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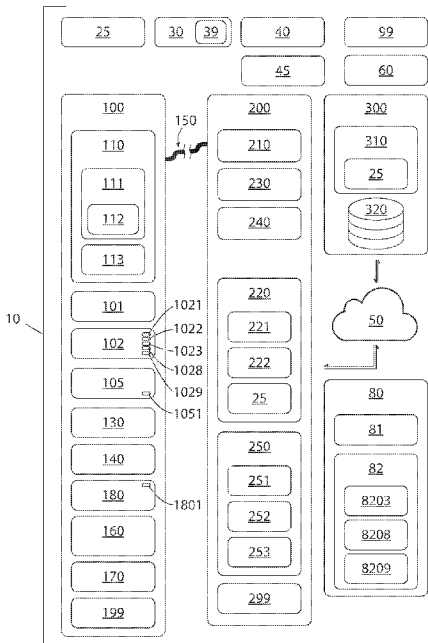


FIG. 1

(57) Abstract: Systems, devices, and methods for treating a medical condition of a patient are described. The system for treating a medical condition of a patient includes: a catheter for insertion into the intestine, the catheter having an elongate shaft with a distal portion; and a functional assembly positioned on the elongate shaft distal portion and including at least one treatment element. The at least one treatment element treats target tissue located in the small intestine of the patient by delivering electrical energy to the target tissue. The delivery of the electrical energy electroporates cells of the target tissue.

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TISSUE TREATMENT SYSTEM**CROSS-REFERENCE TO RELATED APPLICATIONS**

[001] This application claims priority to United States Provisional Patent Application Serial Number 63/506,574 (Attorney Docket No. 41714-731.101; Client Docket No. MCT-060-PR1), entitled “Tissue Treatment System”, filed June 6, 2023, the contents of which is incorporated herein by reference in its entirety for all purposes.

[002] The subject matter of this application is related to that of: United States Patent Application Serial Number 17/222,480 (Attorney Docket No. 41714-703.303; Client Docket No. MCT-001-US-CON2), entitled “Devices and Methods for the Treatment of Tissue”, filed April 5, 2021; United States Patent Application Serial Number 17/864,855 (Attorney Docket No. 41714-704.303; Client Docket No. MCT-002-US-CON2), entitled “Heat Ablation Systems, Devices and Methods for the Treatment of Tissue”, filed July 14, 2022; United States Patent Application Serial Number 17/868,076 (Attorney Docket No. 41714-705.302; Client Docket No. MCT-003-US-CON1), entitled “Tissue Expansion Devices, Systems and Methods”, filed July 19, 2022; United States Patent Application Serial Number 17/879,222 (Attorney Docket No. 41714-706.303; Client Docket No. MCT-004-US-CON2), entitled “Electrical Energy Ablation Systems, Devices and Methods for the Treatment of Tissue”, filed August 2, 2022; United States Patent Application Serial Number 17/192,671 (Attorney Docket No. 41714-707.302; Client Docket No. MCT-005-US-CON1), entitled “Ablation Systems, Devices, and Methods for the Treatment of Tissue”, filed March 4, 2021; United States Patent Application Serial Number 17/568,145 (Attorney Docket No. 41714-708.302; Client Docket No. MCT-009-US-CON1), entitled “Methods, Systems and Devices for Performing Multiple Treatments on a Patient”, filed January 4, 2022; United States Patent Application Serial Number 17/021,798 (Attorney Docket No. 41714-709.303; Client Docket No. MCT-013-US-CON2), entitled “Methods, Systems and Devices for Reducing the Luminal Surface Area of the Gastrointestinal Tract”, filed September 15, 2020; United States Patent Application Serial Number 18/605,655 (Attorney Docket No. 41714-710.302; Client Docket No. MCT-023-US-CON1), entitled “Systems, Methods and Devices for Treatment of Target Tissue”, filed March 14, 2024; United States Patent Application Serial Number 18/467,589 (Attorney Docket No. 41714-711.304; Client Docket No. MCT-024-US-CON3), entitled “Systems, Devices and Methods for the Creation of a Therapeutic Restriction in the Gastrointestinal Tract”, filed September 14, 2023; United States Patent Application Serial Number 16/742,645 (Attorney Docket No. 41714-715.301; Client Docket No. MCT-025-US), entitled “Intestinal Catheter Device and System”, filed January 14, 2020; United States Patent Application Serial Number 17/494,277 (Attorney Docket No. 41714-712.303;

Client Docket No. MCT-027-US-CIP1-CON2), entitled “Injectate Delivery Devices, Systems and Methods”, filed October 5, 2021; United States Patent Application Serial Number 16/798,117 (Attorney Docket No. 41714-714.303; Client Docket No. MCT-028-US-CIP1-CON2), entitled “Systems, Devices and Methods for Performing Medical Procedures in the Intestine”, filed February 21, 2020; United States Patent Application Serial Number 18/526,542 (Attorney Docket No. 41714-714.305; Client Docket No. MCT-028-US-CIP2-CON3), entitled “Systems, Devices and Methods for Performing Medical Procedures in the Intestine”, filed July 23, 2021; United States Patent Application Serial Number 17/096,855 (Attorney Docket No. 41714-713.302; Client Docket No. MCT-029-US-CON1), entitled “Methods and Systems for Treating Diabetes and Related Diseases and Disorders”, filed November 12, 2020; United States Patent Application Serial Number 17/181,969 (Attorney Docket No. 41714-713.501; Client Docket No. MCT-029-US-CIP1), entitled “Methods and Systems for Treating Diabetes and Related Diseases and Disorders”, filed February 22, 2021; United States Patent Application Serial Number 17/516,503 (Attorney Docket No. 41714-713.304; Client Docket No. MCT-029-US-CIP1-CON2), entitled “Methods and Systems for Treating Diabetes and Related Diseases and Disorders”, filed November 1, 2021; United States Patent Application Serial Number 16/400,491 (Attorney Docket No. 41714-716.301; Client Docket No. MCT-035-US), entitled “Systems, Devices and Methods for Performing Medical Procedures in the Intestine”, filed May 1, 2019; United States Patent Application Serial Number 17/859,137 (Attorney Docket No. 41714-721.301; Client Docket No. MCT-039-US), entitled “Tissue Treatment Devices, Systems, and Methods”, filed July 7, 2022; United States Patent Application Serial Number 17/490,947 (Attorney Docket No. 41714-719.301; Client Docket No. MCT-040-US), entitled “Systems, Devices and Methods for Treating Metabolic Medical Conditions”, filed September 30, 2021; United States Patent Application Serial Number 17/942,914 (Attorney Docket No. 41714-723.301; Client Docket No. MCT-041-US), entitled “Systems, Devices and Methods for Treating Diabetes”, filed September 12, 2022; United States Patent Application Serial Number 17/721,937 (Attorney Docket No. 41714-720.301; Client Docket No. MCT-050-US), entitled “Systems, Devices, and Methods for Performing Medical Procedures in the Intestine”, filed April 15, 2022; United States Patent Application Serial Number 17/863,016 (Attorney Docket No. 41714-722.301; Client Docket No. MCT-051-US), entitled “Automated Tissue Treatment Devices, Systems, and Methods”, filed July 12, 2022; United States Patent Application Serial Number 18/062,331 (Attorney Docket No. 41714-724.301; Client Docket No. MCT-034-US), entitled “Tissue Treatment System with Fluid Delivery Console”, filed December 6, 2022; International PCT Patent Application Serial Number PCT/US2022/053531 (Attorney Docket No. 41714-727.601; Client Docket No. MCT-056-PCT), entitled “Methods and Systems for

Treating Mucosal Hyperplasia and other Medical Conditions of a Patient”, filed December 20, 2022; United States Provisional Patent Application Serial Number 63/385,717 (Attorney Docket No. 41714-728.101; Client Docket No. MCT-057-PR1), entitled “Tissue Treatment Devices, Systems, and Methods”, filed December 1, 2022; and International PCT Patent Application Serial Number PCT/US2024/027227 (Attorney Docket No. 41714-730.601; Client Docket No. MCT-059-PCT), entitled “Methods and Systems for Treating One or More Metabolic Conditions of a Patient”, filed May 1, 2024; the contents of each of which is incorporated herein by reference in its entirety for all purposes.

