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## **A New Method for Endoscopic Sampling of Submucosal Tissue in the Gastrointestinal Tract**

### **A Comparison of the Biopsy Forceps and a New Drill Instrument**

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Walther, Jeremiasen, Rissler, Johansson, Larsson, Walther  
*A new biopsy instrument for flexible endoscopy*

**A new method for endoscopic sampling of submucosal tissue in the gastrointestinal tract: a comparison of the biopsy forceps and a new drill instrument**

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## **Abstract**

**Background:** Sampling of submucosal lesions in the gastrointestinal tract through a flexible endoscope is a well-recognized clinical problem. One technique often used is endoscopic ultrasound guided fine-needle aspiration (EUS-FNA), but it does not provide solid tissue biopsies with preserved architecture for histopathological evaluation. To obtain solid tissue biopsies from submucosal lesions we have constructed a new endoscopic biopsy tool and compared it in a cross-over study with the standard double cupped forceps.

**Methods:** 10 patients with endoscopically verified submucosal lesions were sampled. The endoscopist selected the position for the biopsies and used the instrument selected by randomization. After a biopsy was harvested the endoscopist chose the next site for a biopsy and again used the instrument picked by randomization. A total of 6 biopsies, 3 with the forceps and 3 with the drill instrument were collected in every patient.

**Results:** The drill instrument resulted in larger total size biopsies (mm<sup>2</sup>), (Mann-Whitney U-test, p=0.048), and larger submucosal part (%) of the biopsies (Mann-Whitney U-test, p=0.003) than the forceps. Two patients were observed because of chest pain and suspicion of bleeding, respectively in 24 hours. No therapeutic measures were necessary to be taken.

**Conclusion:** The new drill instrument for flexible endoscopy can safely deliver submucosal tissue samples from submucosal lesions in the upper gastrointestinal tract.

The study was registered on ClinicalTrials.gov. NCT02161029

## **Introduction**

Sampling of submucosal lesions in the gastrointestinal tract through a flexible endoscope is a well-recognized clinical problem. In most circumstances, subepithelial tumours lack distinct endoscopic and ultrasonographic features to assess risk of malignancy [1]. Biopsies provided by the forceps are usually epithelial only and also with a bite-on-bite technique and a large-capacity “jumbo” forceps submucosal layers are seldom achieved and are seen in 17 % to 35 % of the biopsies irrespective of technique [1, 2]. The standard technique for sampling submucosal lesions, endoscopic ultra sound guided fine-needle aspiration (EUS-FNA), often requires multiple passes to be diagnostic compared to solid tissue biopsies [3]. FNA material does not preserve the tissue architecture and submucosal lesions are often stromal in nature and the cellularity needed for further investigations is improved by solid tissue biopsies [4, 5]. EUS-guided Trucut® biopsies have been tried but the diagnostic outcome has not been superior to EUS-FNA [6, 7, 8]. Endoscopic mucosal resection (EMR) techniques can provide adequate material as well as removal of the lesion but are time consuming and require anaesthesia. The importance of high quality biopsy material in submucosal lesions is illustrated in gastrointestinal stromal tumors (GIST). A biopsy providing histopathological material is helpful for a correct diagnosis as well as for evaluating the malignant potential using the presence of necrosis and frequency of mitosis. It has been shown in a literary review that EUS- FNA can provide material for an initial diagnosis in about 60 % of cases with submucosal lesions [9]. Nevertheless, to provide adequate solid tissue biopsies with the simplicity of conventional flexible endoscopy would simplify the handling of submucosal tumours. For this purpose we constructed a new biopsy tool for flexible endoscopic use (patent pending). It uses a drilling motion within a casing to harvest solid biopsies from submucosal tissue through the biopsy channel of an ordinary flexible endoscope. Since the

standard biopsy forceps is the biopsy tool always available at endoscopic examinations we chose to compare that initially with the new drill instrument.

We have compared the non-disposable drill instrument with the standard single-use biopsy double cupped forceps in 10 patients with submucosal lesions larger than 10 mm, taking 3 samples with both instruments in each patient.

## **Methods**

### *Patients*

Ten patients with submucosal lesions in the stomach and oesophagus were examined. Six were male and 4 female with an average age of 71 years (range 59-78). The tumours sizes were on average 3.4 cm (range 2-6) [Table 1]. All were investigated with EUS to verify the submucosal localisation and to rule out haemangioma. At time of investigation the endoscopist selected the positions for the biopsies without knowing the order of the two instruments, unique for every of the ten patients due to the closed envelope randomization technique. The instruments were inserted in the order decided by the randomization and the endoscopist sampled the lesion at the location chosen prior to insertion of any instrument. Six consecutive biopsies were harvested, 3 with the conventional forceps and 3 with the drill instrument. All biopsies were harvested, fixated in formalin and sent to the Department of Pathology for microscopic analyses with haematoxylin-eosin staining (HTX). The histological examination was performed by a senior pathologist specialized in gastrointestinal pathology. Which instrument that was used for each biopsy was blinded to the pathologist. A histological diagnosis was performed and the total size of the biopsies as well as the amount of submucosal tissue was measured (mm) from the largest tissue section. Submucosal tissue was defined as tissue beneath the muscularis mucosa layer. The time needed for sampling each biopsy was measured (seconds).

### *Materials*

In all patients a standard gastroscope (GIF-HQ 190, Olympus Sverige AB, Solna, Sweden) was used. The traditional biopsy instrument in the study was a single-use biopsy double cupped forceps, standard capacity with needle, for 2.8 mm working channel (Radial jaw 4, Boston Scientific Corporation, Marlborough, MA, USA). Biopsies were harvested by pushing the open forceps firmly towards the tumor at the different locations chosen for the three biopsies, avoiding hole-in-hole technique. The Endodrill<sup>®</sup> is a new non-disposable biopsy device for flexible endoscopy that we have constructed (Endodrill I, BibbInstruments AB, Lund, Sweden). It has a drill in the distal end covered by a steel casing and a handle that allows for free handling of the rotation and depth of the drill. This gives the examiner freedom to decide both the depth of the sampling and the rotational force and speed of the drill [Fig. 1 A-C]. The length of the biopsy screw is adjusted when the endoscope is close to the tumor to avoid the influence of curvature of the endoscope depending on site of tumor [Fig. 1A]. Before the first biopsy, the drill handle should be moved back and forth a couple of times to check the extension of the biopsy screw and so it was [Fig. 1A]. Specimens from the three chosen locations were sampled by pushing the casing firmly towards the tumor before clockwise drilling into the tumor [Fig. 1B]. Trapping the tissue in the casing was accomplished with a clockwise rotation of the drill while withdrawing it, [Fig. 1C]. We harvested the biopsies from the drill instrument with the help of a tip of a standard 1 mm injection needle [Fig. 2].

