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Waterjet necrostectomy device (WAND) for endoscopic management of pancreatic necrosis: design, development, and preclinical testing (with videos)

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Abstract:	Background and Aims Endoscopic intervention has emerged as a first-line option for management of symptomatic pancreatic necrosis, yet endoscopic debridement limited by the lack of dedicated endoscopic tools intended for this purpose. The objectives of this study were to design and build a prototype necrosectomy device compatible for use with a flexible endoscope and capable of selective tissue fragmentation, and to test the prototype in benchtop and porcine models. Methods A novel prototype, named the WAterjet Necrosectomy Device (WAND), was designed and developed, consisting of a single-use disposable endoscopic waterjet instrument capable of waterjet selection and independent tip articulation while fitting through a 2.8 mm working channel of a standard adult upper gastrointestinal endoscope. Benchtop, ex vivo , and in vivo (porcine) testing was performed in the initial stages of investigation. Results The WAND was constructed capable of delivering a continuous waterjet force with a surface pressure of 0.72 bar at a flow rate of 0.37 L/min. In phase I of testing, the WAND was able to achieve complete fragmentation of gelatin as a surrogate for pancreatic necrosis in benchtop testing. In phase II of testing, the WAND was able to achieve complete fragmentation of freshly explanted human pancreatic necrosis. In phase III of testing for safety in fresh necropsy swine, use of the WAND resulted in no significant tissue trauma even when irrigation was applied at closer proximity and at more extended duration than would be anticipated in clinical use. Conclusion The WAND prototype delivers irrigation capable of fragmenting necrotic debris ex vivo and also avoiding trauma to healthy non-target tissue. Planning is underway for first-in-human studies to assess the efficacy and safety of the WAND for endoscopic pancreatic necrosectomy.

Cover Page

Waterjet necrostectomy device (WAND) for endoscopic management of pancreatic necrosis: design, development, and preclinical testing (with videos)

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Author contributions:

PY: obtained funding, device concept and design, analysis and interpretation of data, drafting of manuscript, critical revision of the manuscript for important intellectual content

CAL: acquisition of data, analysis and interpretation of data, drafting of the manuscript (video component)

FC: device concept and design, acquisition of data, analysis and interpretation of data

PV: device concept and design

KO: obtained funding, device concept and design, acquisition of data, analysis and interpretation of data, critical revision of the manuscript for important intellectual content

Abstract

Background and Aims

Endoscopic intervention has emerged as a first-line option for management of symptomatic pancreatic necrosis, yet endoscopic debridement is limited by the lack of dedicated endoscopic tools intended for this purpose. The objectives of this study were to design and build a prototype necrosectomy device compatible for use with a flexible endoscope and capable of selective tissue fragmentation, and to test the prototype in benchtop and porcine models.

Methods

A novel prototype, named the WAterjet Necrosectomy Device (WAND), was designed and developed, consisting of a single-use disposable endoscopic waterjet instrument capable of waterjet selection and independent tip articulation while fitting through a 2.8 mm working channel of a standard adult upper gastrointestinal endoscope. Benchtop, ex vivo, and in vivo (porcine) testing was performed in the initial stages of investigation.

Results

The WAND was constructed capable of delivering a continuous waterjet force with a surface pressure of 0.72 bar at a flow rate of 0.37 L/minute. In phase I of testing, the WAND was able to achieve complete fragmentation of gelatin as a surrogate for pancreatic necrosis in benchtop testing. In phase II of testing, the WAND was able to achieve complete fragmentation of freshly explanted human pancreatic necrosis. In phase III of testing for safety in fresh necropsy swine, use of the WAND resulted in no significant tissue trauma, even when irrigation was applied at closer proximity and at more extended duration than would be anticipated in clinical use.

Conclusion

The WAND prototype delivers irrigation capable of fragmenting necrotic debris ex vivo and also avoiding trauma to healthy nontarget tissue. Planning is underway for first-in-human studies to assess the efficacy and safety of the WAND for endoscopic pancreatic necrosectomy.

Introduction

Acute pancreatitis results in approximately 275,000 hospital admissions and more than $2.5 billion in health care costs annually [1]. Cases of severe pancreatitis with local adverse events, including pancreatic or peripancreatic necrosis, can be associated with significant morbidity and mortality. Over a period of days to weeks after onset of necrotizing pancreatitis, areas of necrosis may evolve to form mature collections of walled-off necrosis (WON) which, when symptomatic, require intervention/drainage.

Current practice guidelines suggest that endoscopic intervention is preferred over surgical intervention as a first-line approach when drainage of a pancreatic fluid collection (PFC) is indicated [2]. The initial step in endoscopic drainage consists of EUS-guided access to the collection followed by transmural placement of either a lumen-apposing metal stent or double-pigtail plastic stent(s). The resultant fistula tract allows drainage of PFC contents into the GI lumen.

