Original Article

# A Kit for EUS-Guided Access and Drainage of Pancreatic Pseudocysts: Efficacy in a Porcine Model

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**Abstract:**
**Objective:** Transluminal pseudocyst drainage with currently available tools remains technically challenging, time consuming and limited to fluid collections adherent to the GI tract. Multiple tools and steps are still required to achieve pseudocyst drainage. We evaluated a novel kit to facilitate endoscopic ultrasonography (EUS)-guided access, drainage and rapid decompression in a porcine model.
**Methods:** The kit consists of the NAVIX access device and the AXIOS stent delivery system. The NAVIX contains an inner trocar for puncture and an outer dual balloon catheter for anchorage and dilation. The AXIOS stent is a fully covered dual flanged stent. Both are inserted through the working channel of a curved linear array echoendoscope. In a porcine model, a gallbladder was used as a proxy for a pseudocyst.
**Results:** Six Yorkshire pigs underwent this procedure successfully without complication and 3 of them were kept alive. After a 4-week implantation period, the AXIOS stents were removed easily using a snare and the 3 animals were observed for an additional 4 weeks. The stents were well-tolerated by the stomach and gallbladder tissues, as confirmed by weekly endoscopic inspection, gross necropsy and histopathology.
**Conclusion:** EUS-guided transluminal access and drainage of the porcine gallbladder was technical feasible using a novel kit. This kit has the potential to simplify, streamline, and improve the safety of pancreatic pseudocyst drainage.

**Keywords:** pseudocyst; pancreatic fluid collection; pancreatitis; endoscopic ultrasonography

## INTRODUCTION

Pancreatic pseudocysts develop in 10%-20% of patients with acute pancreatitis[1,2] and complicate chronic pancreatitis in 20%-40% of patients.[3] Indication for drainage includes symptomatic pseudocysts or complications such as infection or abdominal pain.[4] Transmural endoscopic drainage of pancreatic pseudocysts has been increasingly accepted as a minimally invasive alternative to surgical drainage.[5-7] Endoscopic drainage entails creating a fistula between the pseudocyst and the enteric lumen and deploying one or more plastic stents into the pseudocyst.[8] Endoscopic ultrasonography (EUS) has significantly extended the reach of endoscopic drainage to include pseudocysts that do not produce a visible bulge in the enteric lumen, and improves safety by visualizing and avoiding intervening organs and vessels.[4,9-13] However current methods of EUS-guided translumenal pseudocyst drainage with multiple plastic stents remains technically challenging. Multiple tools and device exchanges are required, and with each device exchange access to the pseudocyst can be lost.[14] We investigated a novel kit designed to simplify and streamline pseudocyst drainage.

## MATERIALS

The kit consists of the NAVIX access device and the AXIOS stent delivery system (Xlumena, Mountain view, CA). The NAVIX consists of an inner endoscopic trocar with a blade at the tip that creates a 3.5-mm puncture opening and an outer dual balloon catheter. The anchor balloon expands to 8 mm to maintain access within the target and the dilation balloon expands to 10 mm. Radiopaque balloon markers on the catheter shaft aid in fluoroscopic monitoring of balloon dilation, while black band markers aid in endoscopic guidance throughout the procedure. The NAVIX is FDA cleared for transluminal pancreatic pseudocyst drainage.

The AXIOS stent has been previously described (Fig. 1, 2).[15] It is made of braided nitinol wire and measures 8 mm in length and has a 10-mm lumen diameter. Flanges at each end measure 20 mm in diameter and provide apposition of

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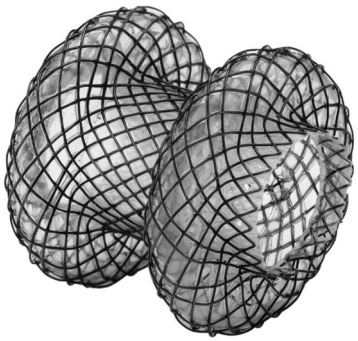

