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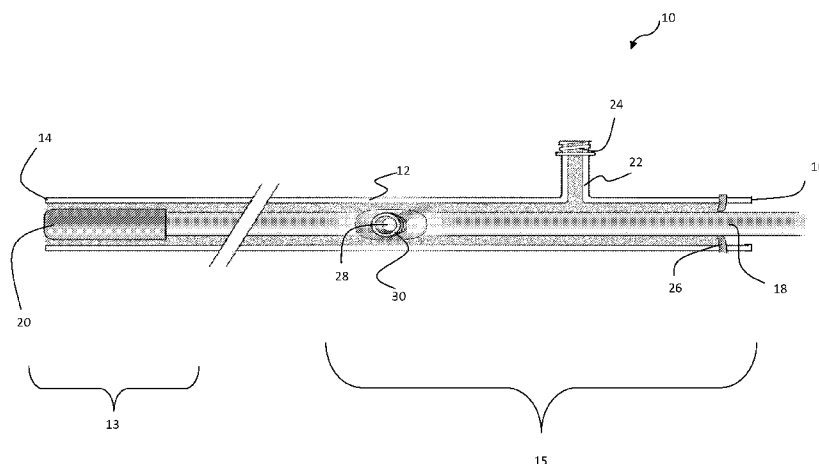
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(54) **Title:** PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY

Figure 1



(57) **Abstract:** This document provides methods and materials involved in obtaining images using pCLE. For example, devices (e.g., pCLE devices) and systems configured to allow a user (e.g., a clinician) to stabilize imaging probes in a manner that minimizes excessive movement during imaging are provided.

PROBE-BASED CONFOCAL LASER ENDOMICROSCOPY

CROSS-REFERENCE TO RELATED APPLICATIONS

5 This application claims the benefit of U.S. Provisional Application Serial No. 61/587,585, filed January 17, 2012. The disclosure of the prior application is considered part of (and is incorporated by reference in) the disclosure of this application.

BACKGROUND

10 1. Technical Field

 This document relates to methods and materials involved in obtaining images using probe-based confocal laser endomicroscopy (pCLE). For example, this document relates to devices (e.g., pCLE devices) configured to allow a user (e.g., a clinician) to stabilize imaging probes in a manner that minimizes excessive movement during
15 imaging.

2. Background Information

 Confocal laser endomicroscopy (CLE) is a technique that allows clinicians to perform microscopic imaging of gastrointestinal mucosa *in vivo*. There are primarily two
20 different types of endomicroscopy systems available to clinicians. One is called a probe-based confocal laser endomicroscopy (pCLE) system, and the other is called an endoscope-based confocal laser endomicroscopy (eCLE) system. The differences between these two systems are discussed elsewhere (Dunbar and Canto, *Techniques in Gastrointestinal Endoscopy*, 12(2):90-99 (2010)).

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SUMMARY

 This document provides methods and materials involved in obtaining images using pCLE. For example, this document provides devices (e.g., pCLE devices) configured to allow a user (e.g., a clinician) to stabilize imaging probes in a manner that
30 minimizes excessive movement during imaging. As described herein, a catheter can be configured to be located within an endoscopic channel that can be advanced into a

patient, and an imaging probe can be configured to be located within the catheter. For example, in some cases, a pCLE system provided herein can include an endoscopic channel configured to be advanced into a patient, a catheter can be configured to be advanced into the endoscopic channel, and an imaging probe configured to be advanced
5 into the catheter. The catheters provided herein can be configured to provide suction to a distal end of the catheter in a manner that stabilizes an imaging probe located within the catheter, thereby minimizing excessive movement during imaging. Having the ability to use the catheters described herein can allow clinicians to stabilize imaging probes *in vivo* and to obtain clear microscopic images during confocal laser endomicroscopy
10 procedures.

In general, one aspect of this document features a system for obtaining an image from the gastrointestinal tract of a mammal during a probe-based confocal laser endomicroscopy procedure. The system comprises, or consists essentially of, a catheter element comprising a proximal end region and a distal end region, wherein the catheter
15 element is configured to be located at least partially within an outer hollow member and defines a lumen configured to receive at least a portion of an imaging probe, wherein the proximal end region comprises a suction port configured to receive suction force and defines a suction release opening, wherein the distal end region defines an opening, and wherein applying suction force to the suction port allows suction force to be delivered to
20 the opening of the distal end region when the suction release opening is closed. The mammal can be a human. The system can comprise the outer hollow member. The system can comprise the imaging probe. The proximal end region can comprise a seal configured to maintain suction force within the lumen and to allow the imaging probe to slide within the catheter element.