Although most patients with predominantly liquefied PFC achieve complete resolution with stent placement alone, other patients with WON containing solid debris may not achieve complete drainage and require further intervention [3]. For patients without complete drainage, a next step often consists of transmural retroperitoneal endoscopy. This can be performed by advancing a flexible endoscope first per os then through the previously created fistula and into the retroperitoneal space. However, in this setting residual pancreatic necrosis may be bulky and/or densely adherent and difficult

to dislodge from the retroperitoneal cavity without further fragmentation. Options for fragmentation include chemical or mechanical debridement, the latter of which is facilitated by off-label use of commercially available endoscopic accessories including polypectomy snares, retrieval nets, forceps, and biliary stone extraction baskets.

There are numerous limitations to this current approach: (1) none of the devices are specifically designed or intended for this use; (2) as such, these devices are inherently limited in their ability to achieve proficient fragmentation of solid necrotic debris; (3) the efficacy and safety of use of these devices for this purpose has not been rigorously investigated; (4) use of multiple devices per case results in equipment waste and excess cost to the health care system; and (5) complete debridement of necrosis is not always achievable in a single endoscopic session, and some patients require multiple endoscopic sessions in order to achieve complete clearance of necrosis.

Development of innovative technologies dedicated for necrosectomy use, capable of fragmenting necrotic debris while sparing viable tissue, has been identified as a critical need in the endoscopic management of WON [3]. The objectives of this study were to design and build a prototype necrosectomy device compatible for use with a flexible endoscope and capable of selective tissue fragmentation, and to test the prototype in benchtop and porcine models.

Materials and Methods

Design, development, and fabrication of the prototype was performed in the Science and Technology of Robotics in Medicine (STORM) Laboratory at Vanderbilt University after Institutional Review Board approval.

The prototype, named the WAterjet Necrosectomy Device (WAND), is a single-use disposable endoscopic waterjet instrument capable of waterjet selection and independent tip articulation while

fitting through a 2.8 mm working channel of a standard adult upper gastrointestinal endoscope (Fig. 1A and B). The WAND is constructed using both "off-the-shelf" and custom 3D-printed parts (Fig. 2). The WAND consists of a handle mechanism, biocompatible polytetrafluoroethylene (PTFE) tubing, and device tip. The waterjet nozzle, device handle, and threaded-filled stopper are manufactured with a 3D printer using biocompatible photopolymers (FormLab Dental SG, FormLab, Mass, USA). The working end device tip of the WAND is composed of a 3D-printed nozzle, bending sleeve, and tri-lumen sleeve used to separate 2 nitinol wires, which facilitate tip articulation.

The handle houses a knob where the nitinol wires attach. The knob rotates on a bearing. The nitinol wires run from the handle, through the length of flexible tubing, to the tip of the WAND. They are separated by a tri-lumen sleeve at the distal end of the WAND to allow for articulation of the tip. Rotation of the knob thereby permits articulation of the tip of the WAND over a range of 120 degrees while housed in a standard adult upper gastrointestinal endoscope, independent of endoscope tip articulation, in order to facilitate precise and accurate targeting of treatment site(s).

The handle adapter attaches to a Y connector to prevent backflow of water. Water enters the Y connector with a pressurized water line and exits into a 135 cm length of biocompatible PTFE tubing coupled with a kink protector and attached with a 3-D printed adapter.

The WAND is designed to provide a controllable waterjet force capable of safely fragmenting necrosis without damage to healthy tissue. The mechanism of tissue fragmentation is irrigation alone, rather than direct contact with the device or mechanical manipulation by the device with necrotic tissue. The water delivery system consists of an ASME-Code pressurized liquid dispensing tank, regulator, control valve, and foot pedal (Fig. 3). The system receives pressurized air from the wall inlet in the procedure room. The air flows into a liquid-dispensing tank that is regulated to have an entry pressure of 90 psi (the vessel has a maximum pressure tolerance of 205 psi at 100 degrees F). The user

can then control the pressure in the vessel to a pressure at or below 90 psi. The air compresses water in the vessel, and an electronic depressible foot pedal controls a water release valve, giving the endoscopist full control of water irrigation. When pressing the foot pedal, water will flow out of the valve and through tubing to the WAND, with water exiting at the tip of the WAND. Irrigation is sustained as long as the foot pedal is depressed. Irrigation ceases with release of the foot pedal.

The WAND is designed to deliver a flow rate up to 0.5 L/minute at a maximum surface pressure of 1.3 bar—well below a tissue safety threshold of 3 bar [5-7]. Both the flow rate and force generated by the WAND are higher than irrigation volumes and pressures generated by commercially laparoscopic irrigation systems used during laparoscopic surgery in the peritoneal and retroperitoneal cavities, yet lower than high pressure water jets used for surgical hydrodissection.