**Figure 1.** AXIOS Stent.

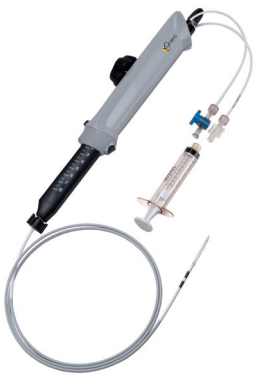

**Figure 2.** NAVIX access device.

the target and enteric lumens to prevent leakage into the peritoneal cavity and stent migration. Anchorage across the lumens also provides a stable conduit for endoscope intubation through the stent to access the target lumen. The stent is fully covered to prevent leakage, tissue ingrowth, and enable removability. The AXIOS stent is preloaded onto a 10.5-Fr delivery system that is inserted through a 'therapeutic' (3.7 mm or greater) working channel of a curved linear array (CLA) echoendoscope. The handle of the delivery system is luer-locked onto the echoendoscope instrumentation channel inlet port, analogous to a standard fine needle aspiration (FNA) needle.

## ANIMAL MODEL

The porcine gallbladder was used as a proxy for the pseudocyst in six 35- to 40-kg female Yorkshire pigs. Institutional review board approval was obtained from the local animal ethics committee, and animals were housed at the animal research facility (ISIS, San Carlos, California). The pigs were fasted for 24 hours before the procedure. Pre-anesthesia sedation and analgesia was administered intravenously and general anesthesia was achieved with isoflurane. For euthanasia, the pigs were anesthetized with Intramuscular (IM) injections of Telazol 2.5-4.0 mg/kg IM and Atropine 0.02 mg/kg IM. A mask was given with ISO/$O^2$ at 2%/2L per minute and an ear vein catheter was placed with a lethal dose of Euthasol or equivalently administered at 1 mL/10 lb. Respiratory and cardiac rates were monitored

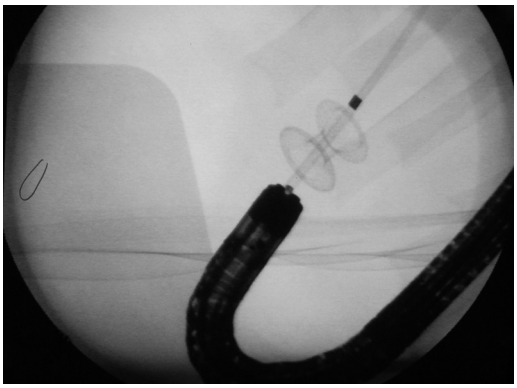

**Figure 3.** Fluoroscopic image of cannulation of gallbladder via the stent.

with a stethoscope until all vital signs ceased.

## TECHNIQUE

The CLA echoendoscope (GF-UCT140; Olympus Corporation, Tokyo, Japan) was advanced into the stomach. The gallbladder was identified and one or two T-tags were first deployed using a modified 19-G needle (Cook Medical, Winston Salem NC) to appose the gallbladder and stomach walls. The endoscopic trocar on the NAVIX access device was used to gain EUS-guided transenteric access to the gallbladder from the stomach. The trocar created a 3.5-mm opening across the stomach and adjoining gallbladder walls. This allowed easy advancement of the balloon catheter directly over the trocar by clockwise rotation of a knob at the handle. The anchor balloon was inflated in the gallbladder to secure access and the trocar was removed. Fluid was aspirated through the balloon catheter, followed by injection of dilute contrast to document the radiological outline of the gallbladder. A 0.035-inch guidewire was inserted and coiled inside the gallbladder through the balloon catheter. The anchor balloon was retracted until 'snug' against the gallbladder wall. The cystoenterostomy tract was then dilated to 10 mm with the dilation balloon (Fig. 3). Both balloons were deflated and the Navix device was removed leaving the guidewire coiled in the gallbladder. The AXIOS delivery system was inserted over the guidewire and the stent was deployed (Fig. 4, 5). The lumen of the AXIOS stent was intubated with a 5.8-mm gastroscope (Fujinon, Wayne, NJ) and the gallbladder was entered for endoscopic inspection. After a 4-week implantation period, the AXIOS stent was removed using a snare.