Complications for the patients were noted in connection with the investigation and at the telephone follow-up, one and seven days after the endoscopy. Any malfunctions of the instruments were registered.

### *Statistical methods*

The primary endpoint of the study was the amount of submucosal tissue harvested with a flexible endoscope. Submucosa of high histopathological quality can be included in 35 % of gastric biopsies from submucosal lesions with a standard biopsy forceps for flexible endoscopy irrespective of technique [2]. Prior to the clinical study, the capacity of the drill instrument to achieve submucosal tissue of acceptable quality was tested experimentally and submucosal layers of good quality was at hand in more than 90 % of the samples (data not shown). Accordingly the number of biopsies needed was calculated from the assumption of an improvement of 55 % that is from 35 % to 90 %, and sample size estimation resulted in 26 biopsies with every of the two instruments. To make sure that our test had adequate data for conclusive results we required a 90 % power ( $1 - \beta$ ) and we accepted statistical significance of 95 % ( $\alpha = 0.05$ ). Estimating a couple of failures we randomized 60 biopsies, 30 to every of the two instruments. As a consequence 6 biopsies, three with the standard forceps and three with the drill instrument, was harvested in every of the 10 patients. Nominal data was calculated with the Chi-2 test. For quantitative data, the Mann-Whitney  $U$  test was used to test the differences between groups. The SPSS statistical package 15.0 basic and advanced modules (SPSS Inc., Chicago, IL) were used for the statistical testing.

The study was approved by the Local Ethical Committee at Lund University, Lund, Sweden (2014/97) and registered at Clinicaltrials.gov (NCT02161029)

## **Results**

Clinical data and results of every biopsy in each patient are at hand in tables 1-3.

Wire break in patient 4 [Table 3] was due to a defect in the attachment of the drill wire to the handle. The disruption occurred at the second biopsy with the drill, with no consequences for the patient or the biopsy. The instrument was substituted and the third drill biopsy could be performed. In patient 9 [Table 3] the drill stuck in the casing. This happened outside the patient and before collecting the specimen but the biopsy procedure took 10 minutes in contrast to the median time of 4 minutes and 15 seconds, (range: 150-600 sec.). Apart from these occasions, the drill instruments worked as they were intended to with no difficulties for the endoscopists or the assistants. The forceps worked without technical problems and a biopsy procedure time of 57 seconds in median, (range: 30-90 sec).

The drill instrument resulted in larger sized biopsies ( $\text{mm}^2$ ), (Mann-Whitney U-test,  $p=0.048$ ), and larger submucosal part (%) of the biopsies (Mann-Whitney U-test,  $p=0.003$ ) compared to the forceps, (Table 2 and Fig. 3). The two extreme values were due to the fact that the forceps in spite of the central needle slipped into a previous biopsy cavity [Fig. 3]. The intention-to-treat design of the study allowed no additional attempt of biopsies. In the Endodrill<sup>®</sup> 18/30 biopsies and in the standard forceps group 10/30 biopsies to some extent contained submucosal tissue, respectively (Chi-2 = 4.286,  $p=0.04$ ).

In patient number 4 the Endodrill<sup>®</sup> showed a GIST and the standard forceps only collected gastric mucosa, [Table 3]. Also, in patient number 8 the drill instrument was the only diagnostic tool to produce the diagnosis, a GIST. In patients number 6 and 7 no submucosal tissue was collected either with the drill or the forceps, [Table 3] and was probably due to the fact that these patients had laborious endoscopy investigations. In patient number 6 the tumor



was later electively resected and the following pathology report showed a GIST. In the study population the time for the investigation was comparable to a standard flexible endoscopy examination with biopsies and was finished within the stipulated 30 minutes, which is ordinary in our open care setting for endoscopy.

In the 10 patients we did not find any serious complications. One patient was observed for 24 hours after the endoscopy due to stomach/chest pains, which were known beforehand and had been extensively examined, without known aetiology. Another patient was admitted 1 week after the examination due to suspicion of gastrointestinal bleeding. The patient was diagnosed with a GIST with the drill instrument and no signs of acute gastrointestinal bleeding were found at the follow-up endoscopic examination. After the observation both patients were discharged without symptoms.

## **Discussion**

We constructed a new biopsy instrument to have the opportunity to take deeper and submucosal biopsies from the gastrointestinal tract at the initial examination using a standard flexible endoscope with a typical working channel of 2.8 millimetres. It was provoked by the clinical situation with increasing numbers of submucosal tumours in the stomach and the fact that most of tumours larger than two centimetres are surgically resected without a preoperative diagnosis [3]. Moreover, guidelines for following small submucosal lesions varies and are influenced more by subjective endoscopic findings than by adequate biopsies, because of absence of the latter. A lot of patients with submucosal tumours are followed, typically those with tumours < 2 centimetres, with intervals of three to 12 months. This is because subepithelial tumours lack distinct endoscopic and ultrasonographic features for assessment whether malignancy or not are at hand. Establishing a tissue diagnosis here is of utmost importance not only for the single patient but also for decreasing the work load of endoscopic follow-ups. Our invention should be seen as the first attempt to accomplish this.

The sample size calculation was performed to evaluate the new instruments capacity to achieve submucosal material from the gastrointestinal tract. Explicitly, we aimed at samples deeper than the muscularis mucosa using a flexible standard endoscope. The diagnostic potential could not be fully evaluated because only three biopsies were sampled from the tumours with each instrument, a concession made after ethical considerations that not more than six biopsies should be taken from each patient simulating an ordinary endoscopy investigation. We demanded a 90 % power compared to the more common, 80 %, to make sure that the test used for comparison of data was reliable for conclusion, because the benefits with a new tool can easily be exaggerated, as well as risks underestimated. To visualize the different sampling capacity between the instruments the results are listed in table 2. To fully

evaluate the capacity of each instrument we sampled all tumours with both instruments. This exposed both instruments to the exact same conditions and thereby testing their ability against each other. This comparison could not have been done using two groups of patients. The amount of submucosal tissue was larger for the drill [Fig. 3].