Results

Preclinical testing phase I: Initial benchtop testing used gelatin as a surrogate for pancreatic necrosis to assess the ability of the WAND to fragment gelatin and necrosis. The WAND was tested for its ability to fragment different densities of gelatin (Video 1). The WAND was passed through the instrument channel of a gastroscope and positioned at a distance of 2.5 cm from the gelatin. Irrigation was delivered by the WAND, both with and without independent articulation of the WAND tip, with a surface pressure of 1 bar at a flow rate of 0.45 L/minute. The WAND was further tested on gelatin to confirm articulation and function in a confined environment, by placing the gelatin in a clear stomach phantom (Video 2). A continuous waterjet force was applied with a surface pressure of 0.72 bar at a flow rate of 0.37 L/minute to achieve adequate gelatin fragmentation. The WAND was then completely removed from the endoscope, and fragmented gelatin was successfully aspirated through the empty working channel of the endoscope. This phase of testing also demonstrated that the WAND could be

successfully and repeatedly re-introduced through the working channel of the endoscope to deliver further waterjet irrigation without compromising the function of the WAND. This would allow for multiple cycles of irrigation, fragmentation, and aspiration as would be anticipated in clinical use.

Preclinical testing phase II: This phase of benchtop testing assessed the WAND's ability to fragment ex vivo freshly explanted pancreatic necrosis from human subjects. The WAND was passed through the instrument channel of a gastroscope and positioned at a distance of 1.5 cm from the necrotic tissue (Video 3). Irrigation was delivered by the WAND, both with and without independent articulation of the WAND tip, at a surface pressure of 0.72 bar and a flow rate of 0.37 L/minute. This resulted in successful fragmentation of necrotic tissue to remnants less than 2.8 mm in diameter, which is less than the inner diameter of the endoscope's suction channel. Due to success in aspirating gelatin, given its more rigorous and homogeneous composition, aspiration of the brittle necrotic pancreatic tissue after it was fragmented to less than 2.8 mm in diameter was not performed. This phase of testing demonstrated the ability of the WAND to fragment pancreatic necrosis as intended for clinical use.

Preclinical testing phase III: Once the WAND's effectiveness for ex vivo fragmentation of necrosis was demonstrated, preclinical testing was performed in a swine model to evaluate system safety (Video 4). In vivo testing was performed using a 40 kg female Yorkshire Landrace cross swine. This testing was performed in fresh necropsy specimens, within 5 minutes of confirmation of death of the swine. The goal of this phase of testing was to demonstrate the absence of tissue trauma caused by the WAND on non-target, non-necrotic tissue. Effects on the pancreas, small intestine, liver, stomach, spleen, and aorta were assessed. We chose to conduct safety testing for "worst case" scenario with irrigation at closer proximity and more extended duration than would be anticipated for clinical use. For each target organ, the WAND was positioned 0.5 cm from the porcine organ or vessel, and continuous irrigation was applied for 30 seconds over a range of 0.4 bar to 1.3 bar to determine whether any tissue damage would

occur. There were 5 cases of mild tissue blanching and erythema at surface pressures above 0.72 bar. None of the organs or vessels sustained perforation, erosion, or excoriation at any pressures including the maximal pressure for the platform. This phase of testing demonstrated that even when applied directly to nontarget tissue at closer proximity and at more extended duration than would be anticipated in clinical use, the WAND creates no significant tissue trauma.

Discussion

The key developmental principle is that the WAND will provide irrigation pressures capable of fragmenting nonviable necrotic tissue yet avoiding injury to healthy tissue. Commercially available endoscopic and surgical irrigation devices currently in routine clinical use have provided guidance in the intentional design strategy of the WAND in an effort to minimize anticipated risks. Waterjet dissection is currently a technique used for liver and kidney surgery. Pulsed waterjet dissection in a swine liver model has demonstrated that the breaking strength of healthy liver parenchymal tissue is 1.41 mPa (14.1bar) and the breaking strength of the hepatic vein is 8.66 MPa (86.6 bar) [4]. Waterjet dissection has also become widely used in endoscopic submucosal dissection (ESD), a flexible endoscopic procedure for removing neoplastic lesions from the luminal gastrointestinal tract. A commercially available waterjet dissection system for ESD capable of achieving a maximum pressure of 80 bar in the endoscopy field was tested in a porcine esophagus model. According to published data, testing at 30 bar demonstrated no evidence of tissue dissection. Testing at 50 bar demonstrated intended and desired tissue dissection. Testing at 70 bar demonstrated perforation of the muscle layer of resection bed when waterjet was applied for 1 minute [5]. A different water jet dissector has been tested on the stomach walls of pigs with the intention of delivering fluid to the submucosal tissue layer. This reported no evidence of perforation when used within the range of 30 to 70 bar [6].

The WAND is designed to deliver a maximum surface pressure of 1.3 bar, which is an order of magnitude less than the lower testing limits in the above waterjet dissection studies, which demonstrated no evidence of tissue or blood vessel injury as established in above studies. Avoidance of vascular injury is particularly important, as a dreaded potential adverse event of endoscopic pancreatic necrosectomy is bleeding caused by damage to the splenic vasculature.