## RESULTS

The NAVIX access device and AXIOS delivery system enabled successful EUS-guided gallbladder drainage without procedural difficulty or complication. Three pigs were kept alive and survived for eight weeks. In all three animals,

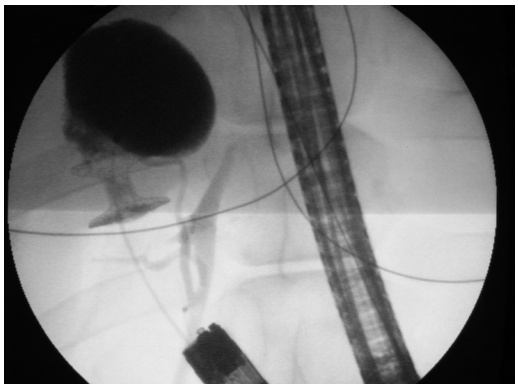

**Figure 4.** Fluoroscopic image of the AXIOS stent creating a cholecystoenterostomy.

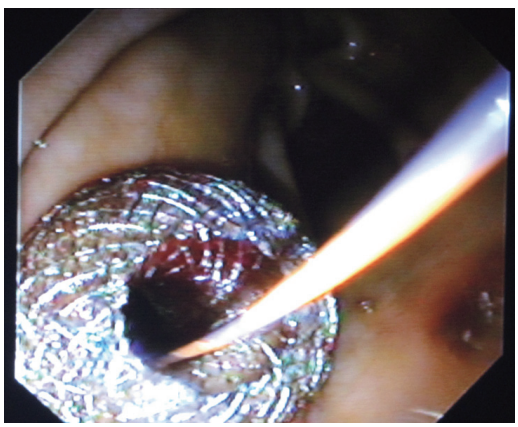

**Figure 5.** Dual-flanged stent having a 10-mm lumen diameter as seen from the stomach.

drainage was visualized from the stent lumen on weekly endoscopic inspection and patency was confirmed by passage of 0.035-inch guidewire and endoscopic retrograde cholangiopancreatography (ERCP) catheter into the gallbladder. Contrast injection through the stent confirmed absence of leakage. The stents were removed in the three pigs without any difficulty using a snare and the pigs were observed for four additional weeks. Visual inspection of the tissue before and after removal as well as histology of the tissue surrounding the flanges of the stent was performed. After stent removal, only changes of chronic inflammation without tissue ulceration or bleeding were seen (Fig. 6). The stomach to gallbladder fistula remained patent throughout the 4-week post-stent removal observation period. No significant complications with the animals were seen after the stent removal. None of the animals developed signs of infection or behavioral change during the entire survival period.

### *Necropsy Results*

Necropsy revealed a residual transenteric "tunnel" in the pig #4509. It was represented by soft fibrous tissue cord in the region corresponding with the intended connection between the stomach and the gallbladder. There was no tunnel lumen in the connective tissue. Although the tunnel opening in the stomach and the gallbladder mucosa were sealed, a shallow crateriform depression remained, reflecting previous mucosal defect following stent withdrawal.

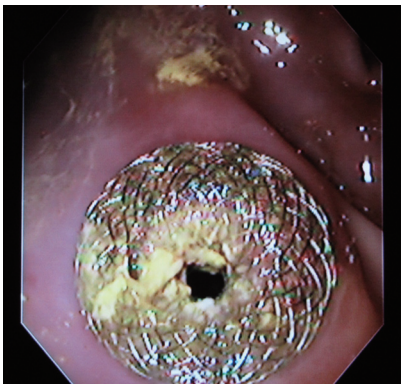

**Figure 6.** Patent stent 7 days post-procedure.

No residual "tunnel" was seen in pig#4510. Other than delicate tissue adhesions between the gallbladder and the stomach wall, there was no gross evidence of solid tissue formation, reflecting previous conduit between the organs following stent removal. A similar fibrous tissue connection was present between the colon and the stomach in pig#4512. Again, the tunnel lumen and the openings on the mucosal surfaces of the adjoined organs were sealed.

### *Histopathology Results*

Histopathology was performed by taking sections of the fibrous tissues connecting the gallbladder and stomach (pig#4509) and stomach to colon (pig # 4512); these sections were processed, embedded in paraffin, sectioned at approximately 4 microns, stained with Hematoxylin & Eosin and examined with a light microscope.

In Pig #4509, sections of the soft tissue connecting the gallbladder and the stomach consisted of mature fibrous bundle surrounded by peritoneal fat layers. In the mid regions of the fibrous cord, a narrow fissure lined by flattened epithelial cells was noted what presumably could be the remains of the original tunnel created by the stent. Elsewhere along the cord, the fissure was not evident. Sections of the stomach and gallbladder mucosa were unremarkable although residual chronic tissue reaction, representing previous tunnel origin, was present in the muscularis, particularly in the stomach wall (Fig. 7AB).

