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(54) **METHODS, DEVICES, KITS AND SYSTEMS FOR DEFUNCTIONALIZING THE GALLBLADDER**

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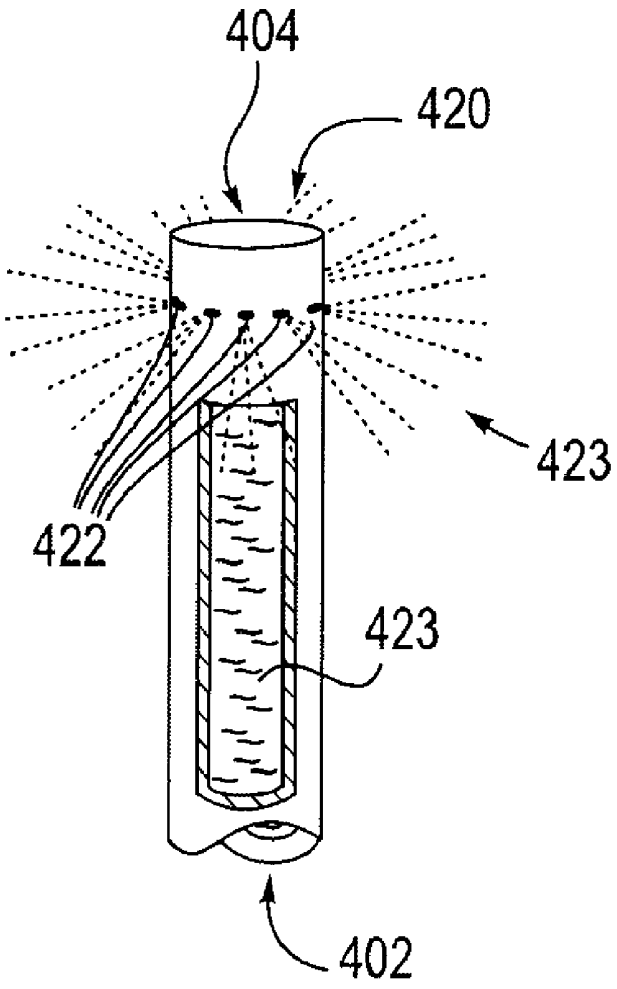
(57) **ABSTRACT**

The application discloses devices, systems, kits and methods for treating biliary disease. Device comprise, for example, a component configured for deployment to a lumen of a gallbladder or gallbladder duct which has a proximal end and a distal end with a lumen extending therethrough and a fluid or gas delivery apparatus at its distal end.