This 1.3 bar estimate reflects a worst-case scenario that would occur if the WAND tip directly contacted tissue during irrigation. However, the WAND is not intended to directly contact necrotic tissue but instead deliver irrigation when positioned 1 to 2 cm from tissue. This should provide an additional margin for safety as prior waterjet dissection data suggests that water pressure drops by 50% at 2 mm from the nozzle tip and by 90% at 3.5 mm from the nozzle tip [8]. This worst-case scenario for damage to the tissue would occur during maximum tissue irrigation with maximum irrigation exit flow. The 5-mm distance from the tissue was chosen for Phase III testing to ensure maximum tissue irrigation, while being very close to the tissue to maintain a focus of the water-jet. In the case of direct or partial tissue contact, the surface pressure would be equal to or less than the perfect irrigation case, because the small-diameter nozzle would most likely be obstructed or partially obstructed and therefore be unable to operate at maximum flow. Placement of a clear cap on the endoscope tip could maintain distance between the endoscope/WAND tip and tissue thereby preventing direct tissue contact; however, we also expect that this modification would constrain independent articulation of the WAND.

Published, peer-reviewed data regarding use of dedicated devices for endoscopic pancreatic necrosectomy are virtually nonexistent. A European report of use of the EndoRotor, a mechanical debridement device, identified no procedure-related adverse events in 2 patients [9]. This small sample size is insufficient to determine a current baseline risk of procedure-related adverse events associated with endoscopic necrosectomy using dedicated necrosectomy devices.

Preclinical testing of the WAND to date is limited in its ability to assess safety for intended use. Risk of procedure-related adverse events such as bleeding is inherent to endoscopic pancreatic necrosectomy. Although the WAND has been designed within precise parameters to avoid tissue injury, it is unknown whether the rate of adverse events and serious adverse events related to WAND use will be increased beyond inherent risks associated with endoscopic pancreatic necrosectomy. And ultimately, the criteria by which endoscopic necrosectomy devices are judged should include demonstration of improved outcomes with shorter recovery times and reduced number of procedures.

It is also possible that further in vivo testing of the WAND will reveal operator challenges or technical factors that require device modification. However, as endoscopic irrigation and irrigation control using a foot pedal are customary tasks for an endoscopist, use of the WAND should pose no unique critical tasks for the endoscopic user. Moreover, the device-user interface is intuitive with cognitive processing required for device use consisting only of customary endoscopic visual feedback.

Based on the above testing, our research team has concluded that the WAND is able to deliver irrigation capable of (1) fragmenting necrotic debris ex vivo and also (2) avoiding trauma to healthy nontarget tissue. Because there is no available animal model of pancreatic necrosis, the logical next step in testing is to assess feasibility and safety of treating pancreatic necrosis in vivo. Planning is underway for first-in-human studies to assess the efficacy and safety of the WAND for endoscopic pancreatic necrosectomy.

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Legends

Figure 1. A, WAND positioned alongside standard adult upper gastrointestinal endoscope. B, WAND housed within standard adult upper gastrointestinal endoscope.

Figure 2: WAND schematic, exploded with parts labeled.

Figure 3: WAND with endoscope, regulator, flow valve, foot pedal.

Acronyms and abbreviations (list all that are used in paper with their spell-outs)

Acronyms and abbreviations

EUS (endoscopic ultrasound)

PFC (pancreatic fluid collection)

PTFE (polytetrafluoroethylene)

WAND (WAterjet Necrosecotmy Device)

WON (walled off necrosis)

Figure 1a :WAND positioned alongside standard adult upper gastrointestinal endoscope

