route, n (% of procedures)			
▪ Antegrade	241 (71.5 %)	211 (74.3 %)	
▪ Retrograde	75 (22.3 %)	58 (20.4 %)	
▪ Combined	21 / (6.2 %)	15 (5.3 %)	
Procedural success rate, n (% of procedures)[1]	295 (87.5 %)	250 (88.0 %)	
Total enteroscopy rate, n (% of patients)			
▪ All indications	46 (15.4 %)	42 (16.7 %)	
▪ Total enteroscopy planned (n = 98 overall; n = 81 core)	46 (46.9 %)	42 (51.9 %)	
Procedure time (median/IQR), minutes			
▪ Time to DMI for antegrade route	39.0 (27–54)	38.0 (25–54)	
▪ Total procedure time for antegrade route	59.5 (45–79)	58.5 (45–79)	
▪ Time to DMI for retrograde route	32.0 (20–50)	29.5 (18–40)	
▪ Total procedure time for retrograde route	48.0 (33–69)	44.5 (28–65)	
Type of anesthesia used, n (%)		General anesthesia	Sedation
▪ Antegrade approach (n = 241)	–	202 (83.8 %)	39 (16.2 %)
▪ Retrograde approach (n = 75)	–	35 (46.7 %)	40 (53.3 %)
▪ Combined approach (n = 21)	–	20 (95.2 %)	1 (4.8 %)
Diagnostic yield per patient, n (%)	251 (84.2 %)	208 (82.9 %)	
Therapeutic yield per patient, n (%)	172 (57.7 %)	151 (60.2 %)	

IQR, interquartile range; DMI, depth of maximum insertion.
[1] Anatomical region of interest reached.

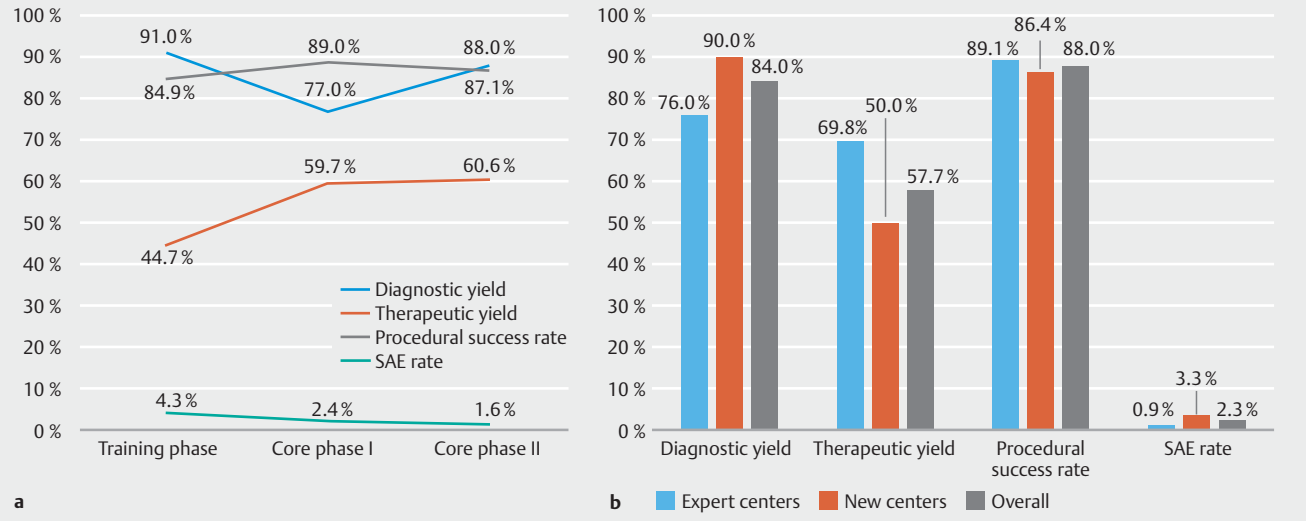
tion (training patients excluded), the SAE rate was slightly lower at 2.0 % (95 %CI 0.6 %–4.6 %). In the training phase group (47 patients), two SAEs occurred, giving an SAE rate of 4.3 % (95 %CI 0.5 %–14.5 %). Details of the SAEs are given in **Table 1 s**.