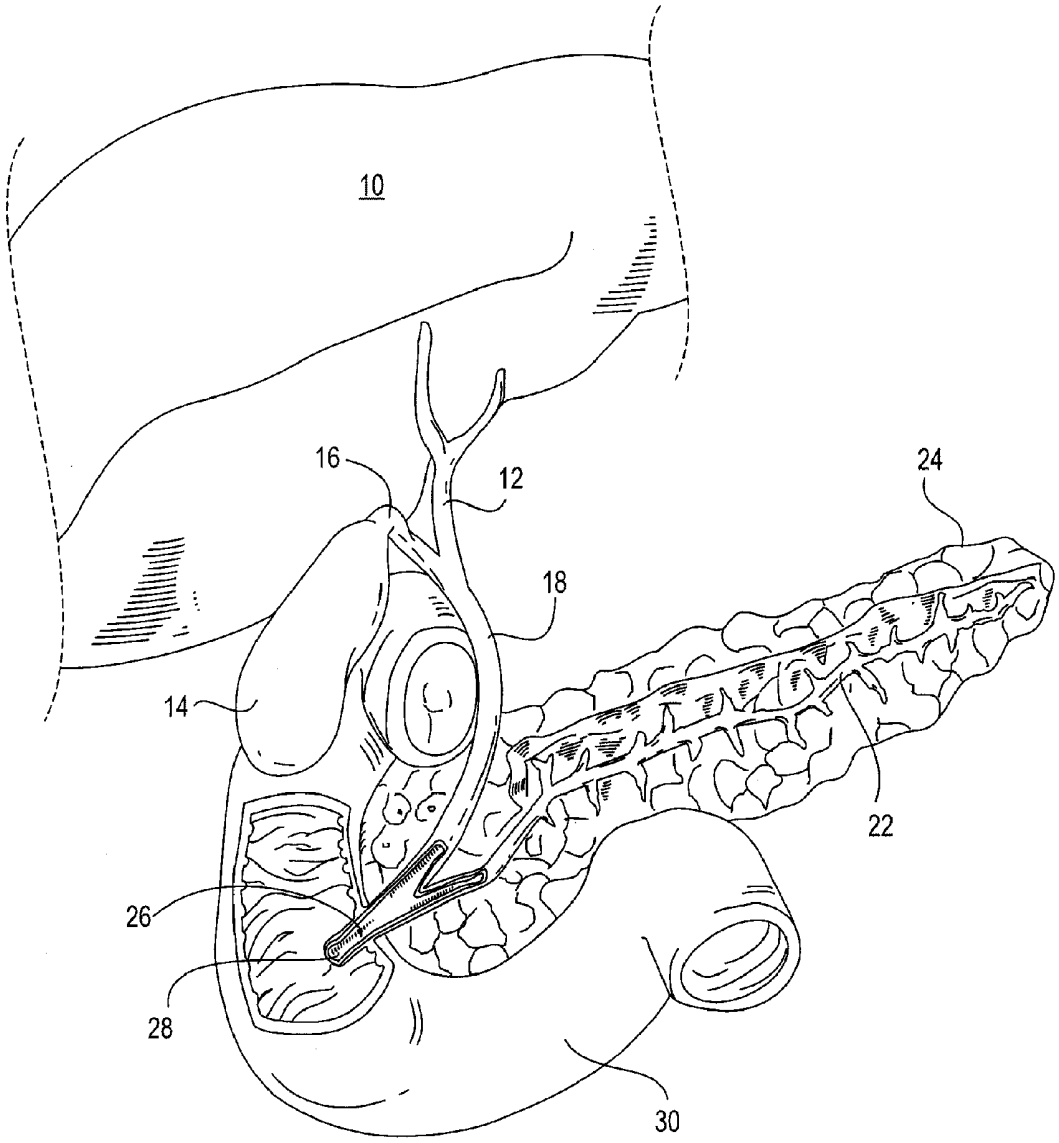


FIG. 1

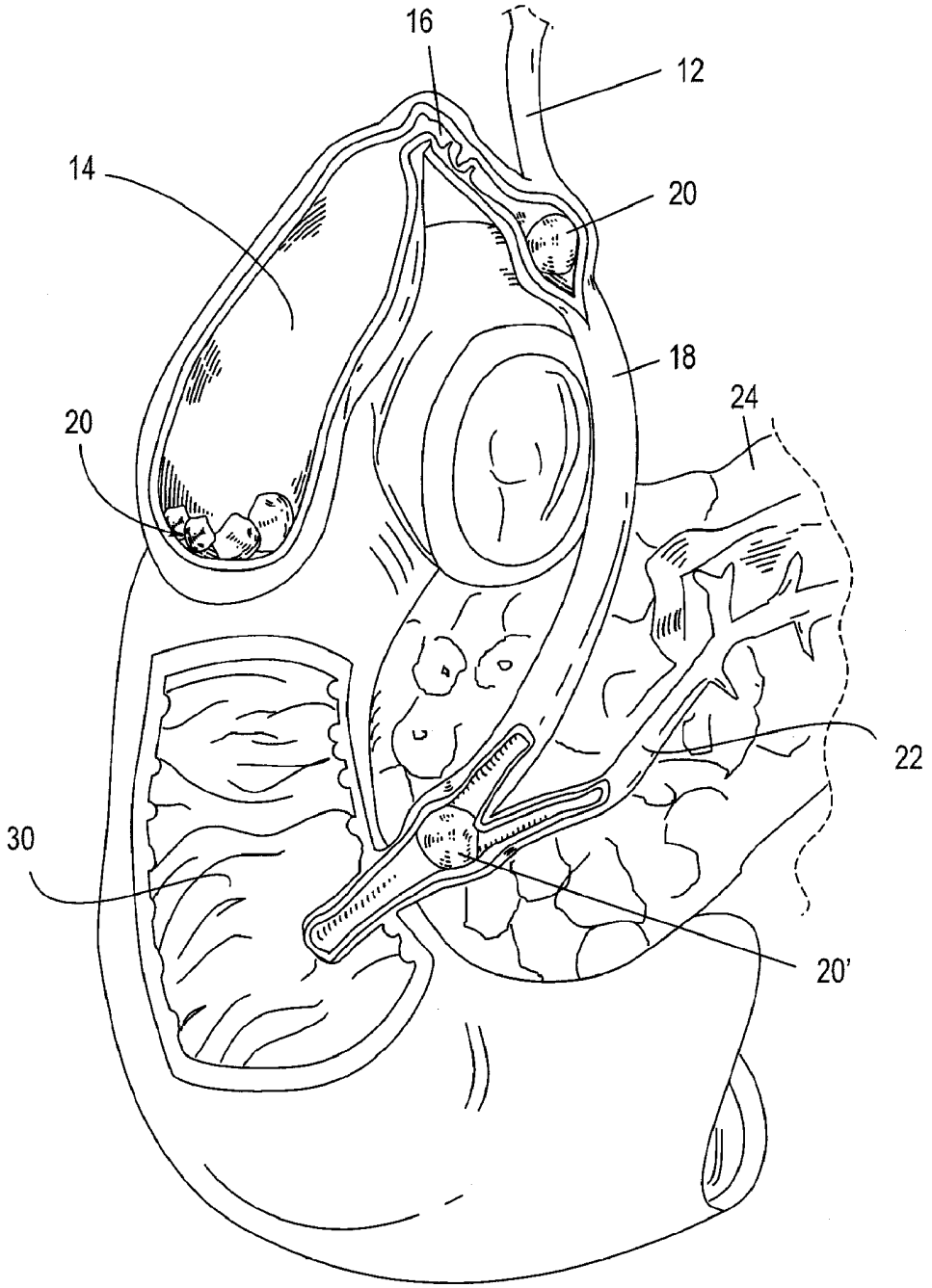


FIG. 2

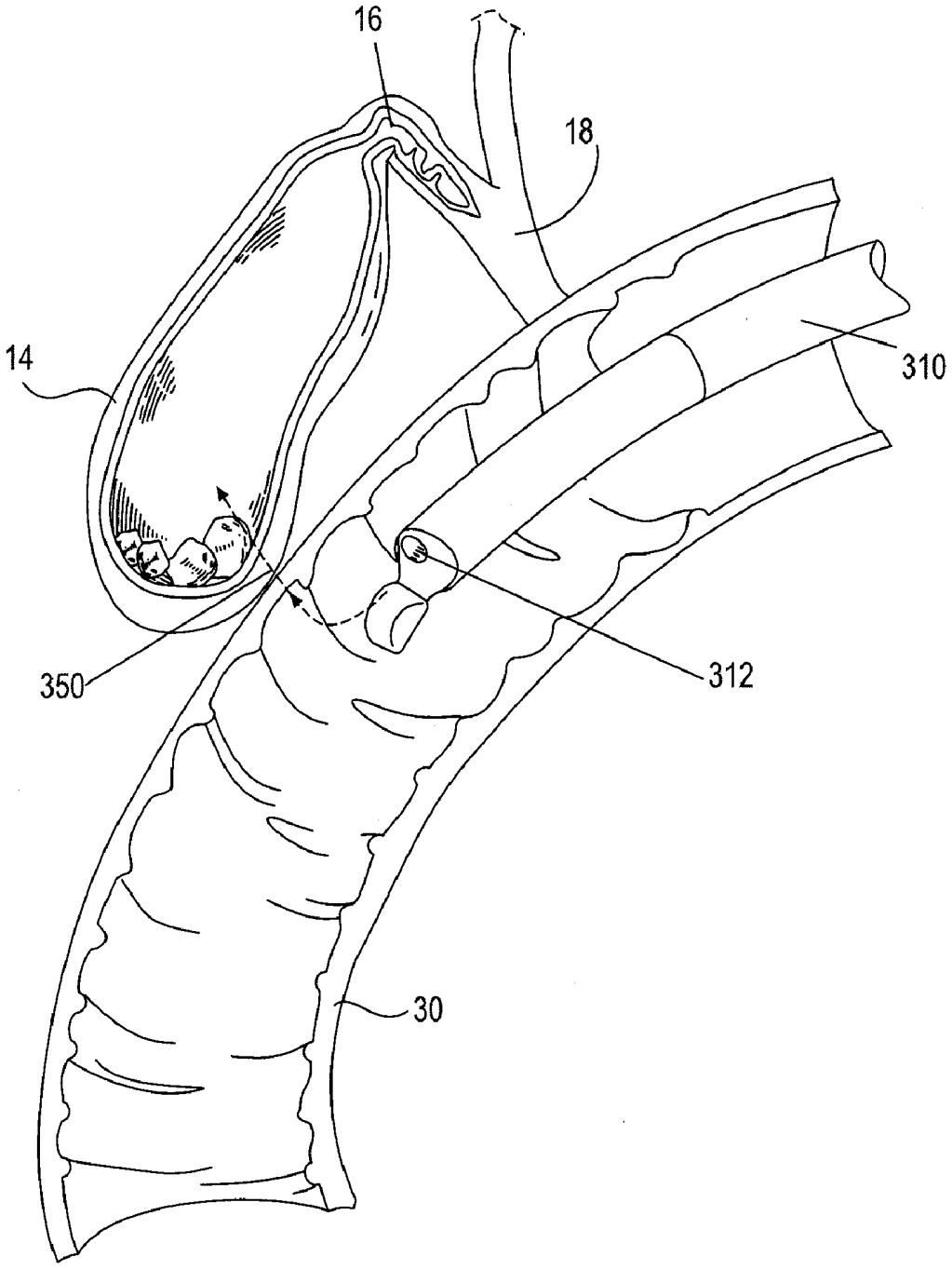


FIG. 3

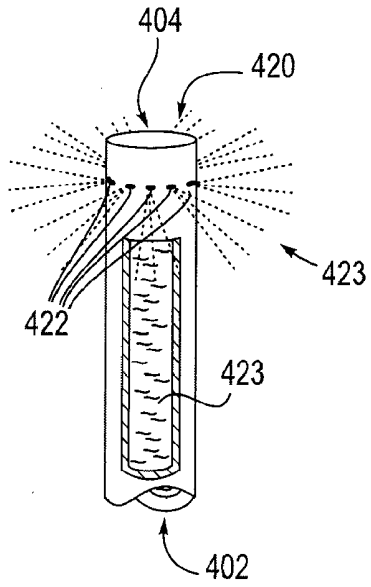


FIG. 4A

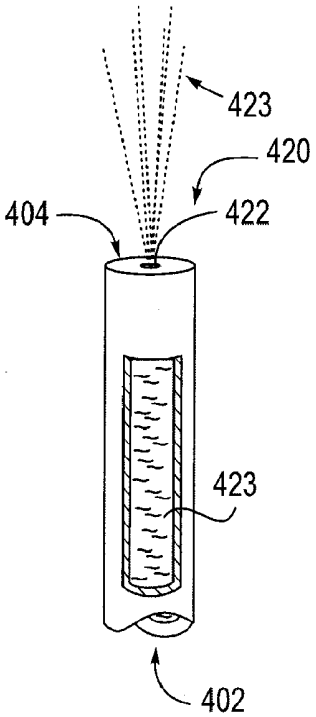


FIG. 4B

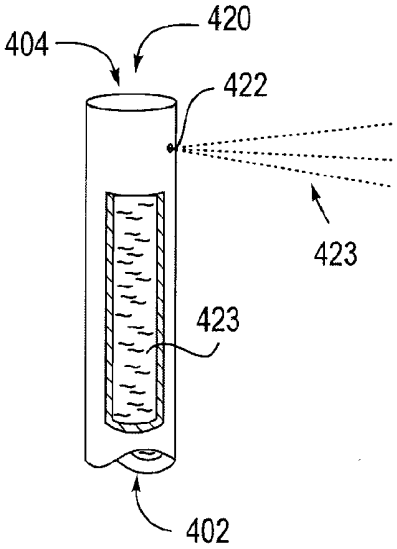


FIG. 4C

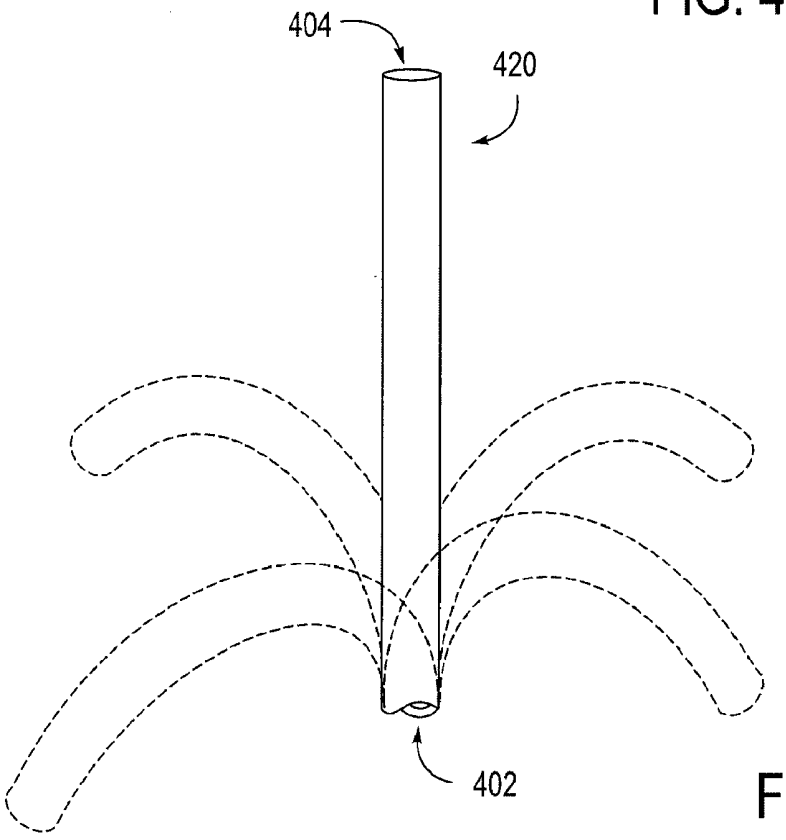


FIG. 4D

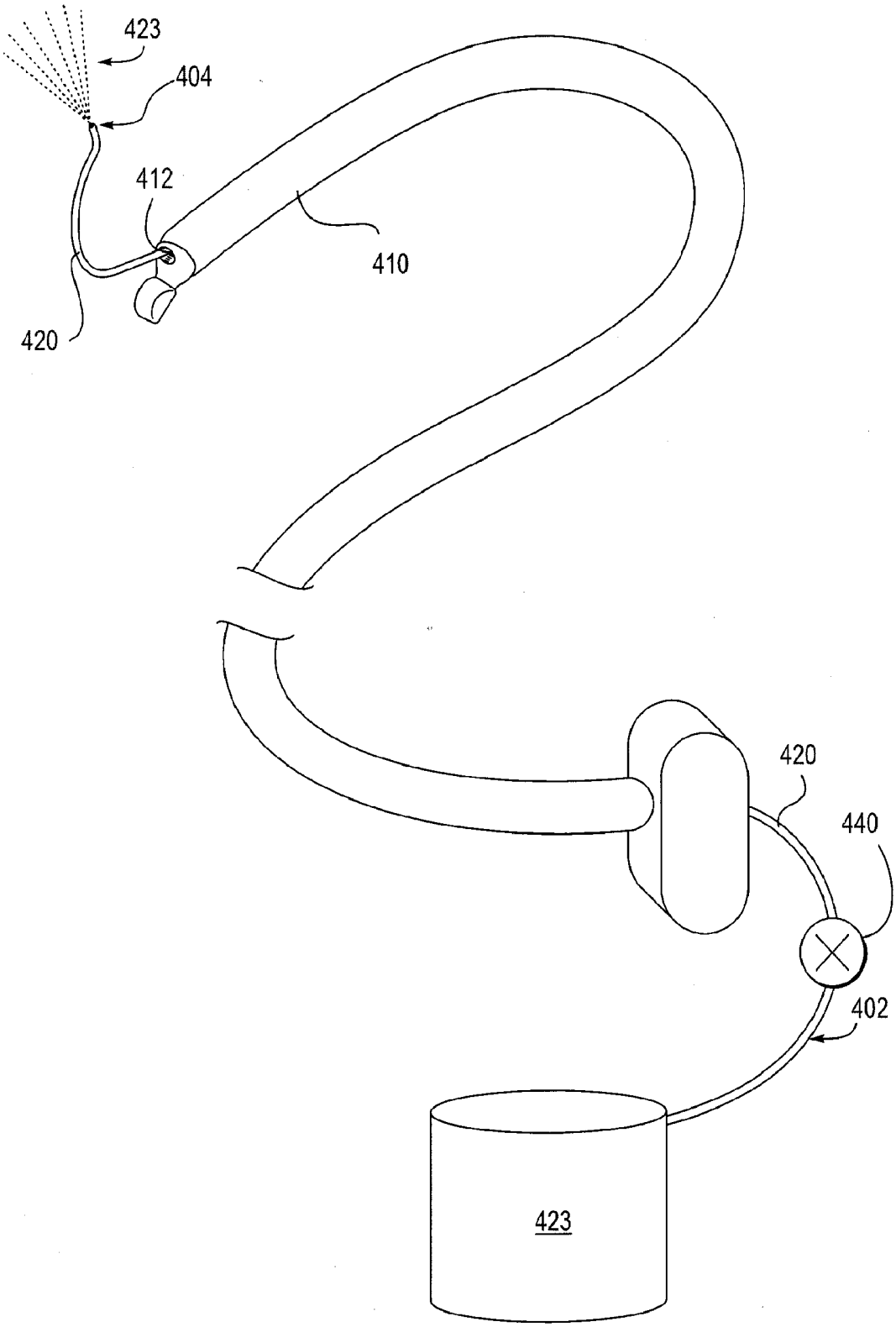


FIG. 4E

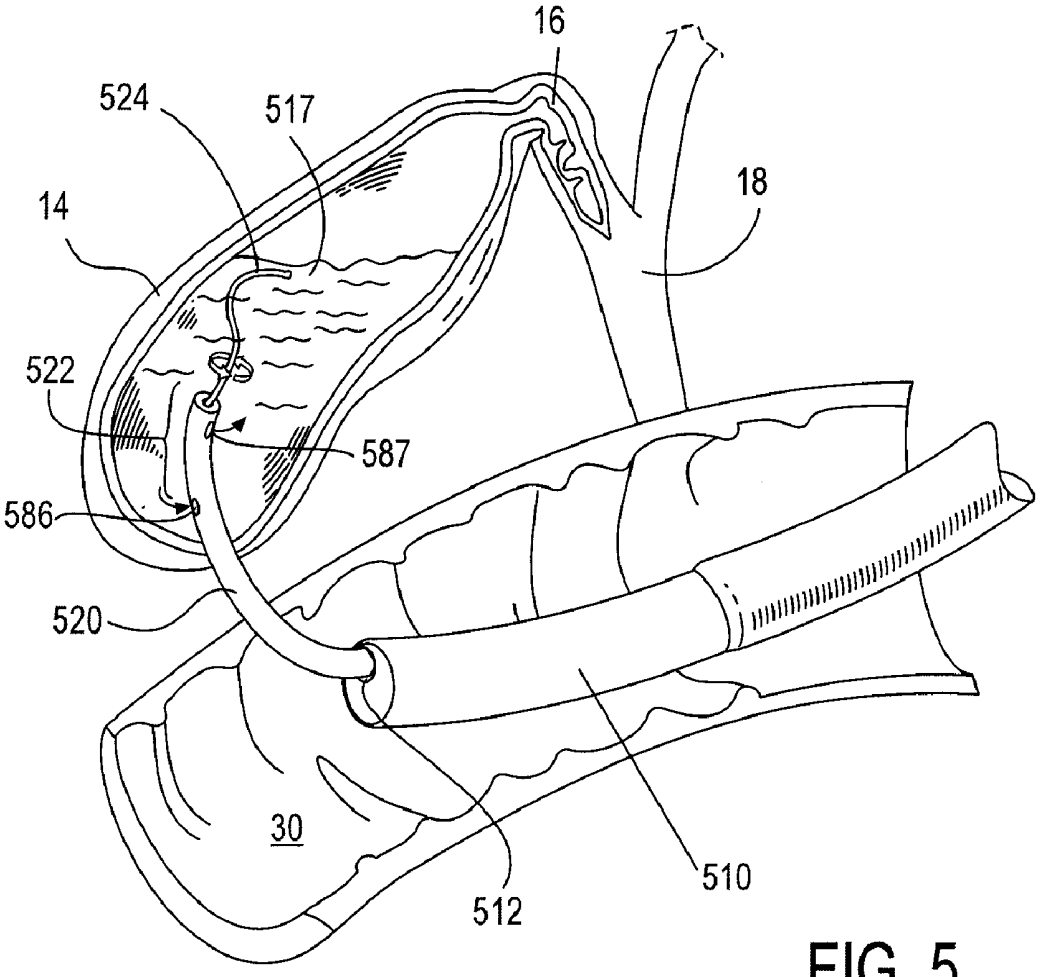


FIG. 5

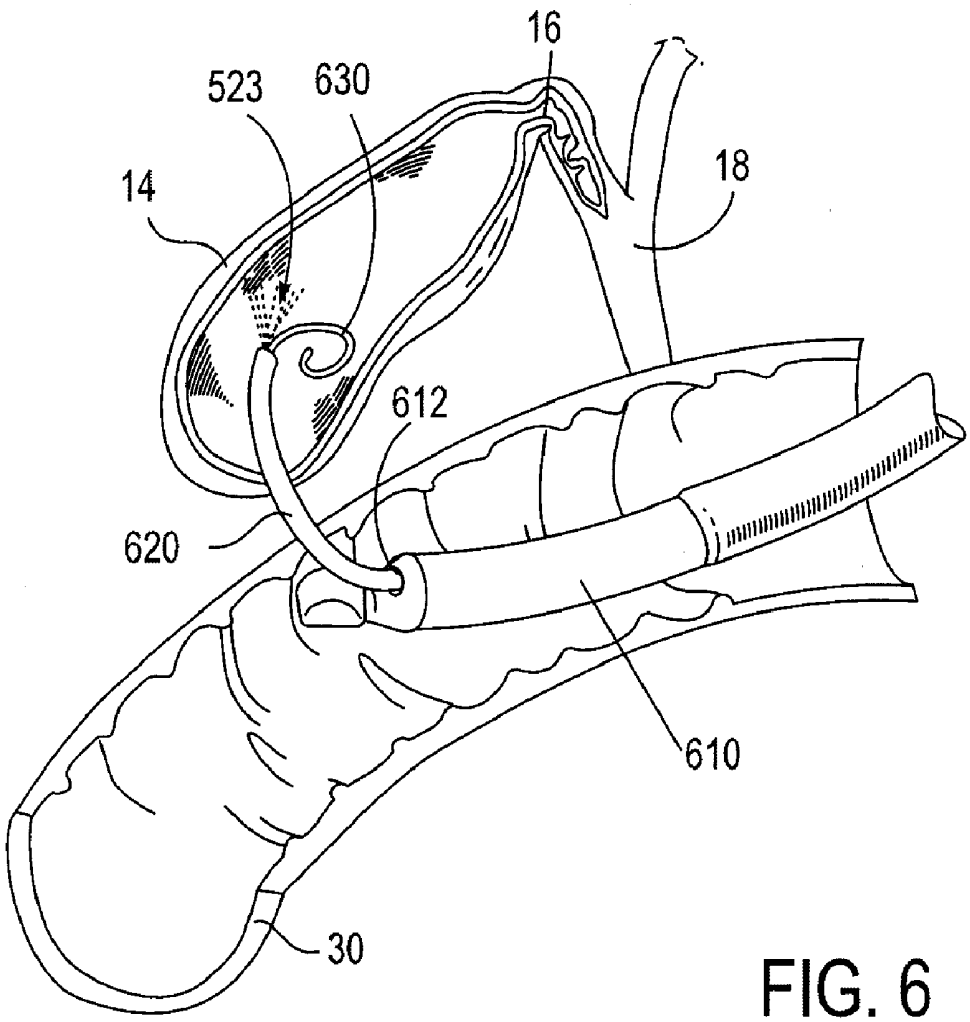


FIG. 6

METHODS, DEVICES, KITS AND SYSTEMS FOR DEFUNCTIONALIZING THE GALLBLADDER

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. 60/991,682, filed Nov. 30, 2007, and Application No. 61/033,368 filed Mar. 3, 2008, which application are incorporated herein by reference.

[0002] This application has related subject matter to U.S. patent application Ser. No. 12/277,338, filed Nov. 25, 2008, entitled "Methods, Devices, Kits and Systems for Defunctionalizing the Cystic Duct" by Jacques Van Dam, J. Craig Milroy, and R. Matthew Ohline and U.S. patent application Ser. No. 12/_____, filed Nov. _____, 2008, entitled, "Biliary Shunts, Delivery Systems, Methods of Using the Same, and Kits Therefor" by Jacques Van Dam, J. Craig Milroy, and R. Matthew Ohline (identified as Attorney Docket No. 36233-701.201), which applications are incorporated herein by reference.

FIELD OF THE INVENTION

[0003] The invention described in this patent application addresses challenges confronted in the treatment of biliary disease. Biliary disease includes conditions affecting the gallbladder, cystic duct, and common bile duct.

Biliary System Function and Anatomy:

[0004] Bile is a greenish-brown digestive fluid produced by the liver **10** illustrated in FIG. **1**, and is vital for the digestion of fatty foods. Bile is secreted by liver cells and collected by a network of ducts that converge at the common hepatic duct **12**. While a small quantity of bile drains directly into the lumen of the duodenum **30** (the section of small intestine immediately downstream of the stomach), most travels