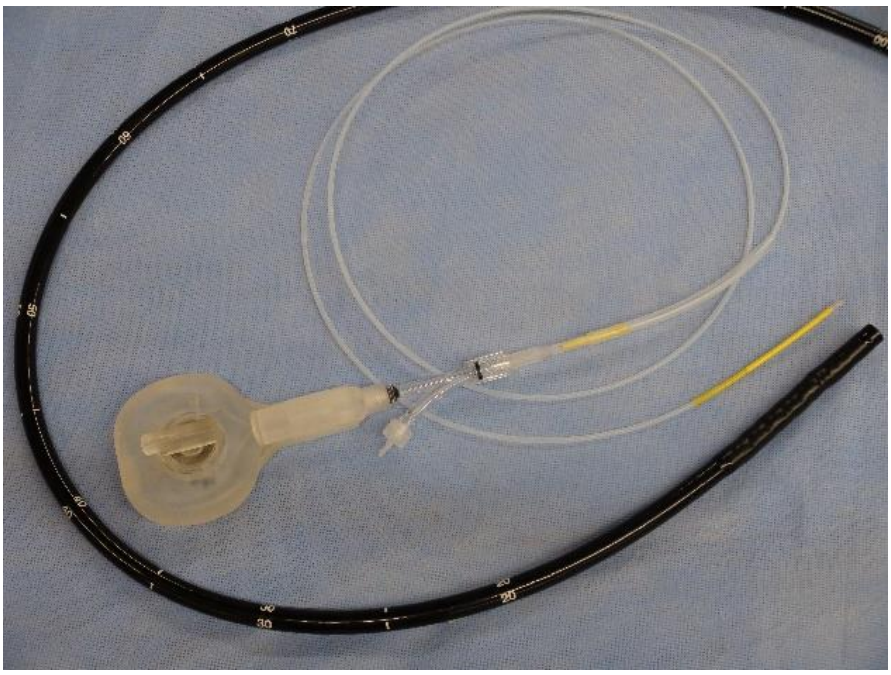

Figure 1b: WAND housed within standard adult upper gastrointestinal endoscope

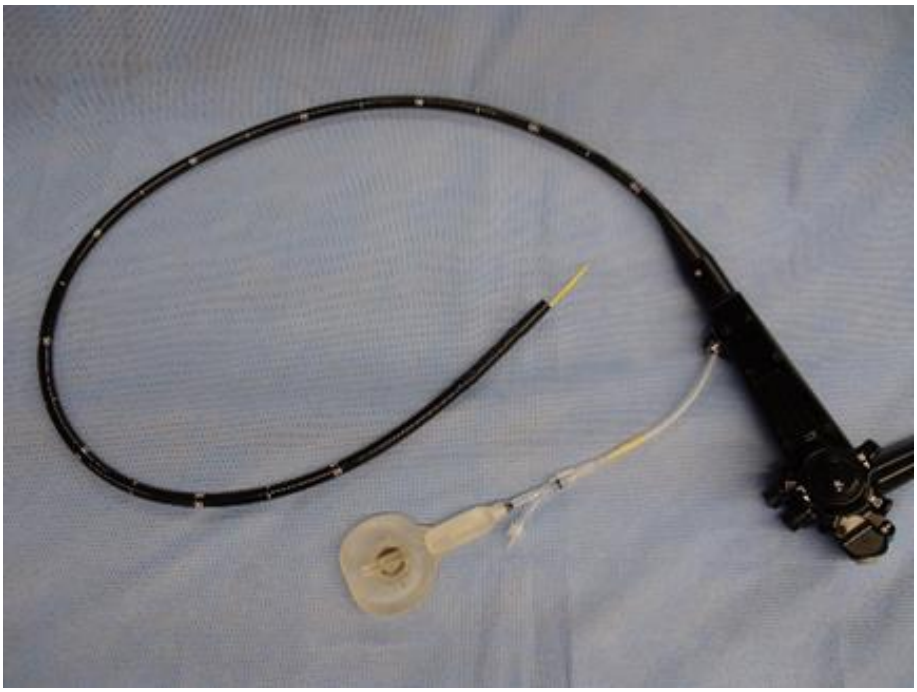

Figure 2: WAND schematic, exploded with parts labeled