In Pig #4510, no histopathology was completed.

In Pig #4512, sections of the soft tissue connecting the stomach and colon represented a partial funnel-shaped fistula and/or colonic invagination into the stent pathway for an approximate distance of 6-8 mm. Beyond this region, the tract was not patent. Residual chronic tissue reaction representing previous tunnel origin was present on the stomach wall (Fig. 8AB).

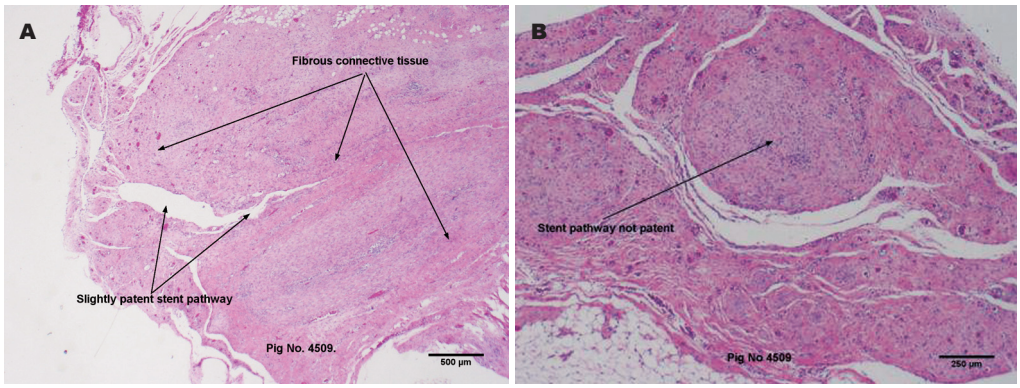


**Figure 7.** Pig #4509. A: Fibrous tissue pathway; B: Occluded stent pathway.

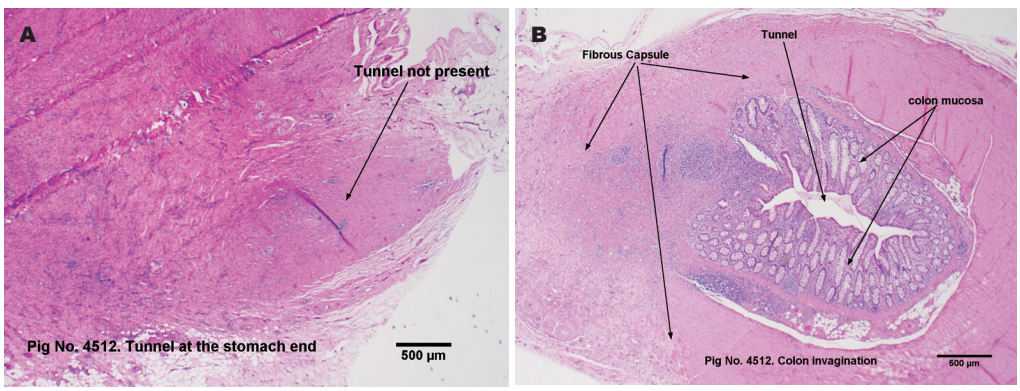


**Figure 8.** Pig #4512. A: Tunnel at the stomach end; B: Colon invagination.

## DISCUSSION

The evolution of EUS has allowed precise characterization of intra- and extramural lesions, tissue aspiration for diagnosis, and access for drainage of extramural fluid collections.[4] EUS has expanded the safety and efficacy of endoscopic drainage of pancreatic fluid collections (PFC) and has been shown to be cost-saving and associated with a shorter length of postprocedure hospital stay when compared with surgical drainage.[8]

Over the last decade, endoscopic drainage of PFC has become the procedure of choice compared to surgery or radiology.[16-17] PFC drainage is indicated for infection, pain, gastric outlet or biliary obstruction, leakage, fistulization, and enlargement.[12,18-21] Indications for drainage have been extended by the evolution of EUS to include pancreatic abscesses, organized liquefied necrosis and non-bulging PFC.[16, 22-25]

