Tissue sampling is the most common manoeuvre performed during endoscopic procedures and histological examination is part of almost every digestive disease investigation. The potential for mistakes is, therefore, widespread and knowledge of the adequacy of the indications and techniques used for tissue sampling during endoscopy, as well as the potential consequences, is indispensable for every gastroenterologist. As such, there are some questions that should always be posed before taking a biopsy sample or tissue acquisition during endoscopy: Why? What for? How? How many? (figure 1).

This manuscript has been organized with these questions in mind. We’ve aggregated examples for the eight most frequent and most correctable mistakes made during tissue acquisition by endoscopy. In addition, most of the recommendations made in this article are supported by existing guidelines and evidence, with a few based solely on the authors’ experience.

**Mistake 1** Not taking biopsy samples for fear of haemorrhagic complications (or stopping antithrombotic medication to take biopsy samples)

Diagnostic upper gastrointestinal endoscopy and colonoscopy, including the acquisition of mucosal biopsy samples, are considered low-bleeding-risk procedures (<1%). Taking mucosal biopsy samples is safe even in patients taking aspirin or clopidogrel as monotherapy and also for those within the therapeutic range for warfarin anticoagulation. Current guidelines do not recommend antithrombotic discontinuation for low-risk endoscopic procedures, with European Society of Gastrointestinal Endoscopy (ESGE) guidelines suggesting an international normalized ratio (INR) check and warfarin dose adjustment one week prior to the procedure.

As evidence on the safety profile of direct-acting anticoagulants is scarcer, and as it is not possible to quantify anticoagulation intensity, ESGE guidelines suggest omitting the morning dose of the anticoagulant on the day of the procedure. Not taking mucosal biopsy samples because of antithrombotic therapy is, therefore, unnecessary and imposes additional redundant examinations on the patient. It is also important to recognize that unneeded antithrombotic discontinuation can have serious consequences in patients at high risk of thrombosis, whereas haemorrhagic complications can usually be controlled endoscopically and are rarely fatal.

**Mistake 2** Failing to take the full clinical information into account

While it is a commonplace recommendation, it is of paramount importance to stress the importance of clinical information and the patient’s history when making the decision on whether and how to obtain tissue samples. During the investigation of chronic diarrhea, for instance, sampling normal-appearing colonic mucosa is the only method available for diagnosing microscopic colitis and is one of the quality indicators in colonoscopy according to the American Society for Gastrointestinal Endoscopy (ASGE). Similarly, patients who have a history of dysphagia or impaction should be evaluated for eosinophilic esophagitis (EoE), with samples taken from the proximal and distal oesophagus during upper endoscopy, even when there is endoscopically normal mucosa.

When there is a clinical and/or serological suspicion of coeliac disease, biopsy samples should be obtained during upper gastrointestinal endoscopy, both from the bulb and distal duodenum, while the patient is on a gluten-containing diet.

Not taking the opportunity to obtain gastric biopsy samples for *Helicobacter pylori* testing during upper gastrointestinal endoscopy is a mistake in patients with dyspepsia or in the setting of a family history of gastric cancer. *H. pylori* eradication persistently improves functional dyspepsia symptoms and is also recommended in the setting of gastric cancer.

Also common is the failure to account for the indication for colonoscopy in inflammatory bowel disease (IBD). When the examination goal is dysplasia surveillance in patients who have long-standing ulcerative colitis or Crohn’s colitis, either chromoendoscopy with targeted biopsy samples should be performed or random four-quadrant biopsy samples taken at 10 cm intervals acquired.

These examples illustrate how not taking the clinical background into consideration can lead to missed diagnoses and repeated examinations. It imperative that the endoscopist is familiar with the indication for the examination and acts accordingly.
**Mistake 3 Putting all tissue samples in the same vial**

Several disease processes require the separation of tissue samples according to location to guide pathological examination and patient follow-up. The staging of atrophic or metaplastic gastritis currently relies on histological confirmation of these changes both in the antrum and corpus. An extensive atrophic or metaplastic phenotype is associated with a higher risk of gastric cancer and endoscopic surveillance is recommended. Tissue samples from the antrum and corpus must be provided in different labelled vials to permit the correct staging of gastritis, as atrophy and metaplasia make it difficult for the pathologist to reliably differentiate between the two gastric areas.

Ideally, each colonic lesion sample should be sent to the pathology department in a separate container. In practice, multiple diminutive polyps found in the same segment are often collected in the same vial because of concerns about extra costs for the patient and the pathologist’s workload. We suggest that only diminutive polyps (≤5 mm) with a benign appearance and removed easily by polypectomy should be grouped together and always separated according to the colonic segment, to allow for endoscopic surveillance and/or a surgical plan in the case of advanced disease.

**Mistake 4 Taking biopsy samples when the results will not (or should not) alter patient management**

There are some situations in which taking biopsy samples will not alter the patient’s future management. After diagnosing extensive atrophic or metaplastic gastritis, taking further random biopsy samples will not alter patient management and are not needed. There is no evidence that any intervention will alter the phenotype, so surveillance should include regular upper gastrointestinal endoscopy with targeted biopsy samples taken for any suspicious lesions.

Barrett oesophagus is now defined as columnar-lined epithelium extending >1 cm above the gastroesophageal line. Shorter segments of columnar-lined epithelium are not classified as Barrett oesophagus due to high interobserver variability in their diagnosis and should be described as ‘irregular Z lines’. Finding intestinal metaplasia in these irregular Z lines does not appear to confer an increased risk of submucosal fibrosis. Extensive biopsy samples or partial resection can hinder lesion elevation and complicate or preclude complete resection by endoscopic mucosal resection (EMR). Granular lateral spreading lesions with Paris type 0-IIa morphology can and should be referred for resection without biopsy samples being taken—they have minimal risk of submucosal invasion and complete excision with EMR is likely.