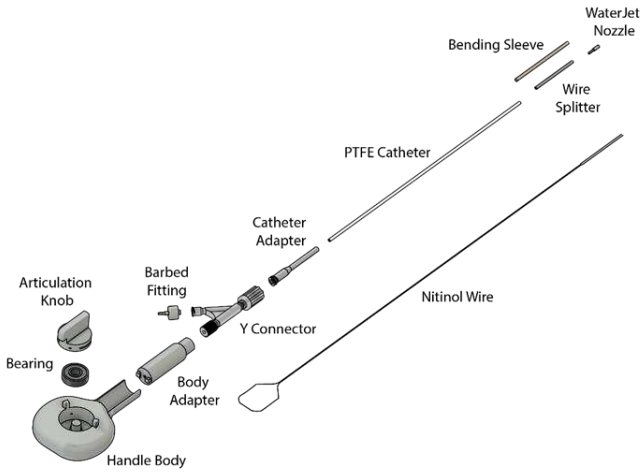

Figure 3: WAND with endoscope, regulator, flow valve, foot pedal

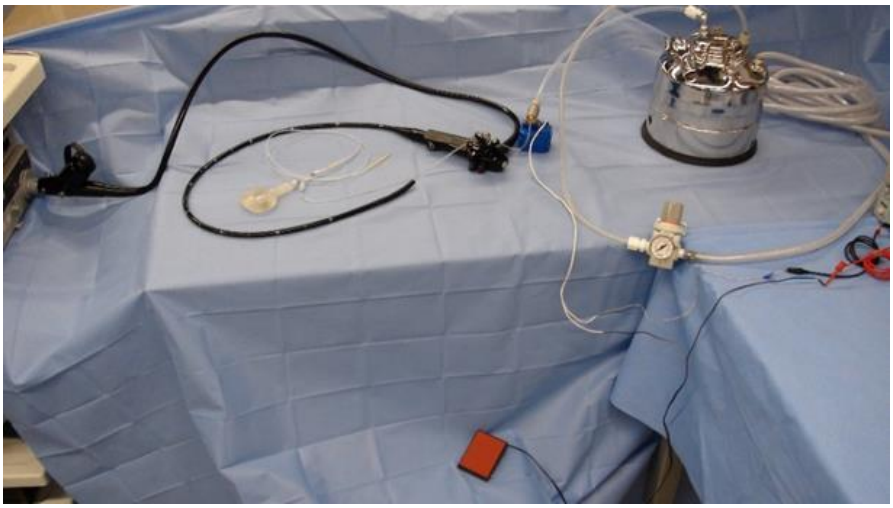

Fig 1A

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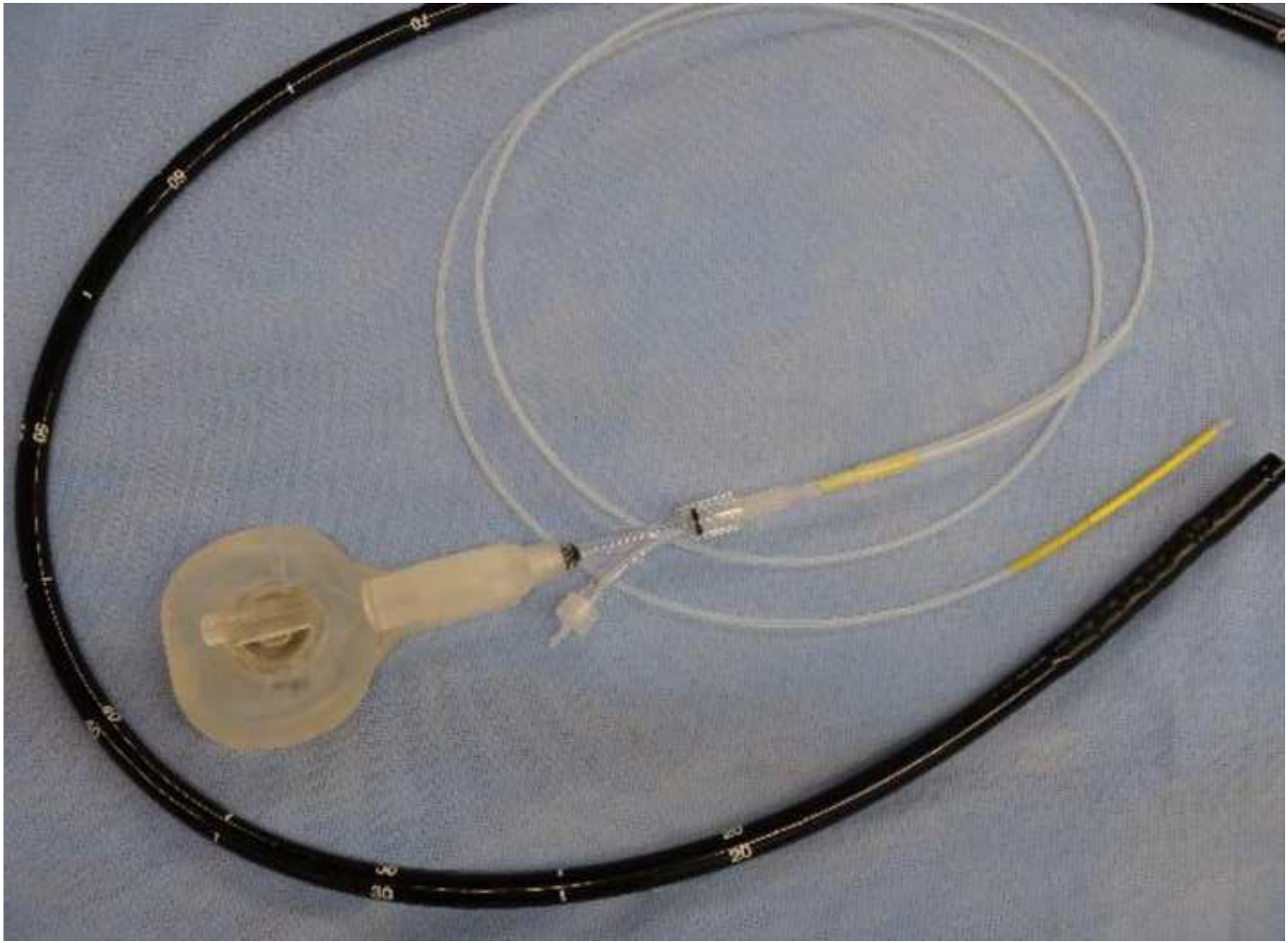

