To promote the appropriate use of new or emerging endoscopic technologies and those technologies that have an impact on endoscopic practice, the ASGE Technology Committee presents relevant information to practicing physicians in the form of technology reviews. Evidence-based methodology is employed wherein a MEDLINE literature search is performed to identify pertinent clinical studies on the topic, a MAUDE (Food and Drug Administration Center for Devices and Radiological Health) database search is performed to identify the reported complications of a given technology, and both are supplemented by accessing the “related articles” feature of PubMed and by scrutiny of pertinent references cited in the identified studies. Controlled clinical trials are emphasized, but in many cases data from randomized controlled trials are lacking; in such cases, large case series, preliminary clinical studies, and expert opinion are utilized. Technical data are gathered from traditional and Web-based publications, proprietary publications, and informal communications with pertinent vendors. Reviews are drafted by 1 or 2 committee members, reviewed in significant detail by the committee as a whole, and approved by the Governing Board of the ASGE. When financial guidance is appropriate, the most recent coding data and list prices at the time of publication are provided. For this review the MEDLINE database was searched through October, 2005 for articles related to devices for tissue sampling by using the keywords “biopsy forceps” and “gastrointestinal endoscopy” plus “cytology brushing,” and “fine needle aspiration.” Practitioners should continue to monitor the medical literature for subsequent data about the efficacy, safety, and socioeconomic aspects of these technologies.

BACKGROUND

Numerous methods and devices have been developed for tissue sampling during gastrointestinal endoscopy, including pinch biopsy, brush cytology, EUS-guided fine-needle aspiration (FNA), true cut needle biopsy, snare excision, suction biopsy, endoscopic mucosal resection, and combinations of techniques. Endoscopic tissue sampling is addressed to various extents in other ASGE clinical practice guidelines and technology status evaluation reports. This report is meant to both complement and update these previous reports, focusing on select, currently available endoscopic tissue sampling devices. Endoscopic mucosal resection (EMR) and EUS-guided tissue sampling are addressed in separate reports.

TECHNOLOGY UNDER REVIEW

Equipment

Biopsy forceps. Single-bite cold-biopsy forceps allow sampling of only a single specimen at a time. Biopsy forceps equipped with a needle-spike between the opposing biopsy cups, sometimes termed double-bite forceps, are most commonly employed because they enhance directed lesion sampling via impalement of the tissue and stabilization of the forceps cups, they provide deeper biopsies than non-needle versions, and they secure the first specimen on the needle during collection of a second in a single pass through the accessory channel. Biopsy cup jaws may be round, oval, or elongated, fenestrated or non-fenestrated, and smooth or serrated. Large-capacity or “jumbo” biopsy forceps sample a larger volume of tissue encompassing 2 to 3 times the surface area compared to standard forceps, but they do not reliably yield deeper specimens; they require a 3.6-mm or greater biopsy channel. Forceps designed to allow for multiple bite sampling have been developed that can obtain up to 4 or more specimens on a single pass through the accessory channel, potentially contributing to decreased operative time when a large number of specimens are to be obtained. Other variations on the standard designs that may offer advantages in challenging circumstances include “swing-jaw,” “rotatable,” and “angled” forceps.

Small, more malleable forceps are available for intra-ductal biopsies of the pancreatic and biliary ducts during ERCP. An alternative wire-guided intraductal biopsy device has a conical tipped circumferential cutting rim that deposits sampled tissue in a cylindrical retrieval chamber.

Monopolar hot biopsy forceps, developed for simultaneous tissue biopsy and coagulation, were reviewed in a previous ASGE technology committee status evaluation report.
report and are not recommended for routine tissue sampling.

**Polyectomy snares.** Polyectomy snares come in a variety of shapes, sizes, and materials, are marketed as disposable or reusable, and may be designed with special features. They are addressed in a separate status evaluation report.16,20-22

**Brush cytology.** A variety of cytology brushes are available for tissue sampling in the luminal GI tract and the pancreatic and biliary ducts. Designs include brushes of variable sizes and stiffness, wire guided or non–wire guided, single or multilumen, and with or without a flexible guide tip. Outer sheaths for brushes used in ERCP are 6 to 8 F.18,19,23 These are described more completely in a previous report.6 A cytology balloon for nonendoscopic esophageal cytological screening and surveillance for infectious and neoplastic diseases has been described.24

**Needle aspiration cytology.** Hollow bore needles may be used for aspiration cytological tissue sampling. ERCP aspiration needles consist of a retractable 7.5 mm 22 gauge needle attached to a ball- tipped catheter.6 The needle is advanced into the target tissue under fluoroscopic guidance and aspiration is applied. Howell et al developed a technique for sampling biliary strictures by endoscopic FNA.25 Other prototypes of aspiration catheters with an extending steel needle have been proposed.26 Needle aspiration of submucosal lesions under direct endoscopic guidance can be performed; however, yields are poor and this technique has not gained broad acceptance. EUS-guided FNA is covered in a previously published ASGE technology committee status evaluation report.27