The **ability of the** conventional forceps to acquire mucosal tissue for histopathological evaluation is good and has been proven through many years of clinical experience. The forceps is also characterized by easiness of handling. However, deeper and submucosal situated tumors are difficult to sample with the forceps, and the drill instrument was constructed to facilitate sampling of these tumours with a demand of preserving the easiness of handling. According to the results we feel confident that the new tool is justified for sampling subepithelial tissues. When we added the possibility to adjust the working length of the drill and retain it with the check-nut we experienced that also the latter demand was fulfilled. Whether the new tool with a drill in a casing will change the present state of circumstances, that the vast majority of larger submucosal lesions are surgically resected without a preoperative diagnosis, can be told only by the future [3].

In our 10 patients we found that the drill instrument provided not only more submucosal tissue (Mann-Whitney U-test,  $p=0.003$ ) compared to the forceps but also over all larger biopsies (Mann-Whitney U-test,  $p=0.048$ ), The figures can be argued but in fact all the endoscopists were instructed to press as hard as possible into the tissue with the forceps, and the site of the biopsies could not be affected by the examiner, due to the randomization.

In two patients we found tumours diagnosed as GIST's with the drill but not with the forceps. The diagnosis was verified on the resected specimen in one patient and the other is scheduled

for gastric resection. During the time period of inclusion of the ten patients 8 others were referred to us because of submucosal gastric tumours but in reality they were misdiagnosed by the referral institution and subsequently no sample attempt was made with the drill instrument. Three of the patients had no tumour at all, two patients had impression on the stomach from the spleen and from a mediastinal tumour respectively, one had an oesophageal cancer, one a gastric carcinoma, and one a gastric ulcer.

The reason that we in this first study compared the drill instrument to a standard forceps and not “jumbo” tongs and used the simple bite method instead of bite-on-bite technique for submucosal tumours is the fact that neither of these standards is superior to the typical technique with a standard forceps in providing submucosal layers from these tumours [1, 2]. To evaluate the diagnostic ability of the drill instrument we have planned a study comparing the drill with the standard of to-day for submucosal lesions, EUS-FNA, also known for its safety. An interesting future perspective would be to perform EUS guided drill biopsies. A comparison between EUS guided “jumbo” biopsies and EUS-FNA has been performed on submucosal tumors and has shown to deliver a higher rate of definitive diagnosis with the “jumbo” biopsies, indicating a beneficial combination between EUS and the drill [10].

That a drill instrument may reach deeper layers than a standard double cupped forceps that our investigation shows goes in many aspects without saying.

There are however many obstacles on the road. In tough tissue we learnt that the rotation in the handle did not fully convey to the drill. The result was a slight backward rotation of the handle due to not a complete torque resistant drill wire. This could be compensated for by two extra turns in the fully inserted position. With this manoeuvre we also achieved more tissue

trapped in the casing. To reduce the effect of backward rotation due to tissue resistance, further technical development has led to the implementation of a more torque resistant wire. The learning curve also included the fact that attaching the instrument to the chosen location of the tumour was easier when 1-2 millimetre of the drill extended out of the casing. By this manoeuvre we avoided to slide with the drill. The result that in 2 patients, prior to this adjustment, no submucosal tissue was sampled with the drill is probably explained by sliding of the instrument. After testing experimentally we used a drill with 6 full turns in 10 millimetres which seemed to be an optimal average for submucous tumours in the stomach. The harvesting of the specimen from the drill instrument is easy but somewhat time consuming [Fig. 2] in comparison to harvesting the sample from the forceps. On the other hand it is atraumatic. During the study the endoscopist and the staff noticed an improved handling of the instrument and the sampling. Although the series was small and many factors influence the time and accuracy of an endoscopic examination there was a positive learning curve. It was above all the time needed to harvest the biopsies from the drill that was time consuming. We have now devised a plate-like nut that is threaded from the tip of the drill and when the nut has reached the base of the drill all the tissue are on the nut and easily removed by the assistant with a needle or a piece of paper. If the series was larger it is possible that there would have been an even larger difference between the instruments due to the learning curve, but the rate of complications might also increase as the experience will inspire to take larger and deeper biopsies.

In routine flexible endoscopy with most of the patient having biopsies with the two cupped forceps the perforation rate at our department is 2/13639, (0.015 %) and increased to 0.43 % in relation to dilatation [11]. The largest series evaluating perforation in connection with

flexible endoscopy and biopsies is from 1999. The frequency here was 0,006 %, that is, 2/39650 (2 - 90 years) examined patients during a 14year period [12].

Capnoperitoneum sometimes at hand in POEM procedures is easily taken care of by expectance or by puncture of the abdomen with a Verres needle [13].

A perforation through a tumor into the peritoneal cavity must be considered, however, a serious oncological adverse event.

Bleeding after harvesting endoscopic biopsies is infrequently a problem. Seiichiro A. et al. did report not a single case where the bleeding after endoscopic resection of submucous tumors, a much larger procedure than harvesting endoscopic biopsies, couldn't be handled solely by endoscopic haemostatic methods [14]. Five patients (0.44 %) in a study of 1135 consecutive EUS-guided FNA for submucosal lesions experienced severe bleeding; four required endoscopic treatment and one blood transfusion [15].

In this series we experienced no serious complication but the series is too small to fully evaluate this. No perforation was seen but in one patient, referred to the hospital because of black stools one week after the endoscopic investigation, anaemia was observed. The patient was examined with endoscopy that revealed no blood, fresh or old, in the oesophagus, stomach, or in the duodenum but a haematin spot was seen in the tumour. The haemoglobin level of 111 gram/litre required no transfusion. Whether the haematin spot was due to the biopsies with one of two instruments or if it was a pathological finding in combination with the tumour is not possible to establish. The patient had, however, a history of intermittent periods of anaemia with two previous haemoglobin values of 111 gram/litre and 112 gram/litre respectively. These findings was in fact the reason for referring the patient for endoscopic investigation and is probably ~~might also be~~ explained by the diagnosed GIST

found in the stomach. The risk of perforation and bleeding are however at hand with a drill.