TECHNICAL FIELD

[003] The embodiments disclosed herein relate generally to methods, systems, and devices for treating a patient, particularly for treating tissue of the gastrointestinal tract to provide a therapy.

BACKGROUND

[004] Numerous diagnostic and therapeutic procedures are performed in the small and large intestine, as well as other locations of the gastrointestinal tract. Devices used in these procedures can be difficult to maneuver and otherwise operate, and they often have limited functionality. There is a need for improved systems and devices for treating and diagnosing tissue of the intestine, as well as a need for methods of treating intestinal tissue to provide an improved therapy for various diseases and disorders.

[005] For these and other reasons, there is a need for improved systems, devices, and methods for the treatment of diabetes and similar patient diseases and disorders.

BRIEF SUMMARY

[006] According to an aspect of the present inventive concepts, a system for treating a medical condition of a patient comprises: a device comprising a first elongate shaft for insertion into the small intestine, the first elongate shaft comprising a distal portion; and a treatment assembly configured to be positioned on the distal portion of the first elongate shaft and comprising an electrode array of one or more electrodes. The at least one treatment assembly is configured to treat target tissue located in the small intestine of the patient by delivering electrical energy to the target tissue via the electrode array. The delivery of the electrical energy electroporates cells of the target tissue, and the system is configured to treat the medical condition of the patient.

[007] In some embodiments, the delivery of the electrical energy irreversibly electroporates the cells of the target tissue.

[008] In some embodiments, the target tissue comprises duodenal tissue. The target tissue can comprise tissue selected from the group consisting of: mucosal tissue; submucosal tissue; nerve tissue; and combinations thereof.

[009] In some embodiments, the medical condition comprises a metabolic condition. The metabolic condition can comprise insulin resistance. The metabolic condition can comprise Type 2 diabetes.

[010] In some embodiments, the medical condition is selected from the group consisting of: Type 2 diabetes; Type 1 diabetes; "Double diabetes"; gestational diabetes; hyperglycemia; pre-diabetes; impaired glucose tolerance; insulin resistance; non-alcoholic fatty liver disease (NAFLD); non-alcoholic steatohepatitis (NASH); obesity; obesity-related disorder; polycystic ovarian syndrome; hypertriglyceridemia; hypercholesterolemia; psoriasis; GERD; coronary artery disease; stroke/TIA; cognitive decline or dementia; diabetic nephropathy; neuropathy; retinopathy; diabetic heart disease and/or heart failure; metabolic dysfunction-associated steatotic liver disease (MASLD); and combinations thereof.

[011] In some embodiments, the treatment assembly further comprises at least one needle for penetrating submucosal tissue of the small intestine, and at least one of the electrodes of the electrode array comprises a hollow tubular shaped electrode, and the system further comprises conductive fluid, and the at least one needle is configured to deliver the conductive fluid to the submucosal tissue, such that the delivered conductive fluid within the submucosal tissue collectively forms a hollow tubular shape that is concentric with the hollow tubular shaped electrode of the functional assembly, and the system is configured to deliver the electrical energy between the hollow tubular shaped electrode of the functional assembly and the hollow tubular shaped conductive fluid in the submucosal tissue to electroporate the tissue between the hollow tubular shaped electrode of the functional assembly and the hollow tubular shaped conductive fluid in the submucosal tissue. The treatment assembly can be configured to removably attach to the distal portion of the first elongate shaft without adversely affecting the functionality of the endoscope. The treatment assembly can include a housing configured to attach to the distal portion of the first elongate shaft, and the endoscope can comprise a working channel, and the housing can include an opening configured to align with the working channel while the housing is attached to the first elongate shaft.

[012] In some embodiments, the system further comprises an endoscope comprising a second elongate shaft and one or more working channels. The first elongate shaft can be configured to be inserted into the small intestine alongside the second elongate shaft. The first

elongate shaft can be configured to be inserted into the small intestine through one of the one or more working channels of the endoscope, and the working channel can comprise an inner diameter. The treatment assembly can comprise an expandable assembly comprising a compact diameter and an expanded diameter, and the compact diameter can comprise a diameter smaller than the inner diameter of the working channel and the expanded diameter approximates the diameter of the small intestine.

[013] In some embodiments, the treatment assembly further comprises an expandable assembly configured to transition between a compact geometry and an expanded geometry. The treatment assembly can further comprise a housing configured to surround the expandable assembly. The expandable assembly can be configured to deploy from the housing and transition from the compact geometry to the expanded geometry. The expandable assembly can comprise one or more radially expandable arms. The electrode array can be furled about the one or more radially expandable arms.

[014] In some embodiments, the treatment assembly further comprises a housing configured to be positioned on the distal portion of the first elongate shaft. The housing can comprise a circumferential channel, and the electrode array can be configured to traverse about the circumferential channel. The electrode array can be positioned on a portion of the housing. The housing can be configured to rotate about the distal portion of the first elongate shaft. The treatment assembly can comprise one or more fluid ports proximate the electrode array, and the system can be configured to apply a vacuum to the one or more fluid ports to pull tissue toward the electrode array. The housing can comprise a first portion and a second portion, and the first portion can be configured to attach to the first elongate shaft and the second portion can be configured to extend from the first portion toward tissue, and the electrode array can be positioned on the second portion. The housing can further comprise a third portion configured to extend from the first portion and opposite the second portion.

[015] In some embodiments, the system further comprises an aspiration assist device comprising a third elongate shaft with a fluid lumen therethrough and one or more aspiration ports positioned on the distal end of the third elongate shaft and fluidly attached to the fluid lumen, and the fluid lumen is configured to attach to a source of vacuum. The device can comprise an endoscope including a working channel, and the aspiration assist device can be configured to be inserted through the working channel. The aspiration assist device and the endoscope can be configured to provide aspiration. The third shaft can be configured to be inserted into the small intestine alongside the first elongate shaft.

[016] In some embodiments, the treatment assembly comprises a radially expandable structure configured to transition between a radially compact and a radially expanded geometry,

and the radially expandable structure is configured transition to the radially expanded geometry when the structure is compacted linearly. The expandable structure can comprise an accordion-like structure. The expandable structure can be biased in the radially compact geometry. The system can further comprise a linkage configured to linearly contract and/or extend the expandable structure to radially extend and/or collapse the expandable structure.

[017] In some embodiments, the treatment assembly comprises an expandable balloon and the electrode array is positioned on the expandable balloon. The electrode array can comprise two or more sets of electrodes, and each set of electrodes comprise two or more electrodes. The two or more sets of electrodes can be configured in an alternating pattern about the expandable balloon.

[018] In some embodiments, the treatment assembly comprises a tissue capture port configured to capture a portion of tissue to be treated by the system. The tissue capture port can comprise two or more tissue capture ports. The tissue capture port can comprise vacuum ports. At least one of the one or more electrodes can comprise a needle and the needle can be configured to penetrate tissue that is positioned within the tissue capture port. The one or more electrodes can be positioned within the tissue capture port.

[019] In some embodiments, the treatment assembly comprises a set of one or more flexible sheets configured to transition between a back-swept geometry and a forward-swept geometry. The electrode array can be positioned on the set of flexible sheets.