**Technique**

Many factors determine the yield of tissue sampling, including adequacy of the specimens, processing of the samples, interpretation of the slides, and effect of tumor type on cancer detection rate.18 The adequacy of the specimens is dependent on the anatomic site, tumor characteristics, and number of samples collected. As a rule, more extensive (number and volume) tissue sampling improves the diagnostic yield. Specimen orientation, fixation, and staining are also important.11

Spiked and nonspiked forceps were compared in a randomized, blinded study using a 2-bite mucosal sampling technique in upper endoscopy. Irrespective of the location of the mucosal sampling, the nonspiked forceps were associated with a significantly higher rate of missing samples than the spiked forceps (28% vs 13%).28

In selected cases, using a combination of techniques can increase diagnostic accuracy. Brush cytology may be a useful adjunct to pinch biopsy and is often helpful in the diagnosis of certain malignancies and infections, particularly esophageal squamous cell carcinoma and esophageal candidiasis.6

Specific techniques and protocols for tissue sampling in different clinical settings, such as when sampling tissue from an ulcer or a polypoid mass, for cancer or dysplasia surveillance (Barrett’s or chronic idiopathic colitis), when testing for *Helicobacter pylori*, or in cases of suspected malabsorption, have been extensively reviewed in an ASGE clinical practice guideline.11

The cancer detection rate for biliary and pancreatic lesions is clearly less than that for endoscopic sampling of lesions in the esophagus, stomach, and colon.5,18,19 Enhanced diagnostic techniques applied to sampled tissue include flow cytometry, digital image analysis, molecular genetic analysis, immunocytochemical techniques, and genotyping.19 None of these, however, are routinely applied.

**INDICATIONS AND EFFICACY**

**Indications**

Histopathologic evaluation is helpful to differentiate malignant, inflammatory, and infectious processes. Tissue biopsy is routinely obtained from any suspicious lesion during endoscopic evaluation.11 When the gross endoscopic appearance is normal, histological analysis may still provide useful information. Tissue analysis is occasionally performed to document the outcome of prior endoscopic or medical therapy. When the gross endoscopic appearance reveals a specific condition, tissue analysis is unnecessary if therapy will not be altered.11 Risks and benefits of tissue biopsy should be considered when there is an increased potential for hemorrhage, such as in patients with coagulopathies,29 although in general standard forceps biopsy techniques may be applied in anticoagulated patients.30 The choice of sampling technique depends on device availability, operator expertise, the endoscopic procedure performed, target tissue, and anticipated amount of tissue required for diagnosis or to guide therapy.

**Efficacy**

**Upper and lower endoscopy.** For the yields of histological sampling according to different clinical situations in upper endoscopy, lower endoscopy, as well as in specific surveillance protocols, please refer to the ASGE clinical practice guideline “Tissue sampling and analysis.”11

**ERCP.** The type of tumor responsible for biliary strictures influences the cancer detection rate for all sampling techniques. Indeed, in most series, brush cytology and forceps biopsy have a higher sensitivity for cholangiocarcinoma (44%-100%) than for pancreatic cancer (30%-65%).18 A recent study suggested that biopsy procurement with a forceps at ERCP appears to be the most sensitive of all tissue sampling techniques for biliary strictures. Brush cytology remains the simplest and most commonly used technique for obtaining tissue samples from biliary strictures at ERCP. Repeated brushing with consecutive
brushes may enhance cancer detection. Stricture dilation before brush cytology does not improve diagnostic yield.\(^{18,19,31}\) Although specificity approaches 100%, the sensitivity of brush cytology for cancer is modest, with an overall mean sensitivity of only 42%, perhaps mainly due to its limited cellular yield.\(^{19}\)

The cancer detection rate at ERCP is increased by combining at least 2 sampling methods, with the highest sensitivity demonstrated for the combination of endoscopic FNA, biopsy, and brush cytology.\(^{6,18,19}\) Sampling from both the pancreatic duct and the common bile duct may also increase the yield.

The forceps biopsy is the best single technique for the diagnosis of neoplasms involving the major duodenal papilla; cancer is detected in 77% to 88% of cases.\(^{32}\)

Proposed algorithms for sampling of suspected biliopancreatic malignancies have recently been published.\(^{19,33}\)

SAFETY

Complication rates of tissue sampling devices used in the upper and lower GI tract in patients without coagulopathies are exceedingly rare.\(^{34-36}\) Complications associated with cold biopsy forceps tissue sampling and cold snare resection include rare instances of bleeding (0.07%) and perforation (0.07%).\(^{21,34,35,37,38}\) There are increased risks associated with the addition of electrocautery to tissue sampling. Complications of hot biopsy forceps and electrocautery snare resection include hemorrhage, perforation, and postcoagulation (transmural burn) syndrome. Bleeding may be acute or delayed, occurring up to 2 weeks after the procedure. The risk of significant hemorrhage from monopolar hot biopsy of diminutive polyps is 0.39%.\(^{38}\) Perforation after using the hot biopsy technique occurs with an estimated frequency of 0.05%.\(^{39}\) The major and most common complication of colonoscopic polypectomy is hemorrhage.\(^{40}\) The reported incidence in large surveys ranges from 0.77% to 2.24%.\(^{40,41}\) Perforation associated with colonoscopic polypectomy is also a major complication, with a frequency of 0.11% to 0.42%.\(^{41}\) In one retrospective review that reported an overall complication rate of 2.2% for colonoscopy polypectomy, a transmural burn was the most common complication after bleeding.\(^{42}\) A retrospective analysis of blended versus pure coagulation current for colonoscopic polypectomy reported no significant differences in the overall complication rates between the 2 groups.\(^{43}\) However, a significant difference was seen in the timing of bleeding with all of the major hemorrhages occurring immediately or within 12 hours when blended current was used, and all were delayed (2-8 days) when pure coagulation current was used.