The overall AE rate was 11.1 % per patient (33/298) and 11.0 % per procedure (37/337). Without the training phase cases, the overall AE rate was 9.6 % per patient (24/251). Most of the reported mild AEs were related to clinically asymptomatic mucosal lacerations at the level of the esophagus, the cardia, and the small bowel, and transient mild abdominal pain.

Subgroup analyses for the primary endpoint

The SAE rates (per patient) were 0.8 % (1/126; 95 %CI 0.02 %–4.34 %) and 3.5 % (6/172; 95 %CI 1.29 %–7.44 %) for diagnostic procedures and when therapeutic interventions were performed during MSE, respectively. The SAE rate was 1.6 % (4/257) when general anesthesia was used and 3.8 % (3/80) when deep sedation was used ($P = 0.24$). All but one SAE occurred during antegrade MSE procedures.

SAE rates for further subgroups were as follows: after previous abdominal surgery, 1.9 % (1/53; the only event occurred in a patient with altered anatomy [4 %; 1/25]); in known or newly diagnosed Crohn's disease, 4.8 % (1/20); patients taking aspirin during the study (80–100 mg daily), 0 % (0/86).



▶ **Fig. 3** Analysis of the learning curve with respect to: **a** study phase; **b** center experience.

Procedural success, insertion depth, and procedure time

The anatomical region of interest could be reached in 295 of 337 procedures in the entire study (87.5 %, 95 %CI 83.5 %–90.9 %) and in 250 of 284 procedures in the core group (88.0 %, 95 % CI 83.7 %–91.6 %). Total enteroscopy was achieved in half of the patients that were initially planned for a total enteroscopy (42/81). Procedural details are shown in ▶ **Table 3**.

Diagnostic yield

In 251 of 298 patients, the procedures with MSE either confirmed a diagnosis from previous studies, or established a new definitive diagnosis at the anatomical location identified in previous studies or findings that could explain the clinical symptoms. Therefore, the diagnostic yield was 84 % (▶ **Table 3**).

Therapeutic yield

In 172 of 298 patients, at least one therapeutic intervention (other than biopsies) was performed. The therapeutic yield per patient was 57.7 %. The time needed for interventions was a mean of 7.8 minutes and a median of 3.0 minutes (IQR 1.0–10.0) (▶ **Table 3**).

Learning curve analysis

Only one SAE occurred at an experienced center (1/116; 0.9 %), whereas the overall SAE rate was 3.3 % at new MSE centers (6/182; $P = 0.25$). The SAE rate, which was 4.3 % (2/47) in the training phase, decreased to 2.4 % (3/124) in core phase 1 and 1.6 % (2/127) in core phase 2 (▶ **Fig. 3a**). As expected, the overall number of SAEs in the entire study population was too low for further subgroup analyses in terms of a learning curve effect.

In all study phases, the rate of procedures that reached the anatomical region of interest (procedural success rate) was high: training phase, 84.9 % (45/53); CP1, 89.0 % (129/145); and CP2, 87.1 % (121/139; $P = 0.70$). The procedural success rate was not significantly different between procedures done at experienced (89.1 %; 123/138) and new MSE centers (86.4 %; 172/199; $P = 0.51$). The diagnostic success rate (per patient) was constantly high throughout all study phases: training phase, 91 % (43/47); CP1, 77 % (96/124); CP2, 88 % (112/127; $P = 0.03$). The overall diagnostic yield was 76 % (88/116) and 90 % (163/182) at experienced and new MSE study centers ($P = 0.002$), respectively. However, the rate of positive imaging tests prior to MSE was lower at the experienced centers (55 % vs. 76 %).