Fig 1B

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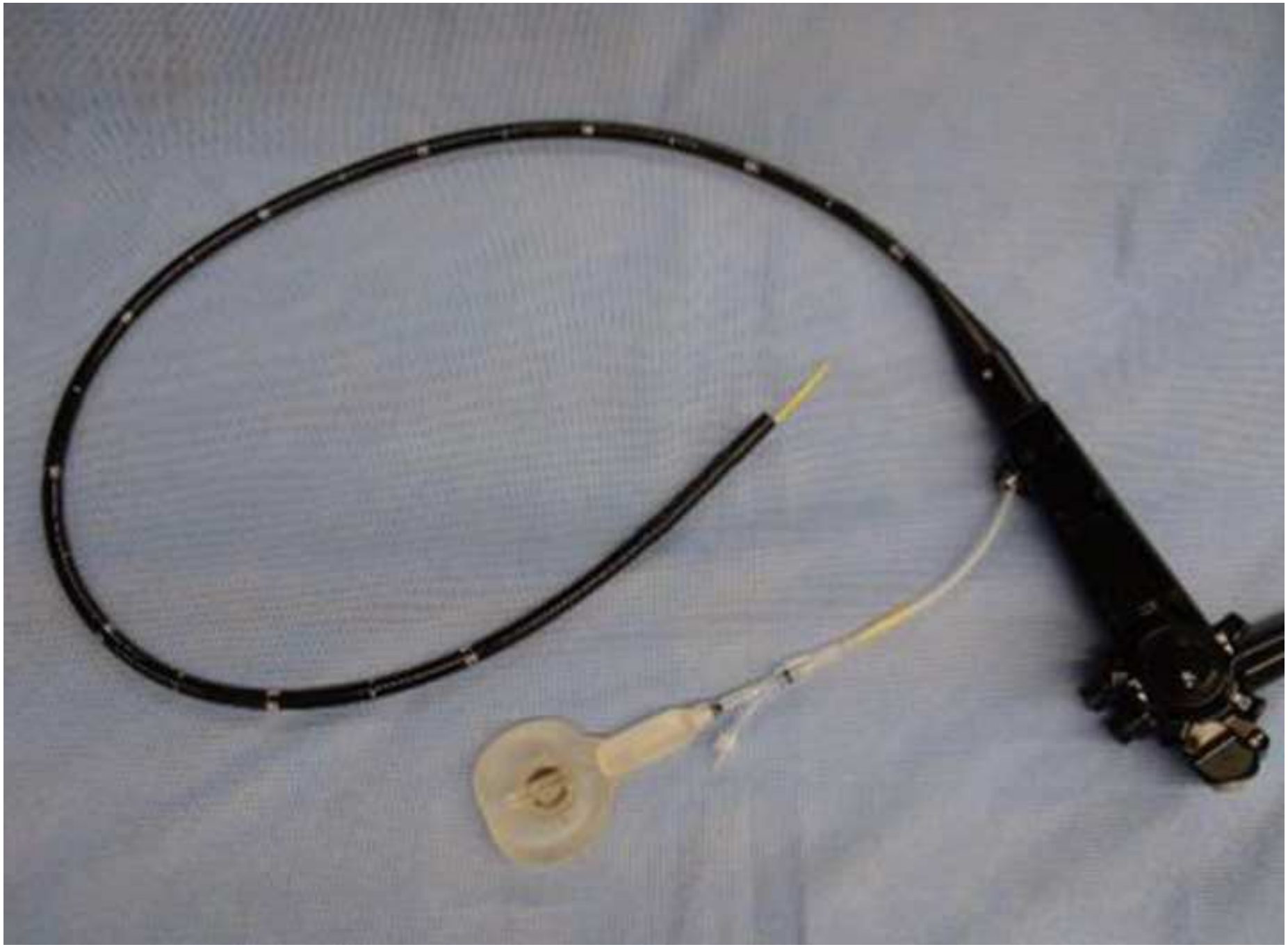