[020] In some embodiments, the first elongate shaft is configured to transition between a linear geometry and an offset geometry, and an axis of the distal portion of the first elongate shaft is offset from an axis of a proximal portion of the first elongate shaft in the offset geometry. The treatment assembly can comprise an expandable structure positioned on the distal portion of the first elongate shaft. The expandable structure can comprise a furlable substrate and the electrode array can be positioned on the furlable substrate. The furlable substrate can be configured to align with the axis of the distal portion of the first elongate shaft in the offset geometry.

[021] The technology described herein, along with the attributes and attendant advantages thereof, will best be appreciated and understood in view of the following detailed description taken in conjunction with the accompanying drawings in which representative embodiments are described by way of example.

INCORPORATION BY REFERENCE

[022] 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

[023] The foregoing and other objects, features, and advantages of embodiments of the present inventive concepts will be apparent from the more particular description of preferred embodiments, as illustrated in the accompanying drawings in which like reference characters refer to the same or like elements. The drawings are not necessarily to scale, emphasis instead being placed upon illustrating the principles of the preferred embodiments.

[024] **Fig. 1** illustrates a system for treating and/or diagnosing gastrointestinal tissue, consistent with the present inventive concepts.

[025] **Fig. 1A** illustrates a flow chart of a method of treating target tissue of a patient, consistent with the present inventive concepts.

[026] **Figs. 2A and 2B** illustrate schematic views of a treatment device inserted into a patient and that device shown in an anatomical shape, respectively, consistent with the present inventive concepts.

[027] **Figs. 3A and 3B** illustrate various views of a treatment assembly comprising a cap positioned on the distal end of an introduction device, consistent with the present inventive concepts.

[028] **Figs. 4A-4D** illustrate various views of a treatment assembly comprising a cap positioned on the distal end of an introduction device and a rotatory electrode, consistent with the present inventive concepts.

[029] **Figs. 5A-5C** illustrate various views of a treatment assembly comprising a pad-like electrode array, consistent with the present inventive concepts.

[030] **Figs. 6A-6F** illustrate various views of a treatment assembly comprising a pad-like electrode array, consistent with the present inventive concepts.

[031] **Figs. 7A-7D** illustrate various views of a treatment assembly comprising a deployable electrode positioned on a needle, consistent with the present inventive concepts.

[032] **Figs. 8A-8C** illustrate side sectional anatomic views and an end sectional anatomic view, respectively, of a treatment assembly comprising a folded expandable structure, consistent with the present inventive concepts.

[033] **Figs. 9A and 9B** illustrate side views of various embodiments of a treatment assembly comprising an expandable balloon and an array of electrodes, consistent with the present inventive concepts.

[034] **Figs. 10A-10E** illustrate various views of a treatment assembly comprising a tissue capture port, consistent with the present inventive concepts.

[035] **Figs. 11A-11C** illustrate various views of a treatment assembly comprising a vacuum channel, consistent with the present inventive concepts.

[036] **Figs. 12A and 12B** illustrate side views of a treatment assembly with an expandable structure comprising one or more expandable petals, consistent with the present inventive concepts.

[037] **Figs. 13A-13C** illustrate various views of an embodiment of a treatment element comprising an “offset spatula” configuration, consistent with the present inventive concepts.

DETAILED DESCRIPTION OF THE DRAWINGS

[038] Reference will now be made in detail to the present embodiments of the technology, examples of which are illustrated in the accompanying drawings. Similar reference numbers may be used to refer to similar components. However, the description is not intended to limit the present disclosure to particular embodiments, and it should be construed as including various modifications, equivalents, and/or alternatives of the embodiments described herein.

[039] It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the invention which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable sub-combination. For example, it will be appreciated that all features set out in any of the claims (whether independent or dependent) can be combined in any given way.

It is to be understood that at least some of the figures and descriptions of the invention have been simplified to focus on elements that are relevant for a clear understanding of the invention, while eliminating, for purposes of clarity, other elements that those of ordinary skill in the art will appreciate may also comprise a portion of the invention. However, because such elements are well known in the art, and because they do not necessarily facilitate a better understanding of the invention, a description of such elements is not provided herein.

[040] Terms defined in the present disclosure are only used for describing specific embodiments of the present disclosure and are not intended to limit the scope of the present disclosure. Terms provided in singular forms are intended to include plural forms as well, unless the context clearly indicates otherwise. All of the terms used herein, including technical or

scientific terms, have the same meanings as those generally understood by an ordinary person skilled in the related art, unless otherwise defined herein. Terms defined in a generally used dictionary should be interpreted as having meanings that are the same as or similar to the contextual meanings of the relevant technology and should not be interpreted as having ideal or exaggerated meanings, unless expressly so defined herein. In some cases, terms defined in the present disclosure should not be interpreted to exclude the embodiments of the present disclosure.

[041] It will be understood that the words "comprising" (and any form of comprising, such as "comprise" and "comprises"), "having" (and any form of having, such as "have" and "has"), "including" (and any form of including, such as "includes" and "include") or "containing" (and any form of containing, such as "contains" and "contain") when used herein, specify the presence of stated features, integers, steps, operations, elements, and/or components, but do not preclude the presence or addition of one or more other features, integers, steps, operations, elements, components, and/or groups thereof.

[042] It will be further understood that, although the terms first, second, third, etc. may be used herein to describe various limitations, elements, components, regions, layers and/or sections, these limitations, elements, components, regions, layers and/or sections should not be limited by these terms. These terms are only used to distinguish one limitation, element, component, region, layer or section from another limitation, element, component, region, layer or section. Thus, a first limitation, element, component, region, layer or section discussed below could be termed a second limitation, element, component, region, layer or section without departing from the teachings of the present application.

[043] It will be further understood that when an element is referred to as being "on", "attached", "connected" or "coupled" to another element, it can be directly on or above, or connected or coupled to, the other element, or one or more intervening elements can be present. In contrast, when an element is referred to as being "directly on", "directly attached", "directly connected" or "directly coupled" to another element, there are no intervening elements present. Other words used to describe the relationship between elements should be interpreted in a like fashion (e.g. "between" versus "directly between," "adjacent" versus "directly adjacent," etc.).

[044] As used herein, the terms **“operably attached”**, **“operably connected”**, **“operatively coupled”**, and similar terms related to attachment of components shall refer to attachment of two or more components that results in one, two, or more of: electrical attachment; fluid attachment; magnetic attachment; mechanical attachment; optical attachment; sonic attachment; and/or other operable attachment arrangements. The operable attachment of two or more components can facilitate the transmission between the two or more components of: power; signals; electrical

energy; fluids or other flowable materials; magnetism; mechanical linkages; light; sound such as ultrasound; and/or other materials and/or components.

[045] It will be further understood that when a first element is referred to as being "in", "on" and/or "within" a second element, the first element can be positioned: within an internal space of the second element, within a portion of the second element (e.g. within a wall of the second element); positioned on an external and/or internal surface of the second element; and combinations of two or more of these.

[046] As used herein, the term "proximate", when used to describe proximity of a first component or location to a second component or location, is to be taken to include one or more locations near to the second component or location, as well as locations in, on and/or within the second component or location. For example, a component positioned proximate an anatomical site (e.g. a target tissue location), shall include components positioned near to the anatomical site, as well as components positioned in, on and/or within the anatomical site.

[047] Spatially relative terms, such as "beneath," "below," "lower," "above," "upper," "under", and the like may be used to describe an element and/or feature's relationship to another element(s) and/or feature(s) as, for example, illustrated in the figures. It will be further understood that the spatially relative terms are intended to encompass different orientations of the device in use and/or operation in addition to the orientation depicted in the figures. For example, if the device in a figure is turned over, elements described as "below" and/or "beneath" other elements or features would then be oriented "above" the other elements or features. The device can be otherwise oriented (e.g. rotated 90 degrees or at other orientations) and the spatially relative descriptors used herein interpreted accordingly.