Using the instrument in conjunction with EUS can probably reduce this risk and will probably increase the safety of the instrument as well as the diagnostic accuracy of the samples. To avoid the risk of going too deep with the drill and accidentally perforating the organ wall the instrument should be angled tangentially.

To fully assess the potential of the drill for achieving correct diagnosis, the endoscopist has to use the instruments to his/her discretion and take as many biopsies that is considered necessary for diagnosis and use the preferred technique with every instrument, for instance hole-in-hole with the “jumbo” forceps and drilling deeper and deeper with the drill instrument. The technique might be suitable for lesions in other organs examined with flexible endoscopy. Especially in the respiratory tract tumors are often deep or outside the bronchial wall and the drill might be a helpful tool to collect diagnostic material.

In mucosal covered carcinomas, for instance not unusual in squamous cell carcinomas of the esophagus, it should be possible to achieve the diagnosis with the drill instrument. Due to the drills perpendicular penetration of the tissue the depth of a lesion might be possible to evaluate in relation to different wall layers.

Passing of a tight stricture under fluoroscopy guidance might be feasible with the drill instrument. Withdrawal of the drill with its wire and insertion of a guide wire through the left behind outer sheath can make dilatation or stent placing possible.

The drill instrument is a new technique that has to be thoroughly tested, but in our admittedly limited series, we have safely delivered diagnostic tissue samples from submucosal lesions in the upper gastrointestinal tract.

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### **Conflicts of interest**

Charles Walther has equity interest the company that has developed the new instrument.

Bruno Walther has equity interest the company that has developed the new instrument.

The remaining authors Jan Johansson, Martin Jeremiasen, Pehr Rissler and Marie Larsson declares no conflicts of interest.

### **Author contributions**

Study concept and design: Bruno Walther, Jan Johansson, Charles Walther

Acquisition of data: Marie Larsson, Martin Jeremiasen

Analysis and interpretation: Pehr Rissler



Study supervision: Charles Walther, Bruno Walther

**References:**

1. Cantor MJ, Davila RE, Faigel DO. Yield of tissue sampling for subepithelial lesions evaluated by EUS: a comparison between forceps biopsies and endoscopic submucosal resection. *Gastrointest Endosc* 2006; 64: 29-34
2. Hedenbro JL, Ekelund M, Wetterberg P. Endoscopic diagnosis of submucosal gastric lesions. The results after routine endoscopy. *Surg Endosc* 1991; 5: 20-23
3. Nishida T, Kawai N, Yamaguchi S, Nishida Y. Submucosal tumors: Comprehensive guide for the diagnosis and therapy of gastrointestinal submucosal tumors. *Digestive Endoscopy* 2013; 25: 479–489
4. Walther CS, Domanski HA, Vult von Steyern F, Mandahl N, Mertens F. Chromosome banding analyses of cells from fine needle aspirate biopsies from soft tissue and bone tumors. Is it clinically meaningful? *Cancer Genet* 2011; 4: 203-6
5. Domanski HA. Fine-needle aspiration cytology of soft tissue lesions: diagnostic challenges. *Diagn Cytopathol.* 2007; 35: 768-73
6. Martinez-Ares D, Varas Lorenzo MJ, Souto-Ruzo J, et al. Endoscopic resection of gastrointestinal submucosal tumors assisted by endoscopic ultrasonography. *Surg Endosc* 2005; 19: 854-58
7. Kojima T, Takahashi H, Parra-Blanco A, Kohsen K, Fujita R. Diagnosis of submucosal tumor of the upper GI tract by endoscopic resection. *Gastrointest Endosc* 1999; 50: 516-22.
8. DeWitt J, Emerson RE, Sherman S, et al. Endoscopic ultrasound-guided Trucut biopsy of gastrointestinal mesenchymal tumor. *Surg Endosc* 2011; 25: 2192-202
9. Hoda KM, Rodriguez SA, Faigel DO. EUS-guided sampling of suspected GI stromal

tumors. *Gastrointest Endosc.* 2009; 7: 1218-23

10. Buscaglia JM, Nagula S, Jayaraman V, et al. Diagnostic yield and safety of jumbo biopsy forceps in patients with subepithelial lesions of the upper and lower GI tract. *Gastrointest Endosc.* 2012; 75 :1147-52

11. Hedenbro JL, Ekelund M. Endoscopic perforation in unsedated patients undergoing endoscopy. *Br J Surg* 1996; 83: 845-6

12. Fernandez FF, Richter A, Freudenberg S, Wendl K, Manegold BC. Treatment of endoscopic esophageal perforation. *Surg Endosc* 1999; 13: 962-6

13. Friedel D, Modayil R, Iqbal S, Grendell JH, Stavropoulos SN. Per-oral endoscopic myotomy for achalasia: An American perspective. *World J Gastrointest Endosc* 2013; 5: 420-7

14. Seiichiro A, Ichiro O, Haruhisa S, et al. Short and long-term outcomes of endoscopic submucosal dissection for undifferentiated early gastric cancer. *Endoscopy* 2013; 45: 703-7

15. Hamada T, Yasunaga H, Nakai Y, et al. Rarity of severe bleeding and perforation in endoscopic ultrasound-guided fine needle aspiration for submucosal tumors. *Dig Dis Sci* 2013; 58: 2634-8

## **Legends to figures**

### **Figure 1**

Working length of the biopsy screw is regulated by the adjustable stop and checked by moving the drill handle back and forth with the instrument tip close to the tumor (A). The check-nut fixes the required length. The biopsy is sampled by pushing the casing towards the surface of the tumor and threads the biopsy screw into the tissue by turning the drill handle

clockwise until it stops towards the adjustable stop (B). By continuing the clockwise rotation while withdrawing the drill into the casing the tissue is trapped within it. (C).

Figure 2

The specimen is harvested by holding a 1 millimetre standard injection needle to the most proximal score of the screw thread and rotating the drill handle counter-clockwise.