In another aspect, this document features a method for obtaining an image from the gastrointestinal tract of a mammal during a probe-based confocal laser endomicroscopy procedure. The method comprises, or consists essentially of, (a)
25 positioning a distal end of a catheter element and a distal end of an imaging probe adjacent to tissue to be imaged, wherein at least a portion of the imaging probe is located within the catheter element, (b) applying suction force to a lumen of the catheter element
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under conditions wherein the distal end of a catheter element attaches to the tissue by suction, and (c) obtaining an image of the tissue using the imaging probe.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention pertains. Although methods and materials similar or equivalent to those described herein can be used to practice the invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

The details of one or more embodiments of the invention are set forth in the accompanying drawings and the description below. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

DESCRIPTION OF THE DRAWINGS

Figure 1 is a side view of a device for obtaining images during pCLE procedures in accordance to some embodiments.

DETAILED DESCRIPTION

This document provides methods and materials involved in obtaining images using pCLE. For example, this document provides devices (e.g., pCLE devices) configured to allow a user (e.g., a clinician) to stabilize imaging probes in a manner that minimizes excessive movement during imaging.

In general, an outer hollow member (e.g., an endoscopic channel, catheter, needle, cannula, or tubular member) can be configured such that it can be advanced within a mammal's body to a position such that an image of gastrointestinal tissue can be obtained. In some cases, the outer hollow member can be the outer most component of a pCLE system described herein, or it can be housed completely or at least partially within another component (e.g., a sleeve or sheath). An outer hollow member can be any appropriate shape. For example, an outer hollow member can have a round or a non-

round shape (e.g., a round or non-round cross-sectional shape). In some cases, the lumen defined by an outer hollow member can have a round or non-round shape. For example, an inner surface of an outer hollow member can have a round cross-sectional shape (e.g., a circular shape) or a non-round cross-sectional shape (e.g., a circular shape with one or more straight or substantially straight edges).

In some cases, the outer hollow member can be configured to receive or contain an inner catheter element. An inner catheter element can be any appropriate shape. For example, an inner catheter element can have a round or a non-round shape (e.g., a round or non-round cross-sectional shape). In some cases, the outer surface of an inner catheter element can have a round or non-round shape. In some cases, the lumen defined by an inner catheter element can have a round or non-round shape. For example, an inner surface of an inner catheter element can have a round cross-sectional shape (e.g., a circular shape) or a non-round cross-sectional shape (e.g., a circular shape with one or more straight or substantially straight edges).

The inner catheter element can be configured to receive or contain one or more imaging probes. An imaging probe can be any appropriate shape. For example, an imaging probe can have a round or a non-round shape (e.g., a round or non-round cross-sectional shape). In some cases, the outer surface of an imaging probe can have a round or non-round shape. For example, an outer surface of an imaging probe can have a round cross-sectional shape (e.g., a circular shape) or a non-round cross-sectional shape (e.g., a circular shape with one or more straight or substantially straight edges).

In some cases, an inner catheter element can be configured such that suction force can be applied to the lumen of the inner catheter element so as to anchor a distal end region of the inner catheter element having an opening to tissue in a manner that minimizes movement of an imaging probe located within the inner catheter element during imaging. For example, a portion of an inner catheter element that remains outside a mammal's body and is not located within an outer hollow member can be configured to include a suction port. When a source of suction force is attached to the suction port and suction force is applied, one or more openings located at the distal end region of the inner catheter element can become attached to tissue, thereby minimizes movement of an imaging probe located within the inner catheter element.

The methods and materials provided herein can be used to obtain images from any appropriate type of gastrointestinal tract tissue such as stomach, small bowel, and/or colon tissue. In some cases, the methods and materials provided herein can be used to obtain images at a selected depth of the desired tissue.

5 With reference to Figure 1, device 10 can include an inner catheter element 12 and an imaging probe 18. Inner catheter element 12 can have a distal end region 13 with a distal end 14 and a proximal end region 15 with a proximal end 16. Inner catheter element 12 can be configured to be located at least partially within an outer hollow member (e.g., an endoscopic channel; not shown). For example, distal end region 13 and
10 the middle section of inner catheter element 12 can be located within an outer hollow member with proximal end region 15 being located outside of the outer hollow member. An outer hollow member can have any appropriate inner and outer diameters. For example, an outer hollow member can have an inner diameter between about 1 mm and about 15 mm (e.g., about 1.2, 2.8, 3.2, 3.8, or 4.2 mm) and an outer diameter between
15 about 2 mm and about 15 mm (e.g., about 2, 3, 4, or 5 mm). In some cases, the inner diameter of an outer hollow member can be a diameter capable of forming a slip fit with the outer surface of inner catheter element 12. An outer hollow member can be made of any appropriate material.