Total enteroscopy was achieved in 19 % (22/116) and 13 % (24/182) of experienced and new MSE centers, respectively ($P = 0.19$). The rate of therapeutic MSE procedures (therapeutic yield) increased slightly throughout the study phases: training phase, 44.7 % (21/47); CP1, 59.7 % (74/124); CP2, 60.6 % (77/127; $P = 0.14$). Procedures performed at experienced centers (69.8 %; 81/116) had a higher overall therapeutic yield than new centers (50.0 %; 91/182; $P < 0.001$) (▶ **Fig. 3b**).

Discussion

MSE was recently introduced into clinical practice for deep enteroscopy in Europe and parts of Asia. The novel technology using a motorized, self-propelling endoscope has demonstrated favorable outcomes for deep enteroscopy in terms of insertion depth, procedural duration, and efficacy of diagnostic and therapeutic interventions in patients without previous abdominal surgery at expert centers [12, 13]. In the current study, MSE was applied to a potentially more vulnerable population of patients who had undergone major abdominal surgery, including those with altered GI anatomy. In addition, when a new technology becomes available, it often involves a learning curve with a potentially higher risk of associated AEs early on. Therefore, safety analysis was chosen as the primary end point of this study. Evaluation was done in a real-life setting with an internal control group, as not only expert centers for MSE but also other

centers, which contributed their learning curve experience, were included.

True complication rates for deep enteroscopy are difficult to estimate because of the limited number of available studies that were primarily designed to evaluate AE rates. Therefore, reported complication rates in the literature mainly derive from the secondary end points of studies with different primary objectives and consecutive meta-analyses.

The latest European guideline on performance measures for small-bowel endoscopy, for the first time, suggested thresholds of 1 % and 5 % for diagnostic and therapeutic DAE procedures, respectively, in unselected populations [14]. In this context, the overall SAE rate in our study of 2.0 % shows that MSE can be safely performed in this real-life and prospectively scrutinized scenario. Even when training phase patients were included in the analysis, the overall SAE rate was only 2.3 %. The distinct SAE rates for diagnostic and therapeutic procedures in our study were 0.8 % and 3.5 %, respectively. While these SAE rates are below the thresholds proposed by the ESGE guideline, the study was not powered for these subgroup analyses and therefore results have to be interpreted with caution and cannot be generalized. However, the current study clearly confirms the findings from a previous large prospective pilot trial, which reported an SAE rate of 1.5 % [12].

Data regarding the use of spiral enteroscopy in patients after major abdominal surgery and with surgically altered anatomy are limited. The available studies therefore do not report an increased rate of AEs [17–20]; however, there is potential concern about an increased rate of AEs using the motorized technique. Recently, a study found no increase in the AE rate for MSE in patients who had undergone previous surgery [21]. In the current study, 21.5 % of the patients had previous abdominal surgery, with 10 % having surgically altered GI anatomy (40.8 % and 19.2 % of the CP2 group, respectively). The SAE rate in this subgroup of patients was only 1.9 %. Remarkably, only one SAE occurred in a patient with altered anatomy.

The most common complications of standard DAE are perforation, bleeding, and pancreatitis. Looking into the details of the current study, only two bleeding-associated SAEs that required endoscopic intervention occurred and a single perforation that required laparoscopic suturing was observed, meaning the rates for both categories were within the anticipated range. Pancreatitis has been reported to occur in 0.3 % of DAE procedures [3]. Remarkably, in the current study, no acute pancreatitis following MSE was registered, indicating that the lower risk for post-DAE pancreatitis reported with spiral enteroscopy is maintained for MSE [6].