through the common hepatic duct **12** and accumulates in the lumen of the gallbladder **14**. Healthy gallbladders are pear-shaped sacs with a muscular wall that, on average, measure 10 cm in length and can store approximately 50 ml of fluid within its lumen. When fatty foods are ingested, the hormone cholecystokinin is released, which causes the gallbladder **14** to contract. Contraction of the gallbladder **14** forces bile to flow from the gallbladder **14**, through the cystic duct **16**, into the common bile duct **18**, out the papilla **28**, and finally into the duodenum **30** of the small intestine. Here, it mixes and reacts with the food that exits the stomach. The Sphincter of Oddi **26** controls secretions from the liver, pancreas **24**, and gallbladder **14** into the duodenum **30** of the small intestine. The opening on the inside of the descending duodenum **30** after the Sphincter of Oddi **26** is called the major duodenal papilla **28** (of Vater). Together, the biliary ducts, the gallbladder **14**, the cystic duct **16** and the common bile duct **18** comprise the biliary system (FIG. **1**).

[0005] The pancreas **24** is a gland organ in the digestive and endocrine system of vertebrates. It is both an endocrine gland (producing several important hormones, including insulin, glucagon, and somatostatin), as well as an exocrine gland, secreting pancreatic juice containing digestive enzymes that pass to the small intestine. These enzymes help in the further breakdown of the carbohydrates, protein, and fat in the chyme. The pancreatic duct **22**, or duct of Wirsung, is a duct joining the pancreas **24** to the common bile duct **18** to supply pancreatic juices which aid in digestion provided by the exocrine pancreas. The pancreatic duct **22** joins the common bile duct **18** just prior to the major duodenal papilla **28**, after which both ducts perforate the medial side of the second portion of the duodenum **30** at the major duodenal papilla.

Biliary Disease:

[0006] The most common problem that arises in the biliary system is the formation of gallstones, a condition called cholelithiasis. Approximately 20 million Americans have gallstones, and about 1-3% will exhibit symptoms in any given year. In the US, gallstones are more common among women, with 25% of women having gallstones by the age of 60 and 50% by the age of 75. Pregnancy and hormone replacement therapy increase the risk of forming gallstones. Prevalence is lower for American men: approximately 25% will develop gallstones by the age of 75. In the US, gallstones are responsible for the highest number of hospital admissions due to severe abdominal pain.

[0007] Gallstones **20**, **20'** are most often composed of cholesterol, but may also be formed from calcium bilirubinate, in which case they are called pigment stones. They range in size from a few millimeters to several centimeters, and are irregularly shaped solids resembling pebbles. They can form in the gallbladder **14**, cystic duct **16**, and/or the common bile duct **18** (FIG. **2**). By themselves, gallstones **20** do not necessarily result in disease states. This is the case 90% of the time. However, stones can cause infection and inflammation, a condition known as cholecystitis, which is generally the result of restricting or blocking the flow of bile from the gallbladder **14** and common bile duct **18**, or the fluids secreted by the pancreas **24**.

[0008] Gallbladder disease may be chronic, and patients who suffer from this may periodically experience biliary colic. Symptoms include pain in the upper right abdomen near the ribcage, nausea, and/or vomiting. The pain may resolve within an hour of onset, may prove unresponsive to over-the-counter medicines, and may not decrease with changes of position or the passage of gas. Recurrence is common, with pain often recurring at the same time of day, but with frequency of less than once per week. Fatty or large meals may cause recurrence several hours after eating, often awakening the patient at night. Patients may elect to suffer from these symptoms for very long periods of time, such as years or even decades.