 Inner catheter element 12 can have any appropriate inner and outer diameters.
20 For example, inner catheter element 12 can have an inner diameter between about 1 mm and about 10 mm (e.g., about 1.2, 2.8, 3.2, 3.8, or 4.2 mm) and an outer diameter between about 2 mm and about 15 mm (e.g., about 3, 4, 5, 6, or 7 mm). In some cases, the inner diameter of inner catheter element 12 can be a diameter capable of forming a slip fit with the outer surface of imaging probe 18. In some cases, the inner diameter of inner catheter
25 element 12 can be a diameter such that there is space available around the outer surface of imaging probe 18 when imaging probe 18 is located within inner catheter element 12. Inner catheter element 12 can be made of any appropriate material.

 Imaging probe 18 can include a distal end region 20 having the ability to capture images of tissue. Imaging probe 18 can have any appropriate outer diameter provided
30 that it has the ability to be located within inner catheter element 12. For example, the

outer diameter of imaging probe 18 can be from about 0.1 mm to about 5 mm smaller than the inner diameter of inner catheter element 12.

Proximal end region 15 of inner catheter element 12 can include a suction port 22 configured to allow suction force to be applied to inner catheter element 12. Suction port 22 can be configured to include an attachment mechanism so that a source of suction force (e.g., a vacuum or a hose attached to a vacuum) can be attached to suction port 22. For example, suction port 22 can be configured to have threads 24 (e.g., Luer-Lok threads). In some cases, proximal end region 15 of inner catheter element 12 can include a seal 26 configured to maintain suction force within the lumen of inner catheter element 12 while allowing imaging probe 18 to slide with respect to inner catheter element 12. Seal 26 can be made of any appropriate material.

In some cases, proximal end region 15 of inner catheter element 12 can define a suction release opening 28. Suction release opening 28 can be configured to allow a user (e.g., a clinician) to place a finger or thumb over suction release opening 28 so as to allow suction force to be applied to distal end 14 when suction force is applied to suction port 22. When a user removes a finger or thumb from covering suction release opening 28, the suction force delivered to distal end 14 can be partially or completely reduced. For example, essentially no suction force can be applied to distal end 14 when suction force is applied to suction port 22 and suction release opening 28 is uncovered. In some cases, inner catheter element 12 can include a raised member 30 that defines suction release opening 28.

During use, an outer hollow member of a system or device provided herein (e.g., device 10) can be introduced into a mammal (e.g., a gastrointestinal cavity of a human). An inner catheter element can be introduced into the mammal by advancing the inner catheter element within the outer hollow member. At this point, an imaging probe can be introduced into the mammal by advancing the imaging probe within the inner catheter element. The imaging probe can be advanced to be within range of the tissue to be imaged. At this point, suction force can be applied to a suction port of the inner catheter element while the user holds a finger or thumb over a suction release opening of the inner catheter element. This can allow the distal end of the inner catheter element to engage the tissue to be imaged in a manner that minimizes excessive movement of the imaging

probe during imaging.

In some cases, the outer hollow member can be introduced into the mammal with the inner catheter element, imaging probe, or both already located within the outer hollow member.

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OTHER EMBODIMENTS

It is to be understood that while the invention has been described in conjunction with the detailed description thereof, the foregoing description is intended to illustrate and not limit the scope of the invention, which is defined by the scope of the appended
10 claims. Other aspects, advantages, and modifications are within the scope of the following claims.

WHAT IS CLAIMED IS:

1. A system for obtaining an image from the gastrointestinal tract of a mammal during a probe-based confocal laser endomicroscopy procedure, wherein said system comprises a catheter element comprising a proximal end region and a distal end region, wherein said catheter element is configured to be located at least partially within an outer hollow member and defines a lumen configured to receive at least a portion of an imaging probe, wherein said proximal end region comprises a suction port configured to receive suction force and defines a suction release opening, wherein said distal end region defines an opening, and wherein applying suction force to said suction port allows suction force to be delivered to said opening of said distal end region when said suction release opening is closed.
2. The system of claim 1, wherein said mammal is a human.
3. The system of claim 1, wherein said system comprises said outer hollow member.
4. The system of claim 1, wherein said system comprises said imaging probe.
5. The system of claim 1, wherein said proximal end region comprises a seal configured to maintain suction force within said lumen and to allow said imaging probe to slide within said catheter element.
6. A method for obtaining an image from the gastrointestinal tract of a mammal during a probe-based confocal laser endomicroscopy procedure, wherein said method comprises:
 - (a) positioning a distal end of a catheter element and a distal end of an imaging probe adjacent to tissue to be imaged, wherein at least a portion of said imaging probe is located within said catheter element,

- (b) applying suction force to a lumen of said catheter element under conditions wherein said distal end of a catheter element attaches to said tissue by suction, and
- (c) obtaining an image of said tissue using said imaging probe.

Figure 1