Figure 3

Boxplot (median and interquartile range (IQR)) of the share (%) of submucosal tissue randomly harvested with a standard single-use biopsy double cupped forceps with needle, (Radial jaw 4, Boston Scientific Corporation, Marlborough, MA, USA) and the non-disposable Endodrill® (Endodrill I, BibbInstruments AB, Lund, Sweden). The extremes (stars) are more than 3 IQR from the upper border of the box and illustrates the hole- in- hole technique with the standard forceps.

Figure 4

An Endodrill® biopsy showing morphology of a malignant gastrointestinal stromal tumour (GIST). A fragment of fibrous tissue is seen in the left lower quadrant. Haematoxylin – Eosin (HTX) at 10 X magnification. Photo: Charles Walther MD, Department of Pathology, Lund University, Lund, Sweden.

Walther, Jeremiasen, Rissler, Johansson, Larsson, Walther  
*A new biopsy instrument for flexible endoscopy*

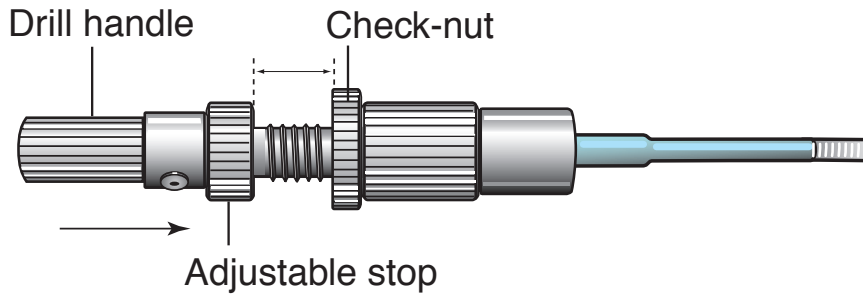
Table 1

Tumour characteristics for the ten patients with subepithelial lesions randomly harvested with a drill instrument and a standard forceps through a standard flexible endoscope.

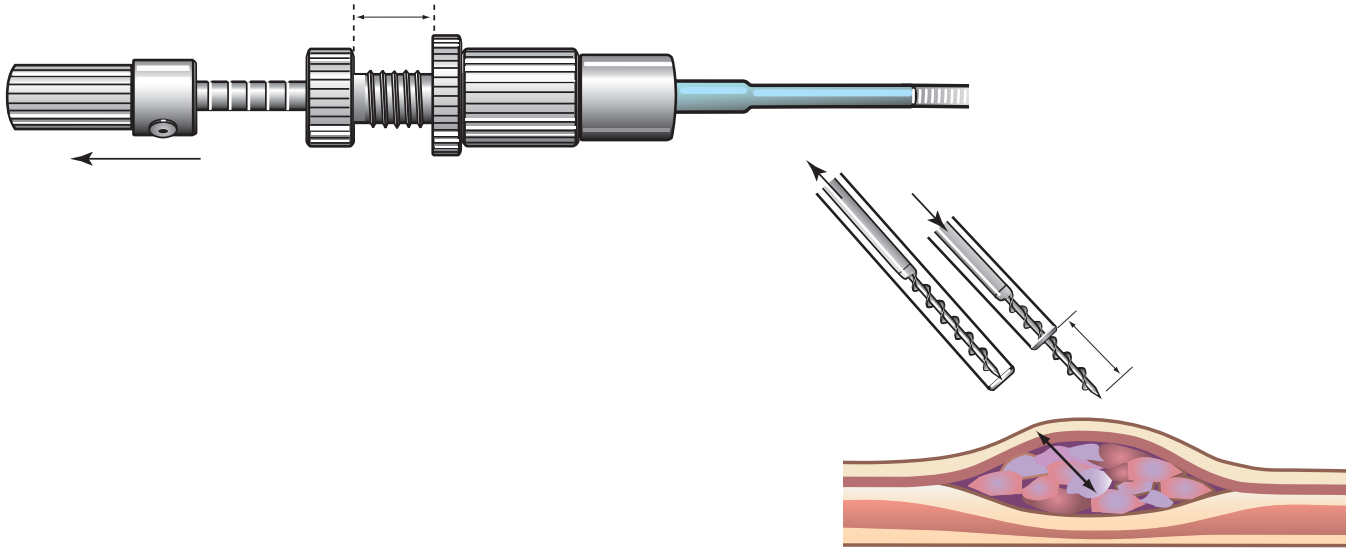
Patient	Sex <sup>a</sup>	Age <sup>b</sup>	Tumor location	Tumor size, largest diameter (cm)
1	F	76	Stomach/corpus-antrum	3
2	M	60	Stomach/corpus	6
3	M	69	Esophagus/middle	4
4	M	78	Stomach/antrum	3
5	F	74	Stomach/cardia	3
6	F	60	Stomach/antrum	4
7	M	73	Stomach/corpus	2
8	M	72	Stomach/fundus	4,5
9	F	66	Stomach/pylorus	3
10	M	70	Stomach/cardia	2

<sup>a</sup> M=male, F=female.