Perforation is a conceivable complication associated with brush cytology. In the case of tissue sampling at ERCP, adverse effects have not been reported with bile collection and biliary brush cytology beyond usual complications associated with the endoscopic procedure.\(^{6}\) Temporary placement of a pancreatic stent after manipulation of the pancreatic duct may decrease the risk of pancreatitis after pancreatic duct brushing.\(^{19}\) There are case reports of pancreatitis related to endoscopic biopsy of the papilla.\(^{11}\) Despite this, complications related to endoscopic biopsy or removal of duodenal adenomas at a distance from the papilla appear to be uncommon.\(^{11}\)

Cases of transmission of infection associated with reusable biopsy forceps have been attributed to breaches in accepted standards of device reprocessing.\(^{36}\) Recently, proper endoscope reprocessing has been identified to be the most important factor in preventing biopsy forceps–related interpatient infection.\(^{44}\)

COMPARATIVE STUDIES

Biopsy forceps

In 2 prospective, randomized, pathologist-blinded trials there were no perceived differences in quality of specimen attained for histological diagnosis among a variety of commercially available reusable and disposable biopsy forceps.\(^{45,46}\) Forceps with central spikes obtain deeper biopsies than nonspiked versions.\(^{15}\) Spikes, however, do not ensure retention of > 2 samples. The quality of biopsy specimens obtained with forceps designed for multiple (> 2) bite sampling is comparable with that of specimens taken with conventional forceps. Use of these forceps saves time in that 4 specimens can be obtained in 1 pass.\(^{47}\) In one study, cholangioscopic biopsy was superior to that done under fluoroscopic control.\(^{48}\)

Polypectomy snares

The limited comparative trials regarding differing snare shapes or configurations, or the use of bipolar versus monopolar snares, do not indicate superiority of modified over standard snares for resection of sessile colon polyps.\(^{16}\)

Brush or aspiration cytology devices

In a study comparing 4 disposable cytology brushes in upper endoscopy, all had adequate cellular yield; however, one brush was associated with less drying artifact.\(^{48}\) There are no published comparative studies of yields of brushing with standard and double lumen biliary cytology catheters.

FINANCIAL CONSIDERATIONS

The functional performance of reusable biopsy forceps ultimately deteriorates with increased number of uses. The durability can be extended with care in use and reprocessing. Cost comparisons depend mainly on the cost of disposable devices.\(^{5}\) When carrying out such estimates, users should also factor in the cost of medical
waste disposal and environmental impact associated with disposal of single-use devices.

A recent ASGE Technology Report reviewed issues and data regarding the costs of disposable versus reusable tissue sampling devices. A study of costs associated with disposable and reusable biopsy forceps concluded that reusable forceps are cost effective after 7 uses. Yang et al more recently found that malfunction of reusable forceps increased with number of uses. At up to 15 to 20 uses, reusable and disposable forceps costs are similar when the cost of disposable forceps is around $40.00. When reusable forceps can be used more than 20 times, they are less expensive. Deprez et al, in a much larger study (7740 sessions), reported that total purchase and reprocessing costs for reusable forceps were 25% of those of disposable devices. Further, an average of 315 biopsy sessions were performed with a reusable forceps, extending their mean life to 3 years. In another study, disposable forceps outperformed their reusable counterparts and offered a cost advantage. These authors also reported a concern over residual proteinacious material observed in reusable forceps, raising an infection-control risk. This charge was countered, however, by a study by Kozarek et al, who performed an ex vivo evaluation of cleaning and in vivo evaluation of function, performance, and durability of reusable forceps. Their analysis concluded that reusable biopsy forceps are confidently sterilized when accepted cleaning and sterilization protocols are followed. Sterilized reusable biopsy forceps were used a mean 91 times, rendering the potential for significant cost saving, again depending on acquisition and reprocessing costs. A German multicenter study recently showed that colonoscopy biopsy forceps can be reliably reprocessed after a standardized protocol.

CONCLUSION

Tissue sampling has become integral to endoscopy and is used to compliment endoscopic imaging. Techniques include pinch forceps biopsy, brush cytology, snare excision, and FNA. Endoscopic tissue sampling is generally safe and effective. Tissue sampling technique and device choice should be determined on the basis of the individual case circumstances.

REFERENCES


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