[048] The terms "reduce", "reducing", "reduction" and the like, where used herein, are to include a reduction in a quantity, including a reduction to zero. Reducing the likelihood of an occurrence shall include prevention of the occurrence. Correspondingly, the terms "prevent", "preventing", and "prevention" shall include the acts of "reduce", "reducing", and "reduction", respectively.

[049] The term "and/or" where used herein is to be taken as specific disclosure of each of the two specified features or components with or without the other. For example "A and/or B" is to be taken as specific disclosure of each of (i) A, (ii) B and (iii) A and B, just as if each is set out individually herein.

[050] The term "one or more", where used herein can mean one, two, three, four, five, six, seven, eight, nine, ten, or more, up to any number.

[051] The terms "and combinations thereof" and "and combinations of these" can each be used herein after a list of items that are to be included singly or collectively. For example, a

component, process, and/or other item selected from the group consisting of: A; B; C; and combinations thereof, shall include a set of one or more components that comprise: one, two, three or more of item A; one, two, three or more of item B; and/or one, two, three, or more of item C.

[052] In this specification, unless explicitly stated otherwise, “and” can mean “or”, and “or” can mean “and”. For example, if a feature is described as having A, B, or C, the feature can have A, B, and C, or any combination of A, B, and C. Similarly, if a feature is described as having A, B, and C, the feature can have only one or two of A, B, or C.

[053] The expression “configured (or set) to” used in the present disclosure may be used interchangeably with, for example, the expressions “suitable for”, “having the capacity to”, “designed to”, “adapted to”, “made to” and “capable of” according to a situation. The expression “configured (or set) to” does not mean only “specifically designed to” in hardware.

Alternatively, in some situations, the expression “a device configured to” may mean that the device “can” operate together with another device or component.

[054] As used herein, the term “threshold” refers to a maximum level, a minimum level, and/or range of values correlating to a desired or undesired state. In some embodiments, a system parameter is maintained above a minimum threshold, below a maximum threshold, within a threshold range of values, and/or outside a threshold range of values, such as to cause a desired effect (e.g. efficacious therapy) and/or to prevent or otherwise reduce (hereinafter “prevent”) an undesired event (e.g. a device and/or clinical adverse event). In some embodiments, a system parameter is maintained above a first threshold (e.g. above a first temperature threshold to cause a desired therapeutic effect to tissue) and below a second threshold (e.g. below a second temperature threshold to prevent undesired tissue damage). In some embodiments, a threshold value is determined to include a safety margin, such as to account for patient variability, system variability, tolerances, and the like. As used herein, “exceeding a threshold” relates to a parameter going above a maximum threshold, below a minimum threshold, within a range of threshold values and/or outside of a range of threshold values.

[055] It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the invention which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable sub-combination. For example, it will be appreciated that all features set out in any of the claims (whether independent or dependent) can be combined in any given way.

[056] As described herein, “room pressure” shall mean pressure of the environment surrounding the systems and devices of the present inventive concepts. Positive pressure includes pressure above room pressure or simply a pressure that is greater than another pressure, such as a positive differential pressure across a fluid pathway component such as a valve. Negative pressure includes pressure below room pressure or a pressure that is less than another pressure, such as a negative differential pressure across a fluid component pathway such as a valve. Negative pressure can include a vacuum but does not imply a pressure below a vacuum. As used herein, the term “vacuum” can be used to refer to a full or partial vacuum, or any negative pressure as described herein.

[057] The term “diameter” where used herein to describe a non-circular geometry is to be taken as the diameter of a hypothetical circle approximating the geometry being described. For example, when describing a cross section, such as the cross section of a component, the term “diameter” shall be taken to represent the diameter of a hypothetical circle with the same cross-sectional area as the cross section of the component being described.

[058] The terms “major axis” and “minor axis” of a component where used herein are the length and diameter, respectively, of the smallest volume hypothetical cylinder which can completely surround the component.

[059] As used herein, the term “fluid” can refer to a liquid, gas, gel, or any flowable material, such as a material which can be propelled through a lumen and/or opening.

[060] As used herein, the term “material” can refer to a single material, or a combination of two, three, four, or more materials.

[061] As used herein, the term “transducer” is to be taken to include any component or combination of components that receives energy or any input and produces an output. For example, a transducer can include an electrode that receives electrical energy and distributes the electrical energy to tissue (e.g. based on the size of the electrode). In some configurations, a transducer converts an electrical signal into any output, such as: light (e.g. a transducer comprising a light emitting diode or light bulb), sound (e.g. a transducer comprising a piezo crystal configured to deliver ultrasound energy); pressure (e.g. an applied pressure or force); heat energy; cryogenic energy; chemical energy; mechanical energy (e.g. a transducer comprising a motor or a solenoid); magnetic energy; and/or a different electrical signal (e.g. different than the input signal to the transducer). Alternatively or additionally, a transducer can convert a physical quantity (e.g. variations in a physical quantity) into an electrical signal. A transducer can include any component that delivers energy and/or an agent to tissue, such as a transducer configured to deliver one or more of: heat energy to tissue; cryogenic energy to tissue; electrical energy to tissue (e.g. a transducer comprising one or more electrodes); light energy to tissue (e.g.

a transducer comprising a laser, light emitting diode and/or optical component such as a lens or prism); mechanical energy to tissue (e.g. a transducer comprising a tissue manipulating element); sound energy to tissue (e.g. a transducer comprising a piezo crystal); chemical energy; electromagnetic energy; magnetic energy; and combinations of two or more of these. A transducer can include a component configured to neutralize an ablative process, such as a transducer configured to cool tissue prior to and/or after a heat ablation of tissue, and/or a transducer configured to warm tissue prior to and/or after a cryogenic ablation of tissue. Alternatively or additionally, a transducer can comprise a mechanism, such as: a valve; a grasping element; an anchoring mechanism; an electrically activated mechanism; a mechanically-activated mechanism; and/or a thermally activated mechanism.

[062] As used herein, the term “functional element” is to be taken to include one or more elements constructed and arranged to perform a function. A functional element can comprise one or more sensors and/or one or more transducers. In some embodiments, a functional element is configured to deliver energy and/or otherwise treat tissue (e.g. a functional element configured as a treatment element). Alternatively or additionally, a functional element (e.g. comprising one or more sensors) can be configured to record one or more parameters, such as a patient physiologic parameter; a patient anatomical parameter (e.g. a tissue parameter); a patient environment parameter; and/or a system parameter (e.g. temperature and/or pressure within the system). In some embodiments, a sensor or other functional element is configured to perform a diagnostic function (e.g. to gather data used to perform a diagnosis). In some embodiments, a functional element is configured to perform a therapeutic function (e.g. to deliver therapeutic energy and/or a therapeutic agent). In some embodiments, a functional element comprises one or more elements constructed and arranged to perform a function selected from the group consisting of: deliver energy; extract energy (e.g. to cool a component); deliver a drug or other agent; manipulate a system component or patient tissue; record or otherwise sense a parameter such as a patient physiologic parameter or a patient anatomical parameter; and combinations of two or more of these. A functional element can comprise a fluid, such as an ablative fluid (as described herein) comprising a liquid, gel, and/or gas configured to ablate or otherwise treat tissue. A functional element can comprise a reservoir, such as an expandable balloon configured to receive an ablative fluid. A “functional assembly” can comprise an assembly constructed and arranged to perform a function, such as is described herein, such as a therapeutic function or a diagnostic function. In some embodiments, a functional assembly is configured to deliver energy and/or otherwise treat tissue (e.g. a functional assembly configured as a tissue treatment assembly). Alternatively or additionally, a functional assembly can be configured to record one or more parameters, such as a patient physiologic parameter; a patient anatomical parameter; a

patient environment parameter; and/or a system parameter. A functional assembly can comprise an expandable assembly. A functional assembly can comprise one or more functional elements.