**Mistake 5 Obtaining too few biopsy samples from malignant lesions**

Traditionally, the number of biopsy samples that should be taken from lesions highly suspicious for malignancy has been six to eight. However, most of the evidence is several decades old and concerns upper gastrointestinal neoplasms only. Recently, it has been suggested that newer endoscopes that produce higher quality images and allow better targeting of biopsy samples may permit diagnostic accuracy with fewer samples.

One study of 59 gastric and 32 colorectal malignancies achieved a cumulative diagnostic yield of 98.3% on the fourth biopsy sample – there was no further increase in diagnostic yield with additional samples. Another study of 180 gastric cancers found cumulative diagnostic yields of >99% after four biopsy samples were taken from ulcerated or polyoid lesions, with only infiltrative lesions benefiting from a fifth sample being taken. By the fifth sample, 100% of malignancies were diagnosed, regardless of morphology.

Arguments in favour of obtaining fewer biopsy samples are reduced bleeding risk, shorter examinations, decreased workload for the endoscopist and pathologist, and reduced costs. Nevertheless, the minimum number of mucosal samples taken from malignant lesions appears to be four, with infiltrative gastric lesions requiring five to six.

**Mistake 6 Acquiring (extensive) biopsy samples from lesions that are probably amenable to endoscopic resection**

Whenever a large colonic polyp or flat lesion is considered for referral to another timeslot, minimal or even no biopsy samples should be taken because of the risk of submucosal fibrosis. Extensive biopsy samples or partial resection can hinder lesion elevation and complicate or preclude complete resection by endoscopic mucosal resection (EMR). Granular lateral spreading lesions with Paris type 0-IIa morphology can and should be referred for resection without biopsy samples being taken—they have minimal risk of submucosal invasion and complete excision with EMR is likely.

**Mistake 7 Not making enough needle passes when taking biopsy samples via fine-needle aspiration**

Endoscopic-ultrasound-guided fine-needle aspiration (EUS-FNA) is considered a safe and useful method for tissue acquisition from lesions of the bowel wall or in its proximity. To be successful the sample must be of the correct quality, which is dependent on several factors, one being the number of times the needle is inserted into the lesion (i.e. the number of passes).

When using rapid on-site evaluation (ROSE), the number of passes is determined by the cytologist/cytotechnician present. Frequently, ROSE is not available and the endoscopist has to decide how many passes should be made. Previous studies of pancreatic masses have shown that sensitivity improves with an increase in the number of passes. It was, therefore, suggested that in the absence of ROSE at least seven passes should be performed. However, more recent prospective studies have shown an excellent diagnostic rate for four needle passes in pancreatic lesions and three passes in malignant lymphadenopathy. Further increases in the number of passes did not improve the diagnostic yield. As such, when performing EUS-FNA, at least three to four passes should be done when sampling pancreatic masses and two to three passes for lymphadenopathies. Visual inspection of the collected sample should not be used to guide the number of passes.
Mistake 8: Being unaware of the instruments you’re using.

The instruments used most frequently for tissue acquisition in endoscopy are biopsy forceps. Although in most instances specialized forceps are not needed, it is important to be aware of some of the differences between them.

Double-bite forceps, which have a needle spike between the cup jaws, are becoming more widespread and allow a second tissue sample to be collected in a single pass through the accessory channel. Some variations in forceps design, such as ‘swing-jaw’ or ‘rotatable’ forceps, may be helpful for lesions in difficult locations. ‘Jumbo’ biopsy forceps have larger cup jaws that allow acquisition of larger tissue samples, while ‘Pelican’ biopsy forceps can obtain up to six specimens in a single pass through the working channel—both of these forceps can reduce the examination time when several tissue samples are needed.1,2

Not all forceps are compatible with all endoscopes, due to the accessory channel diameter and length. For instance, when using ultrathin endoscopes, the forceps used may be smaller, as will be any mucosal samples collected.

Being familiar with the different instruments available on the market and in each endoscopy centre allows better planning and more effective tissue acquisition.

Your tissue acquisition during endoscopy briefing

Online courses

• ‘Coeliac disease’ from ESGPHAN [https://www.ueg.eu/education/online-courses/coeliac-disease/]

• ‘Irritable bowel syndrome’ from UEG [https://www.ueg.eu/education/online-courses/irritable-bowel-syndrome/]

Mistakes in...

• Mistakes in endoscopy and how to avoid them [https://www.ueg.eu/education/latest-news/article/mistakes-in-endoscopy-and-how-to-avoid-them/]

• Mistakes in endoscopic resection and how to avoid them [https://www.ueg.eu/education/latest-news/article/mistakes-in-endoscopic-resection-and-how-to-avoid-them/]

Society conferences

• ESGE & ESDO Quality in Endoscopy 2016—Upper GI Endoscopy & Neoplasia [https://www.ueg.eu/education-conference-files/conference=143]

• ESGE / ESDO Quality In Endoscopy 2015—Colonoscopy & Colonic Neoplasms [https://www.ueg.eu/education/education-conference-files/?conference=110]

UEG Week

• ‘Quality in endoscopy: How to use and interpret performance measures?’ session at 29th UEG Week 2017 [https://www.ueg.eu/education/session-files/?session=1913&conference=149]

• ‘Advanced diagnostic endoscopy’ session at 25th UEG Week 2017 [https://www.ueg.eu/education/session-files/?session=1917&conference=149]


• ‘Does my patient really have GORD?’ session at UEG Week 2016 [https://www.ueg.eu/education/session-files/?session=1614&conference=144]

Standards and Guidelines

• To discover numerous relevant standards and guidelines visit the Standards & Guidelines Repository and filter by category [https://www.ueg.eu/guidelines/]