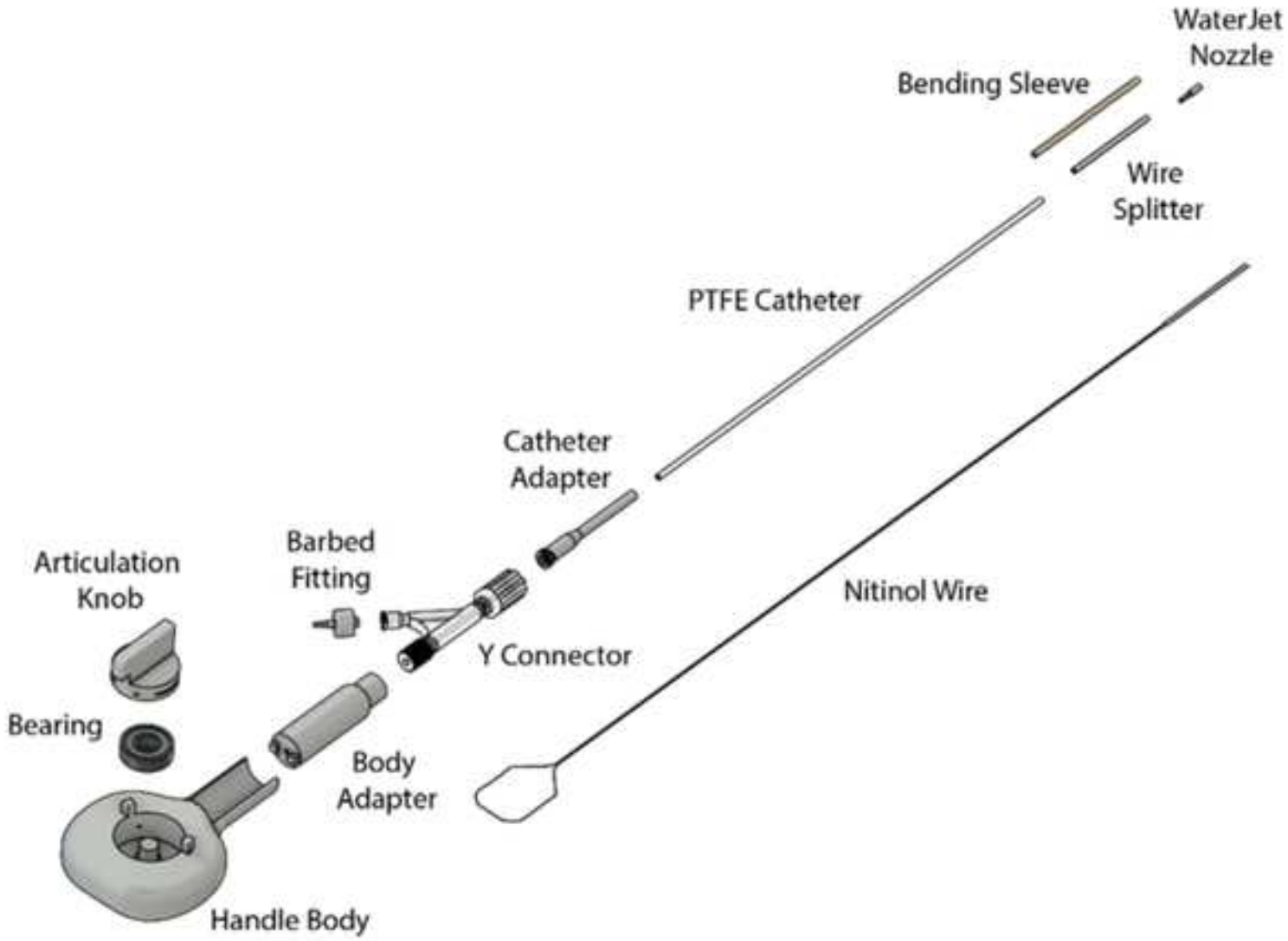

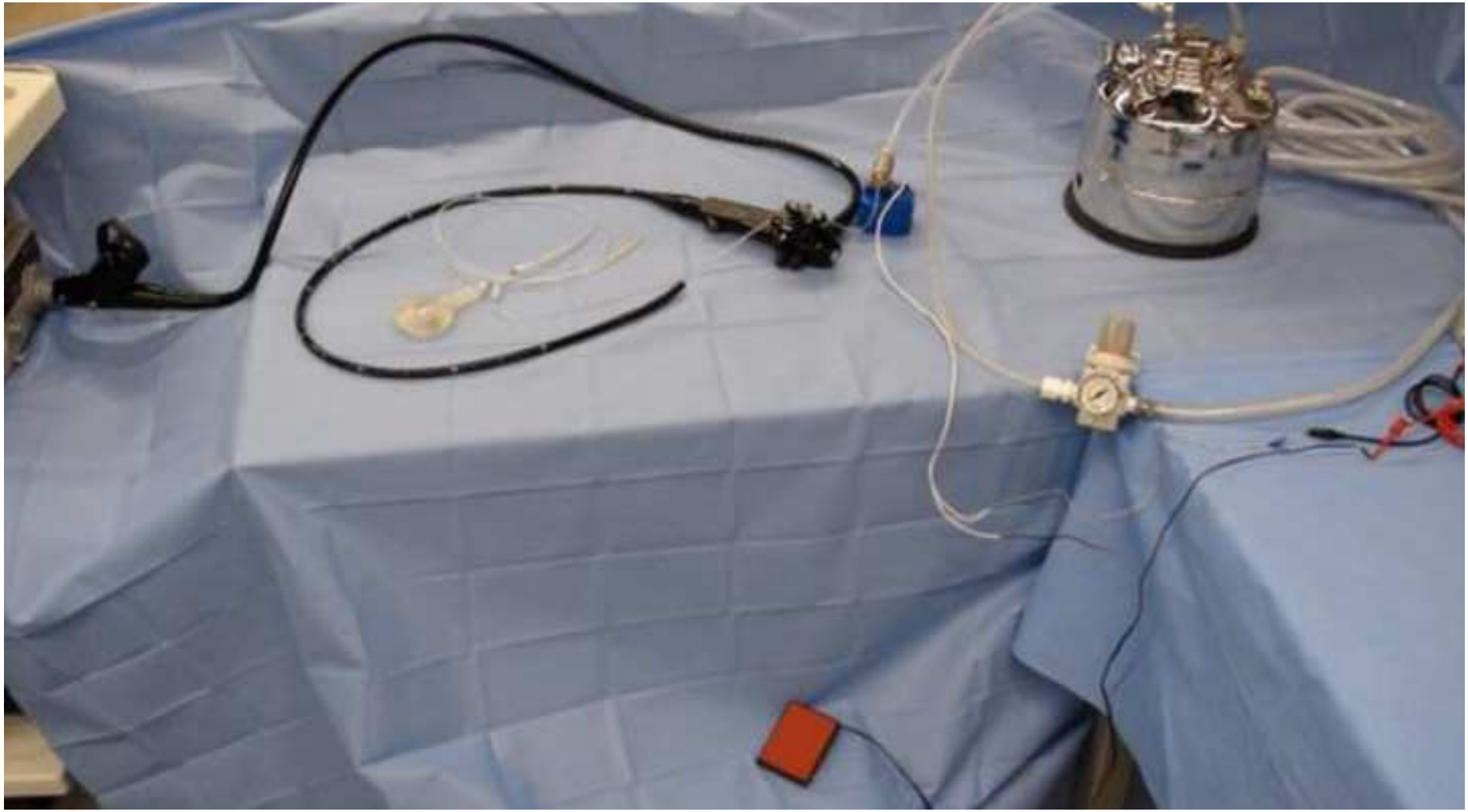

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