[063] As used herein, the term “ablative temperature” refers to a temperature at which tissue necrosis or other desired tissue treatment occurs (e.g. a temperature sufficiently hot or sufficiently cold to cause tissue necrosis). As used herein, the term “ablative fluid” refers to one or more liquids, gases, gels or other fluids whose thermal properties cause tissue necrosis and/or another desired tissue treatment (e.g. one or more fluids at an ablative temperature).

Alternatively or additionally, “ablative fluid” refers to one or more fluids whose chemical properties (at room temperature, body temperature or otherwise) cause tissue necrosis or another desired tissue treatment. A tissue treatment element (e.g. a functional element) of the present inventive concepts can comprise one or more ablative fluids.

[064] As used herein, the term “tissue contacting surface” refers to a surface of a system or device component that makes physical contact with tissue, such as a portion of an external surface of an expandable component (e.g. a portion of a balloon’s surface) which contacts tissue once expanded. In some embodiments, tissue contacting a tissue contacting surface directly receives energy from the tissue contacting surface of the expandable components, however tissue in proximity (e.g. below or alongside) also receives energy (e.g. via conduction of the delivered energy and/or a resultant heat energy).

[065] As used herein, the term “normal level” refers to the level of a physiologic parameter that would be expected to be found in human subjects that are not afflicted with the disease or disorder being treated by the systems and/or methods of the present inventive concepts. In some embodiments, a normal level comprises the level of a physiologic parameter that would be expected to be found in human subjects that are: not afflicted with the disease or disorder being treated by the systems and/or methods of the present inventive concepts (e.g. diabetes, insulin resistance, and/or other metabolic condition); and also are not afflicted with one or more other adverse medical conditions (e.g. a cardiovascular condition). A normal level can be associated with human subjects (e.g. healthy human subjects) that are of similar age, race, and/or sex as the patient being treated by the systems and/or methods of the present inventive concepts.

[066] It is an object of the present inventive concepts to provide systems, methods, and devices for safely and effectively treating and/or diagnosing a volume of tissue (the “target tissue”), such as to treat and/or diagnose a patient disease or disorder. Target tissue can comprise one or more target tissue segments or other target tissue portions, such as target tissue located in the intestine of a patient. Clinical procedures in the duodenum and other locations of the small intestine are challenging for a number of reasons, such as those caused by the long distance between the mouth and the intestine, and the complexities of the gastrointestinal

passageway encountered (including passage through the stomach) during device (e.g. catheter) insertion and operation. Intestinal diameter varies along its length, and effective devices must accommodate this variation. The intestine is quite distensible in the longitudinal and radial directions, further complicating device (e.g. catheter) manipulation and operation (e.g. delivery of energy to tissue). Mobility of intestinal mucosa relative to muscularis is present, as well as mobility of the full wall, but can result in undesired stretching, compression and intussusception. The duodenum is normally closed, and it can require insufflation to open (e.g. for visualization). The insufflation medium (e.g. gas) moves through the intestine, so more must be delivered, while excess gas causes discomfort or other adverse effect for the patient. Duodenal and other intestinal tissue tends to stretch or compress as a device is advanced or retracted, respectively, such as to cause retrograde expulsion of devices if a stabilization force is not maintained. It is difficult to manipulate and control devices that include treatment and other elements positioned in the small intestine. The small intestine wraps around the pancreas, and the curvature is quite variable from patient to patient. The length of the intestine along an outer curve is longer than that along an inner curve. In many procedures, there is a desire to avoid damage to the ampulla of Vater (e.g. to avoid restricting bile and/or pancreatic fluid), tissue which can be difficult to visualize or otherwise identify. There are relatively few endoscopically visualizable landmarks in the intestine, making it difficult to know where in the intestine a portion (e.g. a distal portion) of a device is positioned. Access to the intestine through the stomach via an over-the wire catheter loses one-to-one motion between a proximal handle and a distal portion of the device, as slack can accumulate in the stomach during advancement and slack can be relieved from the stomach during withdrawal. Accessing the intestine can include entering the intestine through the pylorus, a small sphincter, from the stomach, and in obese patients, large stretchable stomachs make it difficult to direct a device to the pylorus. The intestinal mucosa has a very irregular surface due to plicae circulares and mucosal villi, and performing a treatment (e.g. an ablation treatment) of the intestinal mucosa is quite different from a treatment procedure performed in the stomach or esophagus, because of this irregularity. Peristalsis present in the small intestine is dynamic and unpredictable and can alter functional element, functional assembly and/or other device component position and/or contact level with tissue. The intestine is not only thin walled, but the thickness of the wall is highly variable, even within small axial segments of the small intestine, thus complicating preferential ablation of inner layers versus outer layers of the small intestine. The muscularis is innervated and scars and/or stenoses easily, and as such, even minimal trauma to the muscularis should be avoided.

[067] Target tissue can comprise one or more layers of a portion of tubular or non-tubular tissue, such as tissue of an organ or tissue of the gastrointestinal (GI) tract of a patient, such as

tissue of the small intestine or large intestine. The systems and devices of the present inventive concepts can include one or more functional assemblies and/or functional elements configured to treat target tissue, such as a treatment element comprising fluid at an ablative temperature delivered to a balloon (ablative temperature fluid and/or balloon filled with ablative fluid each referred to singly or collectively as a “functional element” or a “treatment element” of the present inventive concepts). One or more functional elements can be provided in, on and/or within an expandable functional assembly or other radially deployable mechanism. Functional assemblies and/or functional elements can be configured to treat target tissue (e.g. deliver energy to target tissue), such as to modify target tissue (e.g. to modify the secretions from the target tissue and/or absorption of the target tissue), ablate target tissue (e.g. to cause the replacement of the target tissue with “new tissue”) and/or to cause a reduction in the surface area of target tissue (e.g. the luminal surface area of an inner wall of tubular tissue) at and/or proximate to one or more locations where the treatment was performed (e.g. at and/or proximate the location where energy was delivered). The luminal or other tissue treatment can occur acutely and/or it can take place over time, such as days, weeks, or months. A tissue surface area reduction can correspond to a reduction in mucosal surface area available to function in an absorptive, neuronal signaling, and/or a hormonal secretory capacity. A target tissue treatment can result in the replacement of target tissue with new tissue with different absorptive and/or secretory capacity and/or other desirable effect related to replacement and/or modification of target tissue. The treatment of target tissue with the systems, devices and methods of the present inventive concepts can provide a therapeutic benefit to the patient, such as to treat one or more diseases or disorders of the patient, as described in detail herein.