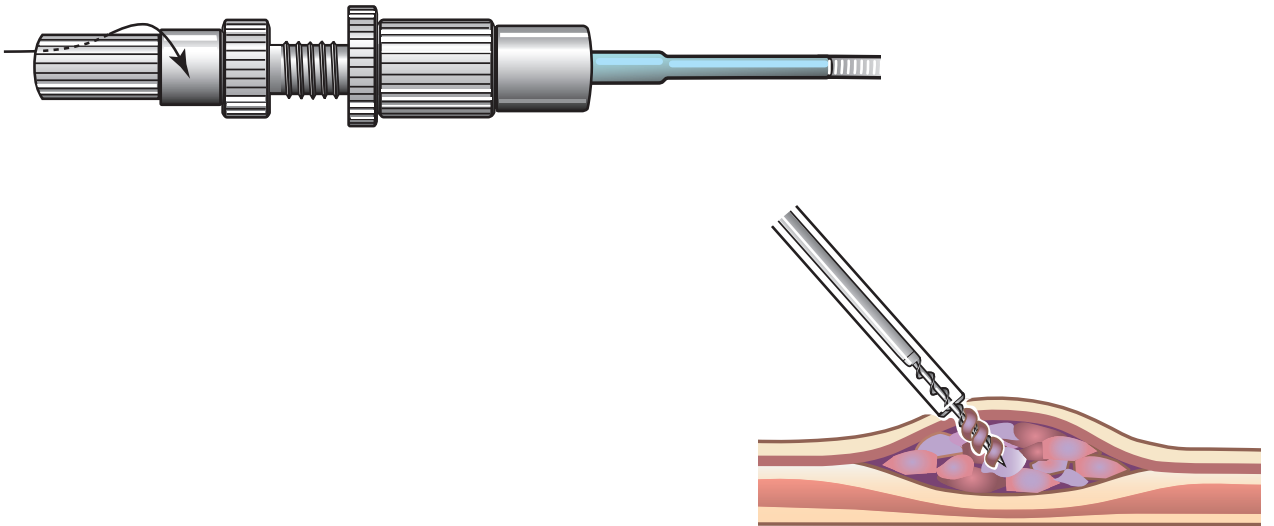
<sup>b</sup> Age in years



A



B



C

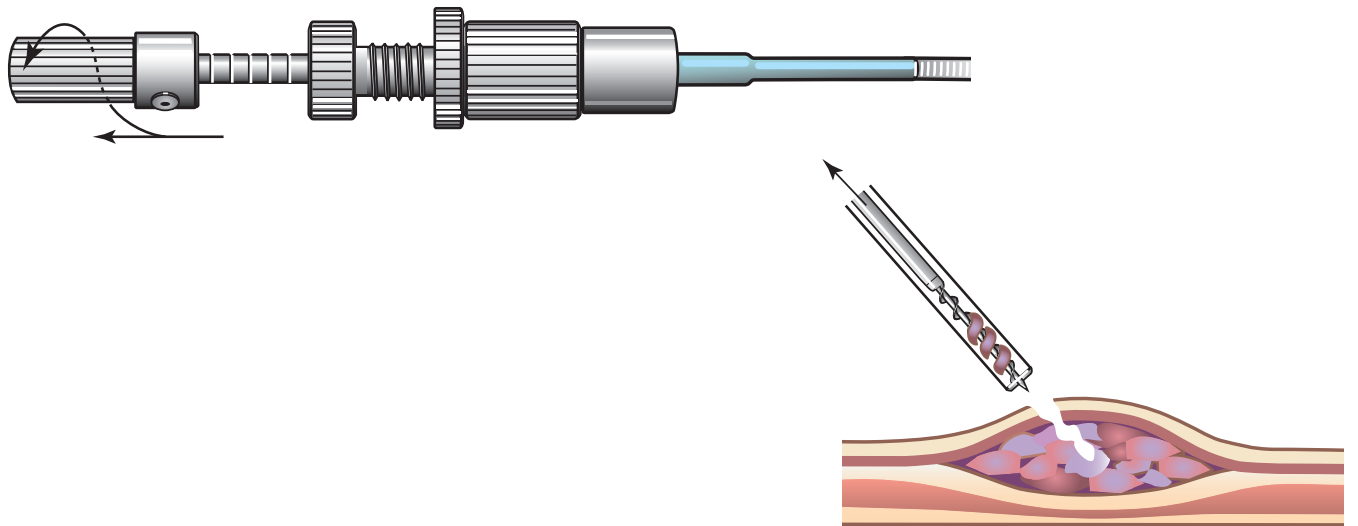


Figure 1

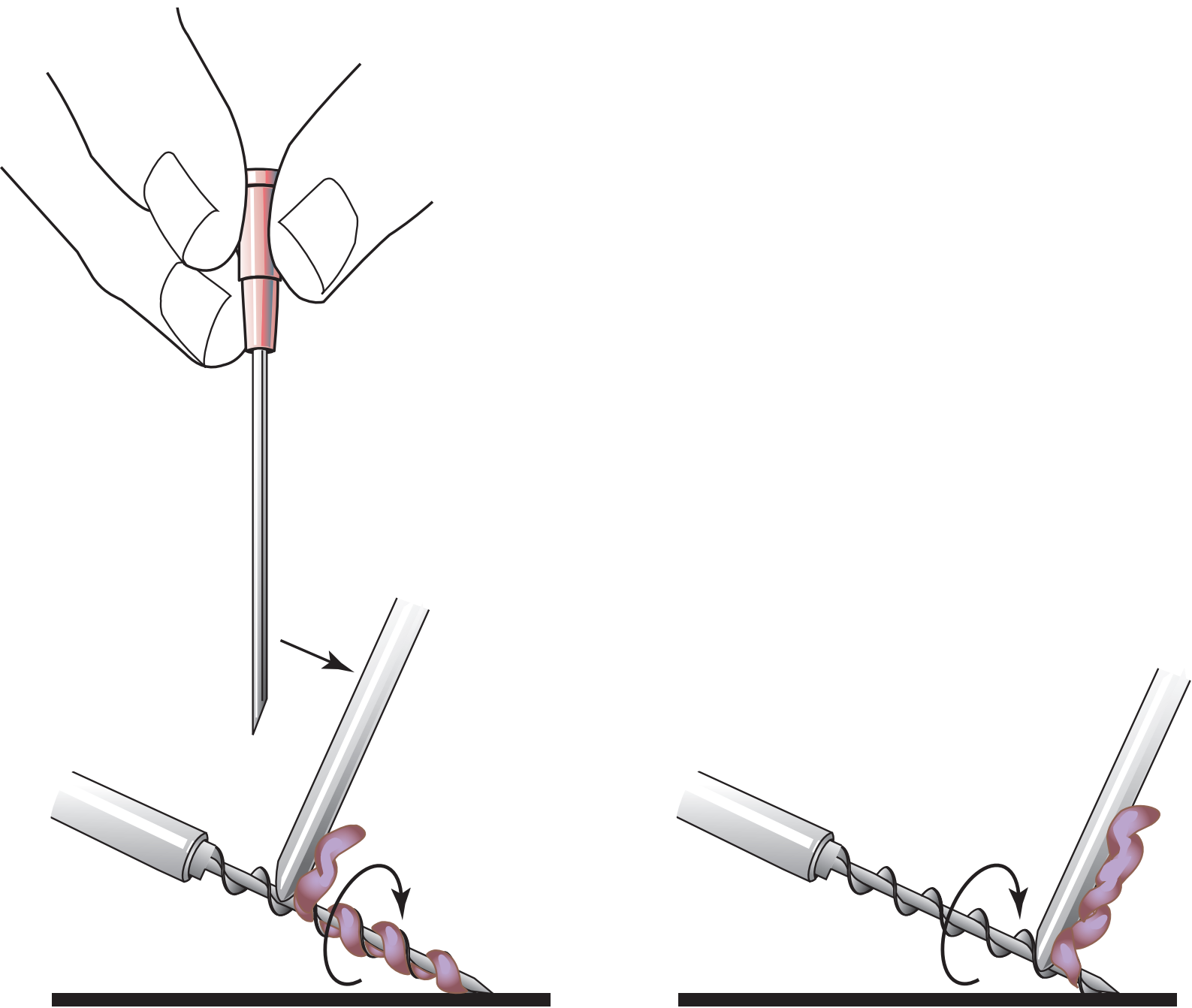


Figure 2

Table 2

Biopsy material from a prospective randomized study comparing a standard two cupped biopsy forceps with a needle (Radial jaw 4, Boston Scientific Corporation, Marlborough, MA, USA) and a new drill instrument surrounded by a casing (Endodrill I, BIBBIstruments AB, Lund, Sweden) for sampling of submucosal lesions through a flexible endoscope.

Patients	Sex <sup>a</sup>	Age <sup>b</sup>	Biopsy number	Total biopsy size (mm <sup>2</sup> )	Submucosal tissue part <sup>c</sup>
1	F	76	1	1.5	F 0
			2	4	F 63
			3	4.5	E 44
			4	0.5	E 0
			5	3	E 33
			6	4	F 0
2	M	60	1	2.5	E 0
			2	9	E 0
			3	2	E 25
			4	2.25	F 0
			5	3	F 0
