A novel flexible cryoprobe for EUS-guided pancreatic biopsies

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Background: EUS-guided FNA (EUS-FNA) is an established technique for the cytologic diagnosis of pancreatic disease. Attempts to obtain adequate histologic specimens have yielded variable and mostly insufficient results.

Objective: To evaluate the safety, feasibility, and quality of histologic biopsy specimens obtained by using a new cryobiopsy probe and to compare them with standard EUS-FNA and (laparoscopic) trucut biopsy specimens of pancreatic tissue.

Design: Animal non-survival study.

Intervention: Eighty-four pancreatic biopsy specimens (12 per group) were obtained in 4 anesthetized pigs by using one of the following the 18-gauge flexible cryoprobe; a conventional, 19-gauge, EUS-FNA needle; or a rigid, trucut biopsy device (18 gauge). The latter, used in laparoscopic surgery, was considered as the criterion standard for obtaining histology specimens.

Main Outcome Measurements: Specimens were evaluated for artifacts and specimen quality by a blinded pathologist who used a 7-point Likert scale to assess histologic adequacy. Biopsy size and bleeding time after biopsy also were recorded.

Results: The new cryoprobe was equivalent to the rigid, trucut needle and superior ($P < .001$) to the conventional 19-gauge FNA needles with respect to artifacts, quality of the specimen, biopsy specimen size, and bleeding.

Limitations: Animal model.

Conclusion: EUS-guided cryobiopsy was associated with better specimen quality for histologic analysis and a shorter bleeding time compared with a conventional 19-gauge FNA needle in the animal model. It is a promising new technique for histologic examination of pancreatic tissue. (Gastrointest Endosc 2013;77:784-92.)

EUS is an established technique for diagnosis and staging of pancreatic lesions. EUS-guided FNA (EUS-FNA) can be used to obtain tissue samples of pancreatic lesions and lymph nodes.[1-6] This is, however, mostly based on cytology, and specimens often lack sufficient quantity and quality for histologic examination because of their small size and sampling artifacts.[7-11] Flexible cryoprobes have been used to debulk endobronchial tumors and have recently been shown to permit high-quality tissue sampling adequate for histologic assessment during bronchoscopy.[12-14] The study hypothesis was that a flexible cryoprobe in conjunction with EUS might allow for pancreatic histology specimens obtained with a

Abbreviations: CB, cryobiopsy; EUS-FNA, EUS-guided FNA; TC, trucut.

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single-pass biopsy technique. This study aims to evaluate the safety, feasibility, and quality of biopsy specimens obtained by using a new cryobiopsy (CB) probe and to compare specimens acquired with the CB to those acquired via standard, EUS-guided FNA and trucut (TC) biopsies of pancreatic tissue.

Take-home Message

- This study reports first results of using cryobiopsy (CB) in conjunction with EUS. EUS-guided CB is tested for tissue acquisition in animal and human cadaver models and is compared with EUS-guided FNA.
- EUS-CB tissue acquisition achieves superior histology specimens compared with EUS-guided FNA with respect to artifacts, quality of the specimen, biopsy specimen size, and biopsy-related bleeding time in the animal model.

MATERIAL AND METHODS

This prospective, preclinical study was designed to compare the quality of pancreatic biopsy specimens obtained by using a novel flexible cryoprobe (18 gauge, Erbe, Tübingen, Germany), a flexible 19-gauge FNA probe (Echotip Ultra, (Cook Medical Inc., Bloomington, IN)), or a TC biopsy probe (18 gauge, Monopty Core Biopsy Instrument, Bard, Tempe, Ariz). The trial was performed in live animals and in human cadaver models. Experiments were conducted under institutional review board approval.

The live animal model was intended to evaluate quality of the tissue obtained with CB as well as bleeding times and compare those of FNA results. The human cadaver model was intended to assess handling of the device with EUS equipment in the human anatomy. The comparator for all experiments was FNA. The cryosurgical equipment used for this study consisted of a cryogen (carbon dioxide) console with an 18-gauge cryoprobe (Erbe, Tübingen, Germany) (Fig. 1). The cooling system is based on the Joule-Thompson effect, whereby the cooling agent is applied under high pressure (57 bar at room temperature) through the central canal of the probe. The gas is delivered through an inner tube located in the other sheath of the probe. The nozzle of the inner gas delivery tube has a diameter of 60 μm and is located in the tip of the probe, which concomitantly serves as a gas expansion chamber. Because of the sudden difference in pressure, the gas expands, resulting in a cooling effect at the tip of the probe. The gas emitted cools the tip of the probe to −35°C. The cryoprobe used in our experiments is a novel prototype with an 18-gauge diameter that resembles an injection needle with a ridge. The ridge incises the tissue before advancing the probe forward into the target tissue. For biopsy extraction, the probe is inserted into the working channel of the endoscope and is advanced into the target tissue under EUS guidance. Once the probe is correctly placed, freezing of the probe is activated. The tip of the cryoprobe is cooled to -35°C after activation. Because of the cryoadhesive effect, the frozen tissue remains adherent at the probe's tip and can be extracted by manual retraction of the probe. There is a positive correlation between biopsy size and freezing time. The biopsy size for the given organ has been determined experimentally before this study was started and was chosen not to be larger than the inner diameter of the oversheath to allow retrieval of the biopsy specimen through the oversheath. The freezing time was standardized in every group and set to 2 seconds. The probe together with the biopsy specimen is then pulled back into an oversheath and withdrawn through the working channel of the endoscope. The stiffness of the probe is not altered when carbon dioxide is delivered.

Biopsy groups in the animal model

Pancreatic biopsy specimens were obtained in 4 anaesthetized pigs under laparotomy control to assess bleeding time associated with each technique. CB was tested as direct puncture with the probe (CB-1) and in conjunction with different specimen retrieval sheaths (1.6-mm sheath, group CB-2; 1.75-mm sheath, group CB-3; 2.53-mm sheath, group CB-4; and via transduodenal puncture (group CB-5), resulting in 5 CB biopsy groups. FNA and TC biopsies also were obtained from each animal. Specimens were obtained from the pancreatic head, body, and tail by using 7 to 10 passes of the FNA needle through the tissue. Specimens were obtained by using a single pass of the TC needle through the tissue. This resulted in 7 groups with 12 biopsy specimens obtained for each group. Overall, 84 biopsy specimens were obtained in the animal model and were sent for histology assessment.

Human cadaver model

To test whether practical application of the cryoprobe introduced through an echoendoscope is feasible in humans by using classical echoendoscope positions such as in the stomach, pancreatic organ biopsy specimens were obtained in two recently deceased human cadavers (<72 hours postmortem), (1) through laparotomy puncture by using each technique (CB, EUS-FNA, and TC) and (2) with standard EUS equipment by using an Olympus GF-UCT140-AL5 (Evis Exera II, Olympus, Hamburg, Germany) echoendoscope with an ALOKA processor (ProSound Alpha 10; Aloka Europe, Zug, Switzerland). The latter experiments were performed to assess maneuverability and handling of the EUS-guided CB. Specimens were obtained via transgastric puncture from the pancreatic body. Specimens were obtained by using a single pass of the cryoprobe needle through the tissue. This resulted in 5 groups with 12 biopsy specimens obtained for each group.