EUS-guided drainage of pseudocysts remains a technically challenging procedure. Using earlier generation echoendoscopes with a restricted working channel size, the role of EUS was restricted to diagnosis and access to the pseudocyst using a FNA needle or needle knife. The echoendoscope was then exchanged over-the-wire for a 'therapeutic' channel endoscope that allows placement of large-bore (10-Fr) stents.[9] Not infrequently, wire access was lost during this endoscope exchange. The availability of large channel echoendoscopes that accommodate large-bore stents and thereby 'single-step' EUS-guided drainage has been a significant advance.[9] Nonetheless, multiple tools and procedural steps to achieve access, tract dilation, and multiple stent placements are still required. The NAVIX access device simplified and streamlined the procedure by enabling access, guidewire placement, and tract dilation with a single device. A blade at the end of the trocar, deployed when the trocar exited the catheter sheath, created a 3.5-mm opening to facilitate subsequent advancement of the balloon catheter over the trocar. Inflation of the anchor balloon secured access to the pseudocyst during the procedure. The anchor balloon also stabilized the position of the dilation balloon during tract dilation, countering the tendency for the balloon to slip forward or backward during dilation.

Multiple large-bore double pigtail plastic stents are widely used for pseudocyst drainage.[4,17] Talreja *et al.*[26] in 2008 reported on the use of a fully covered 10 mm × 60 mm biliary self-expanding metal stent (Viabil; Conmed, Utica, NY) for pseudocyst drainage. A 10-Fr plastic stent was inserted either alongside ($n$ = 4) or through ($n$ = 14) the metal stent lumen to prevent migration. The authors reported a 95% technical success rate with a 75% complete resolution of fluid collections. However, if superinfection were accounted for, there was a high complication rate of over 40%, including one internal stent migration. The AXIOS stent is a dual flanged fully covered nitinol braid stent designed to provide robust anchorage across luminal structures. Unlike tubular stents, the ends do not extend into the lumens. The AXIOS stent's design enables it to appose the pseudocyst or gallbladder to the wall of the duodenum

or stomach. This should permit safer decompression of the collection drained when compared to the Viabil stent, initially manufactured for biliary indication.

In this study, the safety and efficacy of the NAVIX access device used in conjunction with the AXIOS delivery system and stent as a kit was investigated in six pigs. Three pigs were kept alive and were without infection or behavioral changes 4 weeks post-implantation and 4 weeks post-stent removal. Minimal tissue injury was seen after the stents were removed and the fistula between the stomach and gallbladder remained patent throughout the 4-week post-stent removal observation. The AXIOS stent was well tolerated by both the stomach and gallbladder tissues, as confirmed by our weekly endoscopic inspection, gross necropsy and histopathology. This validates our previous experience using the AXIOS stent in the porcine model.[15] Recently, Takao *et al.* reported on the use of the AXIOS stent for internal drainage of pancreatic pseudocysts as well as the gallbladder in humans and the system was found to be feasible, safe and effective.[27] EUS-guided gallbladder drainage can offer the ability to bypass altogether the complications associated with surgery in patients who are at high risk, such as elderly patients or patients with comorbidities. Patients with unresectable malignancies can also benefit from this technique of drainage since it can offer them long-term palliation.

In conclusion, EUS-guided drainage using a kit consisting of the NAVIX access device and AXIOS stent delivery system was found to be technically feasible in the porcine model. This kit can potentially be used to drain other fluid collections adjacent to the gastrointestinal tract as well as to create anastomoses such as gastrojejunal and colo-colonic to bypass obstructing malignancies.[28] The device is currently awaiting FDA clearance after the completion of a multi-center trial. The benefit of this kit, combined with the Axios stent, is the ability to appose the lumen of the gallbladder to the duodenal wall followed by the deployment of a large-diameter stent, creating a permanent fistula. This will enable many future applications such as creating of cystogastrostomy, hepatico-jejunostomy, as well as gastrojejunostomy. Clinical evaluation of this novel kit for transluminal access and drainage are warranted.

## DISCLOSURE

Dr. Kenneth Binmoeller is Chief Medical Officer of and a stakeholder in Xlumena Inc; Dr. Ioana Smith and Dr. Monica Gaidhane have no conflicts of interest or financial ties to disclose; and Dr. Michel Kahaleh has received grant support from Boston Scientific, Fujinon, EMcison, Xlumena, MaunaKea and MI Tech, and He is a consultant for Boston Scientific and Xlumena.

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