			6	7.5	F 0
3	M	69	1	6	E 50
			2	10	E 90
			3	3	F 8
			4	3	E 100
			5	2.5	F 0
			6	2	F 13
4	M	78	1	6	F 4
			2	8	F 0
			3	3.5	E 7
			4	6	E 17
			5	8	F 19
			6	5	E 100
5	F	74	1	6	F 0
			2	6	F 8
			3	6	F 4
			4	6.5	E 23
			5	3	E 33
			6	10	E 100
6	F	60	1	6,5	E 0



			2	2,25	E 0
			3	3	F 0
			4	3,75	F 0
			5	3	E 0
			6	2	F 0
7	M	73	1	2,75	E 0
			2	4	E 0
			3	4,25	E 0
			4	3	F 0
			5	2	F 0
			6	3	F 0
8	M	72	1	8,25	E 100
			2	1,5	F 0
			3	12,5	E 72
			4	1,5	F 17
			5	4,25	E 12
			6	3	F 33
9	F	66	1	5	F 0
			2	0	E 0
			3	15	E 100
			4	4	F 13
			5	17	E 100
			6	3	F 0
10	M	70	1	3	F 0
			2	3	F 0
			3	6	E 0
			4	3	F 0
			5	2,75	E 0
			6	12	E 83

<sup>a</sup> M=male, F=female.

<sup>b</sup> Age in years

<sup>c</sup> E=Endodrill<sup>®</sup>, F=Forceps, submucosal tissue measured in % of total biopsy area