[068] Each functional assembly (e.g. a functional assembly configured as a tissue treatment assembly) can comprise at least one functional element (e.g. at least one tissue treatment element) such as one, two, or more tissue treatment elements selected from the group consisting of: ablative fluid delivered to a balloon or other expandable fluid reservoir; ablative fluid comprising at least steam delivered directly or indirectly to tissue; an energy delivery element mounted to an expandable functional assembly such as an electrode or other energy delivery element configured to deliver radiofrequency (RF) energy and/or microwave energy; an electrode or other energy delivery element configured to deliver electroporation energy, such as reversible and/or irreversible electroporation energy; an electrode, fluid delivery element, and/or other delivery element configured to deliver both reversible electroporation energy and an agent (e.g. a tissue ablating agent whose ablation is triggered and/or enhanced with the delivery of electroporation energy); light delivery element configured to deliver laser or other light energy; fluid delivery element (e.g. needle or nozzle) configured to deliver a necrosis-causing fluid

and/or other ablative fluid directly onto and/or into tissue; sound delivery element such as an ultrasonic and/or subsonic sound delivery element; and combinations of two or more of these. Numerous forms of functional assemblies and/or functional elements can be included. In some embodiments, the functional assemblies and/or the one or more functional elements contained therein are configured as described in: applicant's co-pending United States Patent Application Serial Number 17/222,480 (Attorney Docket No. 41714-703.303; Client Docket No. MCT-001-US-CON2), entitled "Devices and Methods for the Treatment of Tissue", filed April 5, 2021; applicant's co-pending United States Patent Application Serial Number 17/864,855 (Attorney Docket No. 41714-704.303; Client Docket No. MCT-002-US-CON2), entitled "Heat Ablation Systems, Devices and Methods for the Treatment of Tissue", filed July 14, 2022; applicant's co-pending United States Patent Application Serial Number 17/879,222 (Attorney Docket No. 41714-706.303; Client Docket No. MCT-004-US-CON2), entitled "Electrical Energy Ablation Systems, Devices and Methods for the Treatment of Tissue", filed August 2, 2022; and/or applicant's co-pending United States Patent Application Serial Number 17/192,671 (Attorney Docket No. 41714-707.302; Client Docket No. MCT-005-US-CON1), entitled "Ablation Systems, Devices, and Methods for the Treatment of Tissue", filed March 4, 2021.

[069] The functional assemblies and/or treatment elements of the present inventive concepts can be constructed and arranged to deliver one or more treatments (e.g. deliver energy, deliver a chemically ablative fluid, mechanically abrade and/or otherwise treat tissue) directly to a particular area of tissue, the "delivery zone". The area of tissue treated can comprise a segment of the small intestine, or other body lumen, where the delivery zone comprises a length representing the axial length of the segment treated, and a width such as a width representing a full or partial circumferential portion of the segment. A treatment element can be configured to ablate or otherwise treat an energy delivery zone with a "treatment length" and a "treatment width". During a single delivery of treatment, a treatment element can be constructed and arranged to deliver treatment to a relatively continuous surface of tissue (e.g. a continuous surface of tissue in contact with a balloon filled with ablative fluid or a surface of tissue onto which a chemically ablative fluid is sprayed, coated or otherwise delivered). In these continuous-surface treatment delivery embodiments, the delivery zone comprises the continuous surface of tissue receiving the treatment directly. Alternatively, a treatment element can be constructed and arranged to deliver treatment to multiple discrete portions of a tissue surface, with one or more tissue surface portions in-between other surface portions that do not directly receive energy or other treatment from the treatment element. In these segmented-surface treatment delivery embodiments, the delivery zone is defined by a periphery of the multiple tissue surface area portions receiving treatment, similar to a "convex hull" or "convex envelope"

used in mathematics to define an area including a number of discrete locations that define a periphery. A delivery zone can comprise two or more contiguous or non-contiguous delivery zones, and multiple delivery zones can be treated sequentially and/or simultaneously.

[070] For example, in embodiments where the treatment element is hot fluid (e.g. ablative fluid at a sufficiently high temperature to cause tissue necrosis) positioned within a balloon, the delivery zone comprises all tissue surfaces contacted by the balloon that directly receive ablative thermal energy from the ablative fluid through the balloon. In embodiments where the treatment element is a balloon filled with cold fluid (e.g. ablative fluid at a sufficiently low temperature to cause tissue necrosis), the delivery zone can comprise all tissue surfaces contacted by the balloon that have heat directly extracted from them by the cold fluid (e.g. at a sufficient cold temperature to treat the tissue). In embodiments where the treatment element is an array of electrodes configured to deliver electrical energy (e.g. radiofrequency and/or other electromagnetic energy) to tissue, the delivery zone can comprise an area defined by the electrodes on the periphery of the array (e.g. a convex hull as described above), such as when the electrodes are positioned and energy is delivered to treat relatively the entire surface of tissue within the periphery. In embodiments where the treatment element comprises one or more fluid delivery elements delivering ablative fluid directly onto tissue (e.g. an ablative fluid whose chemical nature modifies tissue, at body temperature or otherwise), the delivery zone can comprise a surface defined by the periphery of tissue locations receiving the ablative fluid, such as when the ablative fluid is delivered (e.g. sprayed or otherwise applied, such as via a sponge) to relatively the entire surface within the periphery. In embodiments where the treatment element comprises one or more light delivery elements such as those that deliver laser energy to tissue, the delivery zone can comprise a surface area defined by the periphery of tissue locations receiving the light energy, such as when light is delivered at a set of locations and with a magnitude of energy configured to treat relatively the entire surface of tissue within the periphery. In these embodiments, light can be delivered to relatively the entire energy delivery zone, or to a large number (e.g. greater than 100) of tissue locations within the periphery of the delivery zone (e.g. making up less than 50%, less than 20% or less than 10% of the total surface area of the delivery zone). In embodiments where the treatment element comprises one or more sound delivery elements such as those that deliver sub-sonic and/or ultrasonic sound energy to tissue, the delivery zone can comprise a surface area defined by the periphery of tissue locations receiving the sound energy, such as when ablative sound energy is delivered at a set of locations and with a magnitude of energy configured to treat relatively the entire surface of tissue within the periphery. In embodiments in which the treatment element comprises a mechanical cutter or other abrasion element, the delivery zone can comprise a surface defined by all tissue dissected,

cut, mechanically disrupted and/or otherwise modified during a single abrading step of the mechanical abrader.

[071] A delivery zone can comprise a cumulative set of delivery zones that receive treatment simultaneously and/or sequentially, by one or more tissue treatment elements, such as those described herein. A delivery zone can comprise a first delivery zone defined when a treatment element treats target tissue in a first treatment delivery, plus a second delivery zone defined when the treatment element treats target tissue in a second treatment delivery, and so on. In these embodiments, the treatment element can be translated, rotated and/or otherwise repositioned between treatments (e.g. energy delivery), where each delivery zone is associated with the position of the treatment element during each treatment. Multiple delivery zones can receive treatment in a single procedure, such as within a period of less than twenty-four hours. A delivery zone can comprise a set of multiple delivery zones treated by two or more treatment elements.

[072] Target tissue treated by each energy delivery and/or other treatment delivery comprises the tissue directly receiving treatment (i.e. the tissue defined by the delivery zone) plus “neighboring tissue” which is also modified by the associated treatment delivery. The neighboring tissue can comprise tissue alongside, below (e.g. in a deeper tissue layer) and/or otherwise proximate the delivery zone tissue. The neighboring tissue treatment can be due to one or more of: conduction and/or convection of heat or cold from the delivery zone; flow of ablative fluid from the delivery zone; flow of toxins or other agents that occur during cell degradation and/or cell death; radiation; luminescence, light dissipation; and other energy and/or chemical propagation mechanisms. In some embodiments, an area (i.e. the delivery zone) comprising an inner surface of mucosal tissue directly receives treatment from one or more treatment elements (e.g. an ablative fluid contained within a balloon), and the total volume of target tissue treated by that single treatment delivery includes: the delivery zone tissue (i.e. surface mucosal tissue directly receiving energy and/or other treatment from the treatment element); surface mucosal tissue in close proximity (e.g. adjacent) to the delivery zone tissue; and mucosal and potentially submucosal tissue layers beneath (deeper than) the delivery zone tissue and the treated adjacent surface mucosal tissue.