[0009] Patients with chronic cholecystitis have gallstones and low-grade inflammation. Untreated, the gallbladder **14** may become scarred and stiff over time, leading to a condition called dysfunctional gallbladder. Patients who have chronic cholecystitis or dysfunctional gallbladder may experience gas, nausea, and abdominal discomfort after meals, and chronic diarrhea.

[0010] Acute cholecystitis (a surgical emergency) develops in 1-3% of those with symptomatic gallstone disease, and is due to obstruction of the common bile duct **18** or cystic duct **16** by stones or sludge. Symptoms are similar to biliary colic, though they are more severe and persistent. Pain in the upper right abdomen can be constant and severe, the intensity may increase when drawing breath, and it may last for days. Pain may radiate to the back, under the breastbone or the shoulder blades, and it may be perceived on the left side of the abdomen. In addition to nausea and vomiting, one third of patients experience fever and chills. Complications from acute cholecystitis can be serious and life threatening, and include gangrene, abscesses, perforation of the gallbladder **14** which can

lead to bile peritonitis, pus in the gallbladder wall (empyema), fistulae, and gallstone ilius (when a gallstone creates a blockage in the small intestine).

[0011] When gallstones **20'** become lodged in the common bile duct **18** (FIG. **2**), the condition is known as choledocholithiasis. Symptoms for this condition include pain, nausea and vomiting, and some patients develop jaundice, have dark urine and/or lighter stools, rapid heartbeat, and experience an abrupt drop in blood pressure. These symptoms can also be accompanied by fever, chills, and/or severe pain in the upper right abdomen. Complications from choledocholithiasis can also be very serious, and include infection of the common bile duct **18** (cholangitis) and inflammation of the pancreas **24** (pancreatitis).

[0012] A smaller patient population suffers from gallbladder disease that occurs in the absence of gallstones. This condition, called acalculous gallbladder disease, can also be chronic or acute. Chronic acalculous gallbladder disease, also called biliary dyskinesia, is thought to be caused by motility disorders that affect the gallbladder's ability to store and release bile. Acute acalculous gallbladder disease occurs in patients who suffer from other serious illnesses which can lead to inflammation of the gallbladder **14** because of a reduction in the supply of blood to the gallbladder **14** or a reduced ability to contract and empty bile into the duodenum **30**.

[0013] Cancer can also develop in the gallbladder **14**, though this condition is rare. Gallstones have been found in 80% of patients with gallbladder cancer. Gallbladder cancer typically develops from polyps, which are growths inside the gallbladder **14**. When polyps 15 mm across or larger are observed, the gallbladder is removed as a preventive measure. Polyps smaller than 10 mm are widely accepted as posing low risk and are not generally removed. When detected early, before the cancer has spread beyond the mucosa (inner lining) of the gallbladder, the 5-year survival rate is approximately 68%. However, gallbladder cancer is not usually detected until patients are symptomatic, by which time the disease is more advanced.

Treatment of Biliary Disease:

[0014] The most effective treatment for biliary disease has been surgical removal of the gallbladder **14**, a procedure called cholecystectomy. Surgical removal of the gallbladder **14** is indicated for patients who experience a number of less severe gallstone attacks, cholecystitis, choledocholithiasis, pancreatitis, acalculous biliary pain with evidence of impaired gallbladder **14** emptying, those at high risk for developing gallbladder cancer, and those who have previously undergone endoscopic sphincterotomy for common bile duct stones. Other treatment modalities exist and are frequently used, but gallbladder disease tends to recur in the majority of patients who forgo cholecystectomy and pursue alternatives. Removal of the gallbladder **14** is highly successful at permanently eliminating biliary disease. Cholecystectomy is one of the most commonly performed procedures on women. The gallbladder **14** is not an essential organ, and after a period of adjustment post surgery, patients tend to return to more or less normal digestive function.

[0015] Cholecystectomy can be performed either as open surgery, which requires a single larger incision in the upper right abdomen, or laparoscopic surgery, in which several small instruments are inserted through much smaller incisions in the abdomen. Approximately 80% of cholecystectomies are performed laparoscopically. The primary benefits of this minimally invasive approach are faster recovery for the patient, and a reduction in overall healthcare costs. Patients who receive laparoscopic cholecystectomy are usually released the same day. By contrast, patients receiving open cholecystectomies typically spend 5-7 days in a hospital before release. 5-10% of laparoscopic procedures convert to open procedures when difficulties arise, such as injury to major blood vessels, inadequate access, inadequate visualization, previous endoscopic sphincterotomy, and thickened gallbladder wall. Complications from cholecystectomy (open or laparoscopic) include bile duct injuries (0.1-0.5% for open, 0.3-2% with a declining trend for laparoscopic), pain, fatigue, nausea, vomiting, and infection. In up to 6% of cases, surgeons fail to identify and remove all gallstones present.

[0016] In some cases, the degree of infection and inflammation prevents patients from undergoing immediate cholecystectomy. In these cases, the gallbladder **14** must be treated with antibiotics and anti-inflammatory agents, and drained through a tube into a reservoir outside the abdomen. Placement of this tube occurs in a procedure called percutaneous cholecystostomy, in which a needle is introduced to the gallbladder **14** through the abdomen, fluid is withdrawn, and a drainage catheter is inserted. This catheter drains into an external bag which must be emptied several times a day until the tube is removed. The drainage catheter may be left in place for up to 8 weeks. In cases where no drainage catheter is inserted, the procedure is called gallbladder aspiration. Since no indwelling catheter is placed, the complication rate for gallbladder aspiration is lower than that of percutaneous cholecystostomy.

[0017] Treatment methodologies other than cholecystectomy include expectant management, dissolution therapy, endoscopic retrograde cholangiopanctreatograpy (ERCP) with endoscopic sphincterotomy, and extracorporeal shockwave lithotripsy (ESWL).

[0018] Expectant management is appropriate for patients who have gallstones but no symptoms, and for non-emergency cases with less severe symptoms. This approach is not recommended when patients are in high risk categories (e.g. high risk for gallbladder cancer) or have very large gallstones (e.g. greater than 3 cm).

[0019] Oral dissolution therapy involves the administration of pills containing bile acids that can dissolve gallstones. This approach is only moderately effective, and the rate of recurrence of gallstones after completion of treatment is high. It is not appropriate for patients with acute inflammation or stones in the common bile duct (more serious conditions). Dissolution therapy tends to be more effective for patients with cholesterol stones, and is sometimes used in conjunction with lithotripsy. Despite its relative ineffectiveness, it is costly: treatment can last up to 2 years and the drugs cost thousands of dollars per year.

[0020] Related to oral dissolution therapy is contact dissolution, a procedure that involves injection of a solvent such as methyl tert-butyl ether (MTBE) directly into the gallbladder **14**. This approach is highly effective at dissolving gallstones, but patients may experience severe burning pain.

[0021] ERCP (endoscopic retrograde cholangiopancreatography) is a procedure in which an endoscope is introduced through the mouth of a patient, past the stomach to the papilla **28**, where the common bile duct **18** empties into the duodenum **30**. The overall goal of the procedure is to insert instruments and tools into the common bile duct **18** via the papilla **28** in order to treat biliary disease. Typically, endo-

scopic sphincterotomy is performed, which is a procedure that enlarges the opening of the papilla **28** in the small intestine. This can be accomplished surgically or via balloon dilation. Contrast agent is introduced into the common bile duct **18** to visualize the biliary tree fluoroscopically. Tools for clearing blockages, such as mechanical lithotripsy devices, can be deployed to crush gallstones and remove the resulting debris. Drainage catheters and stents may also be inserted to facilitate the drainage of bile past obstructions. Complications from this challenging procedure occur at a rate of 5-8%, and include recurrence of stone formation, pancreatitis, infection, bleeding, and perforation.

[0022] Extracorporeal shockwave lithotripsy (ESWL) is a technique in which focused, high-energy ultrasound is directed at the gallbladder **14**. The ultrasound waves travel through the soft body tissue and break up the gallstones. The resulting stone fragments are then usually small enough to pass through the bile duct into the small intestine. Oral dissolution therapy is often used in conjunction with ESWL. This treatment is not in common use, as less than 15% of the patient population are good candidates. However, ESWL is used to treat patients who are not candidates for surgery. Complications from ESWL include pain in the gallbladder area, pancreatitis, and failure of the gallstone fragments to pass into the small intestine.