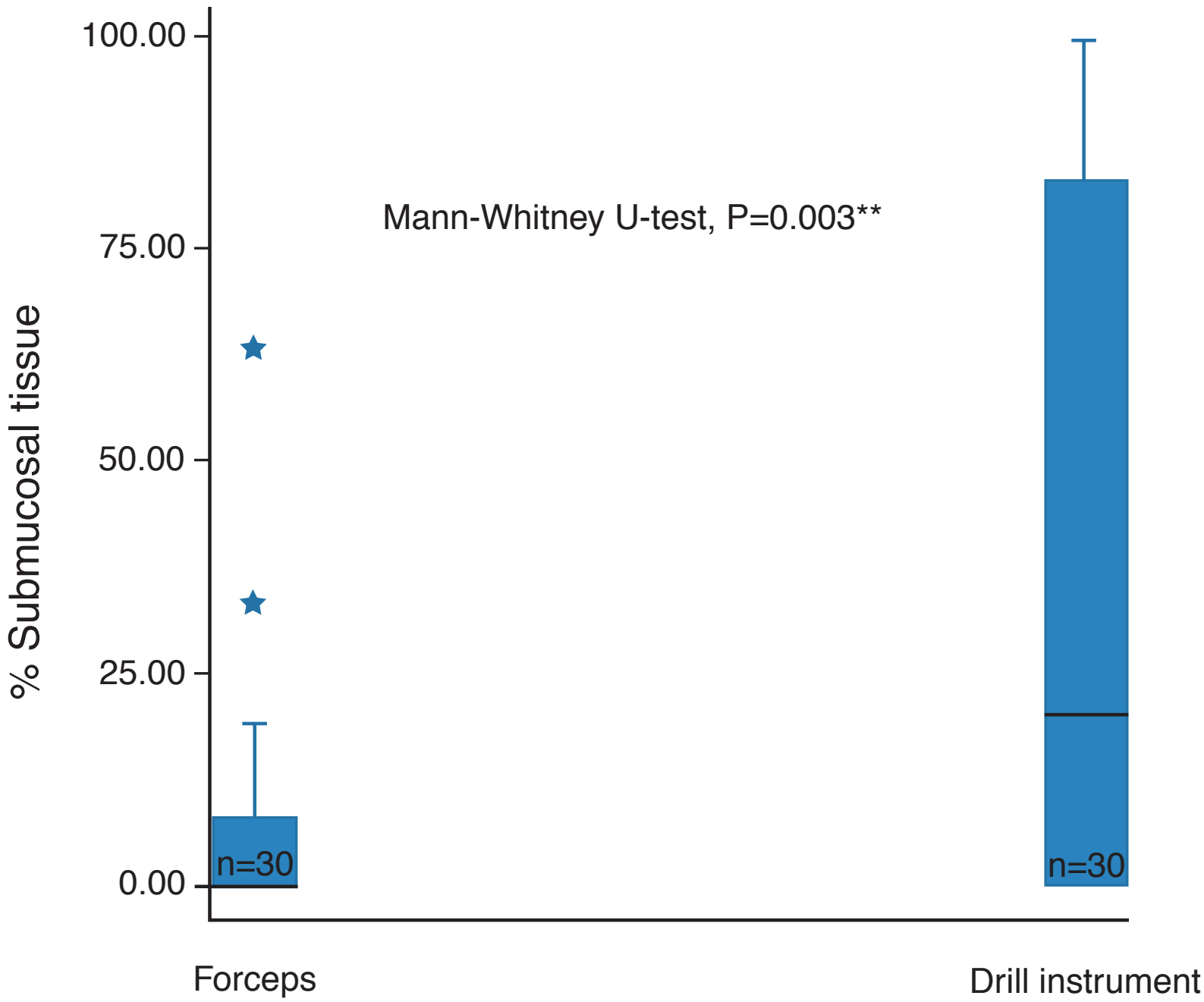


Table 3. Results of randomised sampling with a forceps and a drill instrument through a flexible endoscope in ten patients with submucosal tumours

Nr	Patients		Histopathology		Complications		Follow-up		Crush artefacts	
	Sex <sup>a</sup>	Age <sup>b</sup>	Forceps	Endodrill <sup>®</sup>	Forceps	Endodrill <sup>®</sup>	Day 1	Day 7	Forceps	Endodrill <sup>®</sup>
1	F	76	Gastritis H. Pylori	Gastritis H. Pylori	None	None	No complaints	No complaints	No	No
2	M	60	Gastric mucosa	Gastric mucosa	None	None	No complaints	No complaints	No	No
3	M	69	Fibrosis	Fibrosis	None	None	No complaints	No complaints	No	No
4	M	78	Gastric mucosa	GIST	None	Wire break	No complaints	No complaints	No	No
5	F	74	Gastric mucosa	Gastric mucosa	None	None	No complaints	No complaints	No	No
6	F	60	Fibrosis	Fibrosis	None	None	No complaints	No complaints	No	No
7	M	73	Inflammati on	Inflammation	None	None	No complaints	No complaints	No	No
8	M	72	Normal mucosa	GIST	None	None	No complaints	Black stools	No	No
9	F	66	Inflammati on	Inflammation	None	Drill stuck in casing	No complaints	No complaints	No	No
10	M	70	Inflammati on	Inflammation+ H. Pylori	None	None	No complaints	No complaints	No	No

<sup>a</sup> M=male, F=female.

<sup>b</sup> Age in years

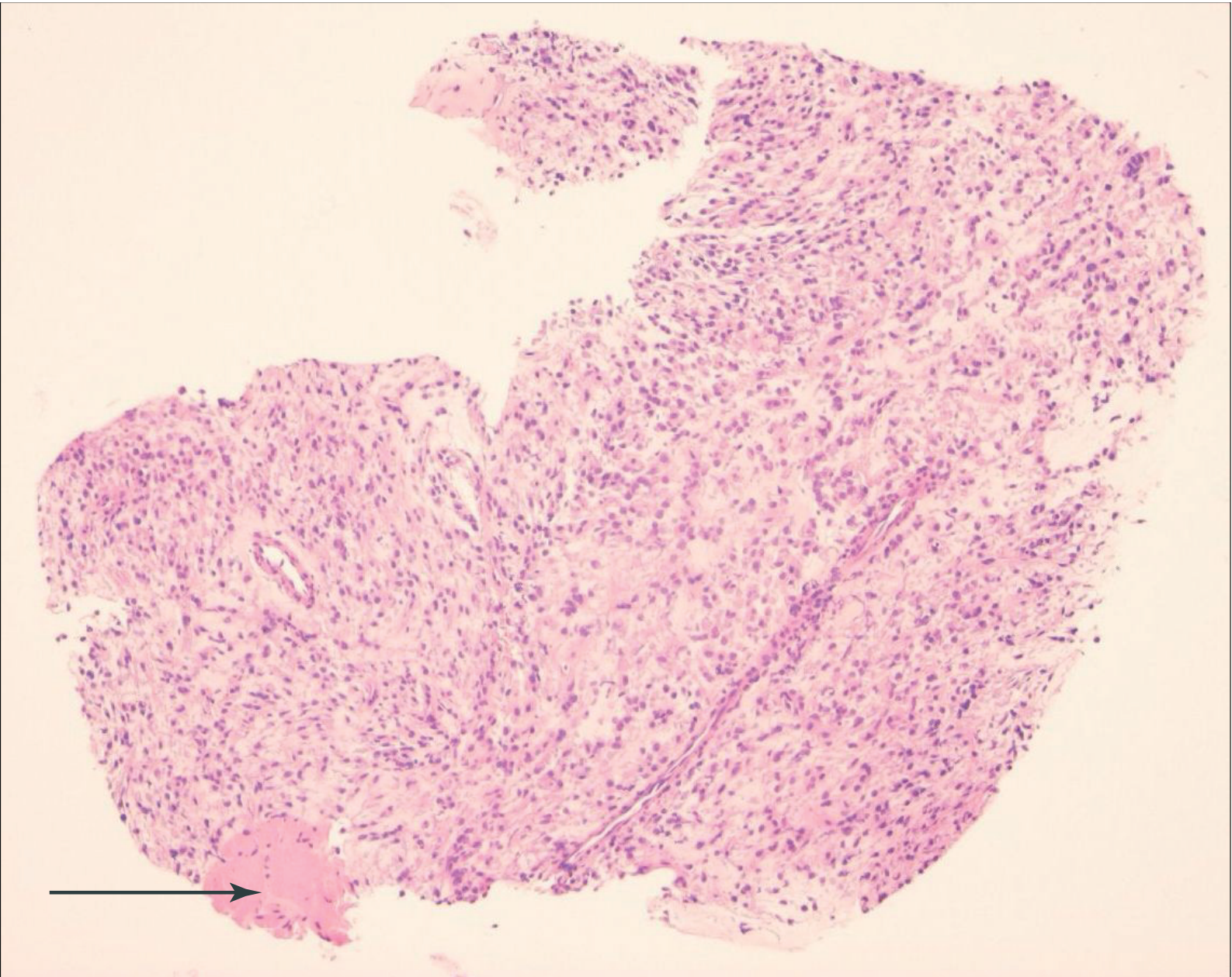


Figure 4