[073] In some embodiments, a “treatment neutralizing” procedure is performed after one or more treatments (e.g. energy deliveries), such as a treatment neutralizing cooling procedure performed after one or more treatment elements deliver heat to treat target tissue, or a treatment neutralizing warming procedure performed after one or more treatment elements deliver cryogenic energy to treat target tissue. In these embodiments, the treatment neutralizing cooling or warming fluid can be delivered to the same functional assembly (e.g. an expandable

functional assembly comprising a balloon) delivering the heat or cryogenic treatment, respectively, and/or the neutralizing fluid can be delivered directly to tissue by the same or different functional assembly or functional element. In some embodiments, a functional element delivers an ablating agent to target tissue (e.g. a chemical or other agent configured to cause target tissue necrosis or otherwise treat target tissue), and a treatment neutralizing procedure comprises delivery of a neutralizing agent (by the same or different functional element) to target and/or non-target tissue to reduce continued ablation due to the delivered caustic ablative fluid (e.g. a base to neutralize a delivered acid or an acid to neutralize a delivered base).

[074] Each functional assembly and/or functional element of the present inventive concepts can be configured to be positioned in one or more intestinal and/or other locations of the patient, such as to perform a function (e.g. perform a treatment, deliver fluid and/or record data) at one or more contiguous or discontinuous tissue locations. Target tissue to be treated (e.g. ablated) comprises a three-dimensional volume of tissue, and can include a first portion, a treatment portion, whose treatment has a therapeutic benefit to a patient; as well as a second portion, a “safety-margin” portion, whose treatment has minimal or no adverse effects to the patient. “Non-target tissue” can be identified (e.g. prior to and/or during the medical procedure), wherein the non-target tissue comprises tissue whose treatment by the functional assembly (e.g. a tissue treatment assembly) and/or treatment element should be reduced or avoided such as to reduce or prevent an undesired effect to the patient.

[075] The target tissue treatment can cause one or more modifications of the target tissue such as a modification selected from the group consisting of: modification of cellular function; cell death; apoptosis; instant cell death; cell necrosis; denaturing of cells; removal of cells; and combinations of two or more of these. In some embodiments, the target tissue treatment is configured to create scar tissue. Target tissue can be selected such that after treatment the treated target tissue and/or the tissue that replaces the target tissue functions differently than the pre-treated target tissue, such as to have a therapeutic benefit for the patient. The modified and/or replacement tissue (singly or collectively “treated tissue”) can exhibit different properties than the pre-treated target tissue, such as different properties that are used to treat a patient disease or disorder. The treated tissue can have different secretions and/or quantities of secretions than the pre-treated target tissue, such as to treat diabetes, hypercholesterolemia and/or another patient disease or disorder. The treated tissue can have different absorptive properties than the target tissue, such as to treat diabetes, hypercholesterolemia and/or another patient disease or disorder. The treated tissue can have a different surface topography than the target tissue, such as a modification of the topography of the inner wall of the GI tract that includes a smoothing or flattening of its inner surface, such as a modification in which the

luminal surface area of one or more segments of the GI tract is reduced after treatment. The effect of the treatment (e.g. the effect on the target tissue) can occur acutely, such as within twenty-four hours, or after longer periods of time, such as greater than twenty-four hours or greater than one week.

[076] Target tissue to be treated can comprise two or more discrete tissue segments, such as two or more axial segments of the GI tract. Each tissue segment can comprise a full (e.g. approximately 360°) or partial circumferential segment of the tissue segment. Multiple tissue segments can be treated with the same or different functional elements (e.g. treatment elements), and they can be treated simultaneously or in sequential steps (e.g. sequential energy delivery steps that deliver energy to multiple delivery zones). Multiple tissue segments can be treated in the same or different clinical procedures (e.g. procedures performed on different days). In some embodiments, a series of tissue segments comprising a series of axial segments of the GI tract are treated in a single clinical procedure. The first and second tissue segments can be directly adjacent, they can contain overlapping portions of tissue, and/or there can be gaps between the segments. Dissimilarities in treatment elements can include type and/or amount of energy to be delivered by an energy delivery-based treatment element. Dissimilarities in target tissue treatments can include: target tissue area treated; target tissue volume treated; target tissue length treated; target tissue depth treated; target tissue circumferential portion treated; ablative fluid type, volume and/or temperature delivered to a reservoir such as a balloon; ablative fluid type, volume and/or temperature delivered directly to tissue; energy delivery type; energy delivery rate and/or amount; peak energy delivered; average temperature of target tissue achieved during target tissue treatment; maximum temperature achieved during target tissue treatment; temperature profile of target tissue treatment; duration of target tissue treatment; surface area reduction achieved by target tissue treatment; and combinations of two or more of these.

[077] Target tissue can include tissue of the duodenum, such as tissue including substantially all or a portion of the mucosal layer of one or more axial segments of the duodenum (e.g. including all or a portion of the plicae circulares), such as to treat diabetes, hypercholesterolemia and/or another patient disease or disorder, such as while leaving the duodenum anatomically connected after treatment. Target tissue can include one or more portions of a tissue layer selected from the group consisting of: mucosa; mucosa through superficial submucosa; mucosa through mid-submucosa; mucosa through deep submucosa; and combinations of two or more of these. Replacement tissue can comprise cells that have migrated from one or more of: gastric mucosa; jejunal mucosa; an untreated portion of the duodenum whose mucosal tissue functions differently than the treated mucosal tissue functions prior to treatment; and combinations of two or more of these. Replacement tissue can include one or more tissue types selected from the

group consisting of: scar tissue; normal intestinal mucosa; gastric mucosa; and combinations of two or more of these. In some embodiments, replacement tissue comprises tissue that has been delivered onto and/or into tissue by a catheter of the present inventive concepts. In some embodiments, target tissue includes a treatment portion comprising the mucosal layer of the duodenum, and a safety-margin portion comprising a near-full or partial layer of the submucosal layer of the duodenum. In some embodiments, the target tissue comprises nearly the entire mucosal layer of the duodenum, and this tissue can include a portion of the pylorus contiguous with the duodenal mucosa and/or a portion of the jejunum contiguous with the duodenal mucosa. In some embodiments, the target tissue comprises all or a portion of the duodenal mucosa distal to the ampulla of Vater (e.g. avoiding tissue within at least 0.5cm, 1.0cm or 1.5cm from the ampulla of Vater while including tissue within 5cm, 10cm or 15cm distal to the ampulla of Vater). In these embodiments, the target tissue can comprise at least 10%, at least 15%, at least 25%, at least 30% or at least 50% of the duodenal mucosa distal to the ampulla of Vater. Alternatively or additionally, the target tissue can comprise no more than 70% or no more than 90% of the duodenal mucosa distal to the ampulla of Vater. In these embodiments, tissue proximal to and/or proximate the ampulla of Vater can comprise non-target tissue (i.e. tissue whose treatment is avoided or at least reduced).

[078] In some embodiments, the target tissue comprises neuronal cells of duodenal mucosal tissue. In some embodiments, the target tissue comprises neuronal cells of duodenal submucosa tissue.

[079] In some embodiments, the target tissue comprises at least a portion of duodenal mucosal tissue, and the systems, methods and devices of the present inventive concepts are configured to counteract duodenal mucosal changes that cause an intestinal hormonal impairment leading to insulin resistance in patients. In these embodiments, the therapy provided can improve the body's ability to process sugar and dramatically improve glycemic control for patients with insulin resistance and/or type 2 diabetes. In some embodiments, target tissue is treated to prevent and/or reduce cognitive decline (e.g. Alzheimer's Disease), such as by improving sugar metabolism in the brain, overcoming insulin resistance in the brain, reducing toxicity of beta amyloid, reducing oxidative stress, and/or reducing inflammation in the brain associated with neuronal death. In some embodiments, target tissue is treated to: prevent liver fibrosis and/or cirrhosis (e.g. non-alcoholic fatty liver disease NAFLD or non-alcoholic steatohepatitis NASH); reduce liver fat; reduce oxidative stress; and/or reduce inflammation in the liver associated with liver fibrosis and toxicity. The systems and methods of the present inventive concepts can be configured to lower insulin requirements by improving insulin resistance (e.g. as opposed to improving insulin secretion), and/or by direct glucose lowering

(e.g. by causing an increase in glucose excretion in the urine). Alternatively or additionally, the systems and methods of the present inventive concepts can be configured to lower insulin requirements by improving hepatic insulin resistance and/or by improving muscle insulin resistance.