SUMMARY OF THE INVENTION

[0023] An aspect of the invention is directed to devices for treating biliary disease. Suitable devices comprise: a component configured for defunctionalizing a gallbladder of a patient which has a proximal end and a distal end with a lumen extending therethrough and one or more apertures at a distal end adaptable to deliver a fluid to a lumen within the gallbladder or a gallbladder duct. Other suitable devices comprise: a means for defunctionalizing a gallbladder of a patient having a proximal end and a distal end with a lumen extending therethrough and one or more means for accessing the lumen at a distal end adaptable to deliver a fluid to a lumen within the gallbladder or a gallbladder duct. The distal end of the device can be configured to provide an angular orientation, to deliver a fluid with at least one of a 360 degree radial pattern, a sharp stream, and a cone shape, and/or to have an articulating member. Additionally, the device can further be adapted to apply a vacuum. The devices can further provide a means for applying a vacuum. In some instances, the lumen includes a means for restricting fluid flow. In some instances, the distal end is adapted to apply an adhesive to a lumen of the gallbladder. Devices can also be configured for deployment by an endoscope, a needle, guidewire, or guidance catheter. In some instances, the lumen is configurable to provide restrictable fluid flow, such as with the use of one or more fluid control components. Alternatively, one or more valves can be used, including at least one of a flow-restrictor or one-way valve. Additionally, devices can be configured such that they are flexible. In some configurations, the device is an elongate tube adapted and configured to extend into the gastrointestinal tract.

[0024] An aspect of the invention is directed to a method of treating biliary disease. The method comprises the steps of: accessing a lumen associated with a gallbladder or a gallbladder duct; defunctionalizing at least one of the gallbladder duct or the gallbladder; and leaving the gallbladder in situ. Additionally, the step of defunctionalizing the gallbladder can further comprise the step of delivering a substance to at least one of the gallbladder duct or the gallbladder, for example, such that it occupies a lumen of at least one of the gallbladder duct or the gallbladder, and/or is one or more of antibiotics, inflammatory agents, and anti-inflammatory agents. Delivery of substances can be performed sequentially or concurrently, as desired. Another aspect of the method includes the step of preventing bile from entering the gallbladder lumen. In some aspects the method further comprises the step of localizing the gallbladder via endoscopic ultrasound. In other aspects of the invention, the method can comprise the step of accessing the gallbladder via the gastrointestinal tract, such as via a duodenum. In still other aspects of the methods the step of defunctionalizing at least one of the gallbladder duct or the gallbladder further comprises one or more of sclerosing, necrotizing or ablating tissue. Suitable ablation techniques include, for example, cryoablation, thermal ablation, chemical ablation, radio frequency ablation, microwave ablation, and ultrasound ablation. Fluid delivery can be achieved with an angular orientation, or with at least one of a 360 degree radial pattern, a sharp stream, and a cone shape. Moreover, the step of delivering a fluid can be achieved with a device comprising an articulating member. Defunctionalizing at least one of the cystic duct or the gallbladder can further comprise applying a vacuum to a lumen of the cystic duct or the gallbladder, applying an adhesive to the lumen of the gallbladder duct or the gallbladder, and/or physically blocking a lumen of the gallbladder duct or the gallbladder. In some instances, the additional steps of altering gallstones and/or removing gallstones can also be performed. Similarly, obstructions can be cleared within the gallbladder. In other aspects of the invention, the method includes the step of visualizing a treatment area. Additionally, the device can be delivered via an endoscope, via a needle, via a guidewire or via a guidance catheter. The method can also include the step of restricting flow from the gallbladder lumen to the gastrointestinal tract, such as by operating a valve to restrict fluid flow. Additionally, the step of defunctionalizing the gallbladder can be performed in situ. The step of defunctionalizing can be achieved by delivering a substance into a space within the gallbladder, such as by delivering a gel or foam. In some instances the delivered substance, such as the gel or foam, can be activated in situ. Moreover, the amount of substance delivered can fill, or substantially fill, the gallbladder lumen either upon delivery or activation. Defunctionalizing can also be achieved by one or more of sclerosing or necrotizing a tissue within the gallbladder, such as by using an ablation technique such as cryoablation, thermal ablation, chemical ablation, radio frequency ablation, ultrasound ablation, and microwave ablation.

[0025] Yet another aspect of the invention is directed to kits for treating biliary disease. Kits can comprise: (a) a device adaptable to deliver to a lumen of a gallbladder or gallbladder duct; and optionally (b) a compound for delivery to a tissue. Additional components of a kit can include, for example, one or more of: a catheter, a needle, a guidewire, and a guidance catheter. Additionally, the kits can include an ablation device. One or more agents can also be included in the kit including, for example, a sclerosing agent, antibiotics, inflammatory agents, anti-inflammatory agents, biocompatible gels, and biocompatible foams. Still other components of the kits can include, for example, one or more of a pair of scissors, a scalpel, a swab, a syringe, a hemostat, a lubricant, a needle, a snare, an antiseptic, and an anesthetic.

[0026] Another aspect of the invention is directed to the use of any of the devices disclosed herein for use in the treatment of biliary disease.

INCORPORATION BY REFERENCE

[0027] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0028] The novel features of the invention will be set forth with particularity in any claims presented based on this application. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0029] FIG. **1** illustrates an overview of the biliary system;

[0030] FIG. **2** illustrates the biliary system with gallstones;

[0031] FIG. **3** illustrates an endoscope accessing the biliary system via the intestinal system;

[0032] FIGS. **4**A-E illustrate fluid applicator embodiments;

[0033] FIG. **5**A illustrates a gallbladder defunctionalization method with a working fluid whose temperature is altered; and

[0034] FIG. **6** illustrates a gallbladder defunctionalization device in combination with a guidance element.

DETAILED DESCRIPTION OF THE INVENTION

[0035] Devices, systems, methods and kits provided herewith can obviate the need for a plurality of procedures, including, for example: 1) percutaneous cholecystostomy, 2) cholecystectomy, 3) percutaneous trans-hepatic cholangiography (PTHC), and 4) endoscopic retrograde cholangiopancreatography (ERCP). Additionally, disclosed treatment modalities enable treatment of a distal common bile duct **18** obstruction, e.g. secondary to pancreatic carcinoma, cholangiocarcinoma, and/or ampullary carcinoma. As will be appreciated by those skilled in the art, the conventional standard of care for treating biliary disease has been surgical removal of the gallbladder **14** and closure of the cystic duct **16**. While this has proven to be an effective mechanism for permanently eliminating biliary disease and its recurrence, the present invention seeks to accomplish the same end in a less invasive and less costly way. This may be achieved by treating biliary disease without requiring the removal of the gallbladder **14**. Methods and apparatus are described in this application that are intended to effectively treat biliary disease with the gallbladder **14** and cystic duct **16** left in situ by defunctionalizing the gallbladder.

Defunctionalization of the Gallbladder:

[0036] By treating the gallbladder in situ in such a way that the biliary disease necessitating treatment is addressed and the likelihood of recurrence is low or altogether eliminated, the need for additional treatment, e.g. cholecystectomy, may be obviated. One method for achieving these goals may be defunctionalization of the gallbladder. A gallbladder that is treated and remains in situ but is otherwise non-functional may lead to the desired result. Alternatively, for example, this goal may be achieved by altering the configuration of the gallbladder **14** in such a way that the underlying condition is addressed and prevented from recurring. The gallbladder can be accessed by any suitable mechanism including, percutaneously, endoscopically, laparoscopically, and the like. Moreover, any of the materials and substances delivered to the gallbladder can be delivered concurrently or sequentially. Delivery of substances can occur sequentially in time or the sequence of delivery can be separated by seconds, minutes, or hours.

[0037] A method of treating biliary disease involves using an endoscope **310** to access a region in the gastrointestinal (GI) tract (FIG. **3**) to which the gallbladder **14** is in close proximity **350**, locating the gallbladder **14**, accessing the gallbladder **14**, and then treating the underlying condition that led to the need for intervention (FIG. **3**). Treatments may also include, but are not limited to: providing for drainage of the gallbladder **14** and/or the biliary tree, delivering suitable substances or materials, such as antibiotics, inflammatory, and/or anti-inflammatory agents (any of which may be short-term acting, fast acting, or time release), and/or other substances (e.g. adhesives, bioadhesives, etc.) to the gallbladder **14** and/or biliary tree, removing gallstones **20**, facilitating the destruction and subsequent removal of gallstones, clearing obstructions, delivering catheters, delivering stents (drug coated or not drug coated), temporarily or permanently defunctionalizing the cystic duct **16**, temporarily or permanently defunctionalizing the gallbladder **14**. Devices and therapies can be delivered in a single treatment, with minimal likelihood of or necessity for follow-up or repeat procedures.