Rotation of the spiral overtube, that is needed for movement of the endoscope, depends on the functionality of the integrated electric motor and its peripherals. Thus, there is concern among users about the durability of the MSE system and consequences of a major equipment failure, like a motor breakdown, when the spiral is fixed deep within the small bowel. Therefore, before starting a new procedure (after start-up of the system), the operator is obliged to follow an inspection protocol to ensure normal functionality of the system. However, the manufacturer provides a specific emergency protocol (use of CO_2 insufflation, fluid irrigation, and repetitive tip deflection under fluoroscopic guidance to free the entrapped small bowel from the endoscope without spiral movement), that has been successfully validated in animal models prior to first-in-human application. Furthermore, in MSE, compared with manual spiral enteroscopy, the tactile feedback of spiral rotation is replaced by a graphical rotation force indicator that displays the direction and the resistance of the spiral rotation to the operator. The system continuously monitors the current that is needed for spiral rotation as a surrogate for the applied force. Automatic motor stops occur when a certain threshold is exceeded. The system functionality check also includes a mandatory test of this “limit function”.

Rotation of the spiral overtube, which is needed for movement of the endoscope, depends on the functionality of the integrated electric motor and its peripherals. Therefore, there is concern among users about the durability of the MSE system and the consequences of a major equipment failure (**Appendix 3 s**). No failures were observed during any of the 337 MSE procedures. Premature disassembly of the spiral overtube from the rotation coupler would result in the inability to further apply spiral rotation and might lead to a total loss of the overtube within the patient’s small bowel. In the current study, this situation occurred once, when the overtube was already in the patient’s esophagus during the withdrawal phase and it could be manually extracted. This situation may have occurred because a standard mouthpiece was used instead of the approved mouthpiece with a larger diameter. Furthermore, it has become evident that strict adherence to the manufacturer’s procedure guideline is needed.

In the previous prospective trials using MSE, diagnostic success rates were reported to be as high as 74.2 % for antegrade MSE [12] and 80 % when applying an antegrade and/or retrograde approach [13]. In the current study, where 87.5 % of the procedures successfully reached the region of interest, the overall diagnostic yield was 84 %. This clearly indicates that the high diagnostic success rates of MSE can also be reproduced in the real-life setting of this multicenter study.

Looking at the learning curve, we found a higher SAE rate of 4.3 % in the training phase, compared with 2.0 % in the entire core phase and 1.6 % in core phase 2 only, when postsurgical patients, including those with altered anatomy, were also enrolled. Although these results must be interpreted with caution because of the limited number of patients and only two events in the training phase population, this indicates a trend towards a (short-term) learning curve effect. Only one SAE occurred during a procedure that was done at a center with previous MSE experience.

Remarkably, procedural and diagnostic success rates remained constantly high throughout all study phases, including the training phase, and were not inferior at new MSE centers compared with those with more experience. There was a trend for higher rates of total enteroscopies at experienced centers (19.0 % vs. 13.2 %). Furthermore, although the rate of therapeutic interventions slightly increased throughout the study phases (from 44.7 % to 60.6 %), no increase in the complication rate was noted.

Although our study represents the first large-scale international multicenter prospective evaluation of the novel technique of MSE, it also has limitations. Firstly, the study was powered for the overall rate of SAEs. Important subgroup analyses (i. e. training phase, postsurgical and altered anatomy patients, or patients with specific small-bowel diseases) are limited by small numbers of subjects in the respective groups. Secondly, no control group was included in the study. In addition, the heterogeneous composition of the study centers, with different levels of experience in terms of MSE, may be seen as a limitation. However, it may also represent a strength of our study, as it serves as an internal control. The involvement of centers with two differing levels of MSE experience and different study phases related to the complexity of patients reflects real-life clinical practice and addresses the learning curve effect.

In conclusion, this prospective multicenter study showed that MSE was feasible and safe in a large cohort of patients in a real-life setting at centers with experience in deep enteroscopy after a short learning curve. MSE was shown to be feasible in postsurgical patients, including those with altered anatomy, without an increase in the rate of AEs. These results justify further evaluation of MSE in further prospective studies for various indications, including biliopancreatic interventions in postsurgical/altered anatomy patients, preferably with the inclusion of a control group.

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Competing interests

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