[0038] Localization of the gallbladder **14** can be performed via endoscopic ultrasound (EUS) by accessing the wall of the GI tract with an endoscope **310** as shown in FIG. **3**. Localization may also be achieved by any other method that visualizes anatomical features, such as fluoroscopy, x-rays, magnetic resonance imaging (MRI), computed axial tomography (CT) scans, ultrasound imaging from outside the body, or any method of anatomical imaging and visualization.

[0039] Once the gallbladder **14** has been located, it may be accessed and/or treated **350** through the wall of the GI tract (or any lumen in proximity to the gallbladder **14**) with tools and devices (e.g. needles, guidewires, guidance catheters, dilators, shunts, etc.) delivered through or by, for example, an endoscope **310**. Such tools and devices may be inserted down the length of the endoscope's working channel **312**, or loaded onto or near the distal end of the endoscope **310**. Alternately, tools and other devices may be used that do not require the aid of the endoscope for navigation or delivery. Direct visualization may be provided by the endoscope **310** during the procedure, as well as irrigation, suction, and insufflation.

[0040] Though the preferred location for accessing the gallbladder lumen is the duodenum **30**, it may also be readily achieved through the wall of other regions of the GI tract, such as the stomach or the jejunum, for example. Thus, any lumen in close proximity to the gallbladder **14** is a candidate for access to and treatment of the gallbladder **14** and other members of the biliary system.

[0041] In order to defunctionalize the gallbladder **14**, it may be beneficial to sclerose or necrotize the tissue inside the lumen of the gallbladder **14**. This may involve only the tissue within the gallbladder **14**, but it may also include, for example, the tissue comprising the cystic duct **16**, which is the passageway leading into the gallbladder **14** from the common bile duct **18**. Sclerosing or necrotizing the tissue within the gallbladder **14** may be achieved by using any ablating tech-

nique, such as cryoablation, thermal ablation, chemical ablation, radio frequency (RF) ablation, microwave ablation, and ultrasound ablation.

[0042] In the case of cryoablation, cold fluids (such as liquids, sprays, mists, and gases) may be applied to the walls of the lumen of the gallbladder **14** with an applicator **420** having a proximal end **402** and distal end **404** (FIG. **4**). Any non-solid sclerosing agent may be similarly applied with an applicator. Such fluids may be applied evenly so that the effect is consistent throughout the affected areas, or they may be applied selectively or unevenly. The applicator **420** optionally includes a user controllable valve **440**, as illustrated in FIG. **4**E, within its lumen to facilitate control and application of the fluids or gases during the defunctionalization process. The user controllable valve can be positioned proximally from the delivery tip.

[0043] During defunctionalization part or all of the walls may be treated. In order to have the ability to apply therapy anywhere within the gallbladder, it may be necessary to direct the application of such fluids by the applicator **420** at a variety of depths within the gallbladder **14**, and at any or all angular orientations. The applicator **420** has one or more apertures **422** in communication with a central lumen through which fluid **423** or material is delivered. As discussed above, a valve **440** is positioned within the interior lumen of the applicator **420** to provide control of the amount and timing of delivery. Different applicators **420** or nozzles may be useful for achieving this, such as those configurable to direct flow in a 360° radial pattern (FIG. **4**A), a sharp stream or a cone shape directed forward by the applicator (FIG. **4**B), or a sharp stream or a cone shape directed sideways by the applicator (FIG. **4**C). The applicator **420** may be capable of articulating so that it may be selectively aimed (FIG. **4**D). In order to distinguish treated areas from untreated areas, a pigment may be added to the fluid. Alternately, treated tissue may have a different appearance from untreated tissue due to the resulting sclerosis or necrosis. Applicators may be guided by one or more of a needle, a guidewire, and/or a guidance catheter, and controlled proximally by a clinician, as illustrated in FIG. **6**. Alternately, applicators may navigate freely within the gallbladder. Applicators may be delivered to the gallbladder lumen **14** through the tool channel **612** of an endoscope **610** and may remain within the endoscope during their use, or they may be guided into the gallbladder **14** using alternate guidance elements **630** (e.g. a needle, a guidewire, and/or a guidance catheter). In some instances, directly visualizing the devices and navigational devices used may also be desirable, and may facilitate control and treatment. Visualization may be achieved by any suitable mechanism known in the art, including, for example, endoscopic ultrasound (EUS), or by using a small daughter endoscope (e.g. a cystoscope), or by using catheters incorporating small imaging sensors at the distal end (e.g. Avantis' Third Eye) and fiber optic imaging bundles (e.g. Boston Scientific's SpyGlass). Visualization and guidance may also be achieved via external imaging methods, such as fluoroscopy (with or without the use of contrast agent), ultrasound, X-ray, etc.

[0044] Additionally, cryoablation can be used to effect treatment by flooding the entire gallbladder lumen or duct lumen with a fluid **517** (FIG. **5**). This can, for example, be performed with a liquid, but a gas may also be used. Filling the lumen, or substantially filling the lumen, with such a working fluid **517** ensures even distribution of treatment. The fluid or gas may be initially a first temperature and then be altered such that the temperature achieves a desired therapeutic level. An applicator for this approach may have one or more apertures **522** for introducing fluids **587** into the gallbladder and optionally withdrawing fluids **586** from the gallbladder. A stirrer **524** can be provided that stirs or mixes the fluid or gas **517** that is delivered into the lumen. This feature may ensure uniformity of properties throughout the working fluid or gas and increase the rate of temperature change (FIG. **5**). The working fluid **517** may be left in place, or actively withdrawn after treatment is completed. As will be appreciated from FIG. **5**, access to the gallbladder **14** can be achieved through the wall of the duodenum **30**.

[0045] In cases when the activatable material, such as a working fluid or gas **517**, remains in the gallbladder lumen or duct lumen, it may be selected so that it becomes a biocompatible gel or foam once it has reached a specific state, such as a low or high temperature, or contact with an activating agent, or when sufficient time has passed. The activating agent may be selected to be bile, so that the gel or foam becomes further activated in the presence of flow of bile. In this way, it a self-sealing mechanism is established. Such a foam or gel may also be selected so that it is bioabsorable, and is self dissipating after a desired period of time.

[0046] An amount of fluid, gas, or material delivered as described throughout can be such that it fills the gallbladder, substantially fills the gallbladder (e.g., fills more than 50% of the gallbladder, more than 75% of the gallbladder, more than 85% of the gallbladder, more than 90% of the gallbladder, more than 95% of the gallbladder, or more than 99% of the gallbladder) or is activatable to fill or substantially fill the gallbladder. Alternatively, in some instances, e.g., where a vacuum is applied, the amount of fluid, gas, or material delivered as described throughout can be such that it coats the interior lumen of the gallbladder, or substantially coats the interior lumen of the gallbladder (e.g., coats more than 50% of the gallbladder, more than 75% of the gallbladder, more than 85% of the gallbladder, more than 90% of the gallbladder, more than 95% of the gallbladder, or more than 99% of the gallbladder).

[0047] In contrast to cryoablation, thermal (or heat) ablation may be applied to effect treatment. The same methods outlined above for cryoablation may also be used in the application of therapies based on heat ablation. This includes using working fluids that may be applied using a spray applicator, working fluids that completely fill, or substantially fill, the lumen, working fluids that are introduced at a non-therapeutic temperature and then altered so that the temperature is increased to therapeutic levels, and fluids that becomes gels or foams at a desired elevated temperature. These techniques may be used with any fluid or non-solid sclerosing agents in addition to those described above. In another approach thermal ablation is achieved through the use of infrared light to heat the tissue comprising the gallbladder **14** and/or cystic duct **16**.

[0048] Another alternate method of defunctionalizing the gallbladder **14** involves applying a vacuum. After occlusion of, for example, the cystic duct **16**, application of a vacuum to the gallbladder lumen causes it to collapse to a smaller volume. The internal volume of the gallbladder lumen may be eliminated altogether. Making this collapsed volume permanent or semi-permanent results in the goal of defunctionalizing the gallbladder **14**. Substances may be applied to the gallbladder walls prior to the application of vacuum, such as a bioadhesives, sclerosing agents, or fluids used in cryo- or

thermal ablation. These fluids may serve to enhance the outcome or improve the efficacy of the treatment.

[0049] The devices and methods disclosed herein facilitate defunctionalizing the gallbladder without the need for surgery.

Kits:

[0050] All of the devices required to deliver and install a conduit, treat and/or defunctionalize the gallbladder, may be packaged in a kit. Bundling all devices, tools, components, materials, and accessories needed to perform these procedures into a kit may enhance the usability and convenience of the devices, and also improve the safety of the procedure by encouraging clinicians to use the items believed to result in the best outcomes. The kit may be single-use or reusable, or it may incorporate some disposable single-use elements and some reusable elements. The kit may contain, but is not limited to, the following: implantable and/or non-implantable devices; delivery devices (e.g. needles, guidewires, guidance catheters, dilators, etc.); balloon inflation/deflation accessories; syringes; fluid flow, temperature, and pressure measurement instruments; scissors; scalpels; clips; ablation catheters; endoscopic tools (e.g. lithotripsy devices, snares, graspers, clamps, forceps, etc.); fluids; gels; gas cartridges adaptable to communicate with the devices. The kit may be supplied in a tray, which organizes and retains all items so that they can be quickly identified and used.

Description of Other Uses:

[0051] The techniques and devices described in this application may prove beneficial in applications beyond their initial use in the treatment of biliary disease.

[0052] For example, they may prove to be an effective mechanism of treating cholangitis (infection of the common bile duct **18**). This condition is usually bacterial, and occurs when the bile duct is blocked by gallstones **20'** or a tumor. Traditional treatment involves the insertion a stent or drainage catheter into the common bile duct **18** to allow bile to drain into the duodenum from locations above the obstruction. Placement of a conduit into the gallbladder **14** may allow for an alternate method of draining bile and/or other fluids into the duodenum. Any blockage in the common bile duct **18** between the entrance of the cystic duct and the duodenum may be treated in this way. See FIG. **2**.

[0053] Another use of the devices and techniques described herein is for drainage of any body lumen into another body lumen in proximity, for example, the drainage of pancreatic pseudocysts.

[0054] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

What is claimed:

1. A device for treating biliary disease comprising: a component configured for defunctionalizing a gallbladder of a patient which has a proximal end and a distal end with a lumen extending therethrough and one or more apertures at a distal end adaptable to deliver a material to a lumen within the gallbladder or a gallbladder duct.

2. The device of claim **1** wherein the distal end has an angular orientation relative to a length of the component.

3. The device of claim **1** wherein the distal end is adapted to deliver a material with at least one of a 360 degree radial pattern, a sharp stream, and a cone shape.

4. The device of claim **1** wherein the distal end has an articulating member.

5. The device of claim **1** further is adapted to apply a vacuum.

6. The device of claim **1** wherein the distal end is adapted to apply an adhesive to a lumen of the gallbladder.

7. The device of claim **1** wherein the device is configured for deployment by an endoscope.

8. The device of claim **1** wherein the device is configured for deployment using at least one of a needle, guidewire, or guidance catheter.

9. The device of claim **1** wherein the lumen is configurable to provide restrictable fluid flow.

10. The device of claim **9** further comprising one or more fluid control components.

11. The device of claim **1** further comprising a valve.

12. The device of claim **11** wherein the valve is at least one of a flow-restrictor or one-way valve.

13. The device of claim **1** wherein the device is flexible.

14. The device of claim **1** wherein the device is an elongate tube adapted and configured to extend into the gastrointestinal tract.

15. A method of treating biliary disease comprising:

a. accessing a lumen associated with a gallbladder or a gallbladder duct;

b. defunctionalizing at least one of the gallbladder duct or the gallbladder; and

c. leaving the gallbladder in situ.

16. The method of claim **15** wherein the step of defunctionalizing the gallbladder further comprising the step of delivering a substance to at least one of the gallbladder duct or the gallbladder.

17. The method of claim **16** wherein the substance occupies, or substantially occupies, a lumen of at least one of the gallbladder duct or the gallbladder.

18. The method of claim **16** wherein the substance is one or more of antibiotics, inflammatory agents, and anti-inflammatory agents.

19. The method of claim **15** further comprising the step of preventing bile from entering the gallbladder lumen.

20. The method of claim **15** further comprising the step of localizing the gallbladder via endoscopic ultrasound.

21. The method of claim **15** further comprising the step of accessing the gallbladder via the gastrointestinal tract.

22. The method of claim **21** wherein the step of accessing is performed in the gastrointestinal tract at a duodenum.

23. The method of claim **15** wherein the step of defunctionalizing at least one of the gallbladder duct or the gallbladder further comprises one or more of sclerosing, necrotizing or ablating tissue.

24. The method of claim **23** wherein an ablation technique is selected from the group comprising cryoablation, thermal ablation, chemical ablation, radio frequency ablation, microwave ablation, and ultrasound ablation.

25. The method of claim **15** further comprising the step of delivering a fluid with an angular orientation relative to a length of body of a fluid delivery device.

26. The method of claim **15** further comprising the step of delivering a fluid with at least one of a 360 degree radial pattern, a sharp stream, and a cone shape.

27. The method of claim **15** further comprising the step of delivering a fluid with a device comprising an articulating member.

28. The method of claim **15** wherein the step of defunctionalizing at least one of the cystic duct or the gallbladder further comprises applying a vacuum to a lumen of the cystic duct or the gallbladder.

29. The method of claim **28** further comprising the step of applying an adhesive to the lumen of the gallbladder duct or the gallbladder.

30. The method of claim **15** wherein the step of defunctionalizing at least one of the gallbladder duct or the gallbladder further comprises physically blocking a lumen of the gallbladder duct or the gallbladder.

31. The method of claim **15** further comprising the step of removing gallstones.

32. The method of claim **15** further comprising the step of altering gallstones.

33. The method of claim **32** further comprising the step of removing the altered gallstones.

34. The method of claim **15** further comprising the step of clearing obstructions within the gallbladder.

35. The method of claim **15** further comprising the step of visualizing a treatment area.

36. The method of claim **15** further comprising the step of delivering a device via an endoscope.

37. The method of claim **15** further comprising the step of delivering a device via a needle, guidewire or guidance catheter.

38. The method of claim **15** further comprising the step of restricting fluid flow from the gallbladder lumen to the gastrointestinal tract.

39. The method of claim **38** further comprising the step of operating a valve to restrict fluid flow.

40. The method of claim **15** further comprising the step of defunctionalizing the gallbladder in situ.

41. The method of claim **40** wherein the step of defunctionalizing is achieved by delivering a substance into a space within the gallbladder.

42. The method of claim **41** wherein the delivered substance is selected from the group consisting of gel and foam.

43. The method of claim **41** further comprising the step of activating the delivered substance in situ.

44. The method of claim **41** further comprising delivering an amount of substance sufficient to fill or substantially fill the gallbladder lumen.

45. The method of claim **15** wherein the step of defunctionalizing is achieved by one or more of sclerosing or necrotizing a tissue within the gallbladder.

46. The method of claim **45** wherein the step of sclerosing or necrotizing can be achieved by an ablation technique.

47. The method of claim **45** wherein the ablation technique is selected from cryoablation, thermal ablation, chemical ablation, radio frequency ablation, ultrasound ablation, and microwave ablation.

48. A kit for treating biliary disease comprising: (a) a device adaptable to deliver to a lumen of a gallbladder or gallbladder duct; and optionally (b) a compound for delivery to a tissue.

49. The kit of claim **48** further comprising a catheter.

50. The kit of claim **48** further comprising one or more of a needle, a guidewire, and a guidance catheter.

51. The kit of claim **48** further comprising an ablation device.

52. The kit of claim **48** wherein the compound comprises a sclerosing agent.

53. The kit of claim **48** wherein the compound comprises antibiotics.

54. The kit of claim **48** wherein the compound comprises one or more of inflammatory agents and anti-inflammatory agents.

55. The kit of claim **48** further comprising one or more biocompatible gels and biocompatible foams.

56. The kit of claim **48** further comprising one or more of a pair of scissors, a scalpel, a swab, a syringe, a hemostat, a lubricant, a needle, a snare, an antiseptic, and an anesthetic.

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专利名称(译)	用于使胆囊功能化的方法，装置，试剂盒和系统		
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摘要(译)

该申请公开了用于治疗胆道疾病的装置，系统，试剂盒和方法。装置包括例如构造成用于部署到胆囊或胆囊管腔的部件，该部件具有近端和远端，其具有穿过其延伸的内腔以及在其远端处的流体或气体输送装置。