[080] Hormones released from the intestinal mucosa play an important role in modulating glucose homeostasis, and different axial segments of the intestinal mucosa release different hormones in the fasting and post-prandial state, in order to modulate blood glucose in the fasting and post-prandial states, respectively. After a meal, the proximal intestinal mucosa senses the intestine for ingested glucose and releases a collection of hormones in response to this signal. These hormones initiate the process of insulin release into the bloodstream after a meal, but they also induce some insulin resistance to prevent the released insulin from causing hypoglycemia before the body has a chance to absorb the ingested glucose. One such hormone that plays a role in this is GIP. Distal gut hormones (produced in the jejunum or a more distal location), on the contrary, allow the release of more insulin but also play a role in helping the body now become sensitive to its circulating insulin. Teleologically, the explanation for this difference in the type of gut hormones produced by different segments of the intestine is that enough glucose will have been absorbed by the time nutrients reach the distal intestine to allow the insulin to begin to function to reduce blood glucose levels. Releasing different hormones at different times (e.g. from different segments of the intestine) enables the body to absorb and process glucose in such a way as to avoid hypoglycemia (blood sugars that are too low) and hyperglycemia (blood sugars that are too high). In this way, intestinal hormonal signaling is important for whole body glucose homeostasis in the fasting and post-prandial states. The treatment can also lead to weight loss through decreased absorption of nutrients, increased sensation of satiety, altered food preferences, increased energy expenditure, and combinations of two or more of these.

[081] In patients with type 2 diabetes, a lifetime of exposure to fat and sugar can lead to intestinal changes that occur in regions with the highest exposure to these nutrients, predominantly in the proximal intestine. These changes are characterized by an excess proximal intestinal mucosa's hormonal contribution to the fasting and post-prandial glucose homeostasis. The net result of these intestinal changes is to create a condition of insulin resistance and impaired glucose tolerance. Treatment of duodenal mucosal tissue with the systems, devices and methods of the present inventive concepts can be performed to alter the intestinal mucosal hormone production from the region of treated tissue. The treated tissue can then have an altered hormonal secretion pattern that affects blood glucose levels in the fasting and post-prandial states. The tissue treatment of the present inventive concepts can be performed to effect duodenal mucosal tissue secretion of GIP and/or GLP-1. The tissue treatment can lead to

changes in the blood levels of GIP and/or GLP-1 (and other gut hormones) that can lead to changes in glucose homeostasis in the fasting and/or post-prandial states. The treatment can lead to changes in insulin and/or glucagon secretion from the pancreas and/or insulin and/or glucagon levels in the bloodstream. The treatment can lead to changes in pancreatic beta cell function and/or health through direct hormonal consequences of the treated duodenal tissue and/or indirectly through improved blood glucose levels. In some embodiments, the treatment of the present inventive concepts is configured to at least one of reduce a blood glucose level and/or reduce a lipoprotein level.

[082] Treatment of intestinal tissue (e.g. duodenal mucosal tissue) using the systems, devices, and methods of the present inventive concepts can be performed to treat a medical condition (e.g. a disease and/or disorder) selected from the group consisting of: diabetes; pre-diabetes; impaired glucose tolerance; insulin resistance; a condition caused by or otherwise related to insulin resistance; obesity or otherwise being overweight; a metabolic disorder and/or disease; a condition caused by or otherwise related to a metabolic disorder and/or disease; and combinations of two or more of these. In some embodiments, treatment of intestinal tissue (e.g. at least duodenal mucosal tissue) using the systems, devices and/or methods of the present inventive concepts can be performed to treat one or more medical conditions selected from the group consisting of: type 2 diabetes; type 1 diabetes; "Double diabetes"; gestational diabetes; hyperglycemia; pre-diabetes; impaired glucose tolerance; insulin resistance; non-alcoholic fatty liver disease (NAFLD); non-alcoholic steatohepatitis (NASH); obesity; obesity-related disorder; polycystic ovarian syndrome (PCOS); hypertriglyceridemia; hypercholesterolemia; psoriasis; GERD; coronary artery disease (e.g. as a secondary prevention); stroke; TIA; cognitive decline; dementia; Alzheimer's disease; neuropathy; diabetic nephropathy; retinopathy; heart disease; diabetic heart disease; heart failure; diabetic heart failure; hirsutism; hyperandrogenism; fertility issues; menstrual dysfunction; cancer such as liver cancer, ovarian cancer, breast cancer, endometrial cancer, cholangiocarcinoma, adenocarcinoma, glandular tissue tumor(s), stomach cancer, large bowel cancer, and/or prostate cancer; diastolic dysfunction; hypertension; myocardial infarction; microvascular disease related to diabetes; sleep apnea; arthritis; rheumatoid arthritis; hypogonadism; insufficient total testosterone levels; insufficient free testosterone levels; metabolic dysfunction-associated steatotic liver disease (MASLD); and combinations of two or more of these. In some embodiments, two, three, or more of the above medical conditions listed immediately hereabove are treated using the systems, devices, and methods of the present inventive concepts. A near full circumferential portion (e.g. approximately 360°) of the mucosal layer of one or more axial segments of GI tissue can be treated. In some embodiments, less than 360° of one or more axial segments of tubular tissue is

treated, such as one or more circumferential portions less than 350°, or between 300° and 350°, such as to prevent a full circumferential scar from being created at the one or more axial segment locations. In order to achieve a desired therapeutic benefit, a minimum amount of mucosal tissue can be treated, such as is described herein.

[083] In some embodiments, the systems, devices, and methods of the present inventive concepts are used to treat arthritis, such as rheumatoid arthritis. In these embodiments, arthritis and another disease or disorder of the patient can be treated, such as when one, two, or more of the following are treated in addition to arthritis: insulin resistance, diabetes, non-alcoholic fatty liver disease (NAFLD); non-alcoholic steatohepatitis (NASH); polycystic ovarian syndrome (PCOS); and combinations of these. For example, patients with arthritis may exhibit abnormal and/or dysfunctional glucose metabolism. In some embodiments, a patient exhibiting insulin resistance as well as arthritis (e.g. rheumatoid arthritis) has their small intestinal mucosa (e.g. their duodenal mucosa) treated with the systems of the present inventive concepts.

[084] Target tissue can be selected to treat two or more patient diseases or disorders, such as two or more patient diseases or disorders as described herein.

[085] Target tissue can comprise tissue of the terminal ileum, such as to treat hypercholesterolemia and/or diabetes. In these embodiments, the target tissue can extend into the proximal ileum and/or the colon.

[086] Target tissue can comprise gastric mucosal tissue, such as tissue regions that produce ghrelin and/or other appetite regulating hormones, such as to treat obesity and/or an appetite disorder.

[087] Target tissue can comprise tissue selected from the group consisting of: large and/or flat colonic polyps; margin tissue remaining after a polypectomy; and combinations of two or more of these. These tissue locations can be treated to treat residual cancer cells.

[088] Target tissue can comprise at least a portion of the intestinal tract afflicted with inflammatory bowel disease (e.g. chronic inflammatory bowel disease), such that Crohn's disease and/or ulcerative colitis can be treated.

[089] Target tissue can comprise GI tissue selected to treat Celiac disease and/or to improve intestinal barrier function.

[090] The functional assemblies, functional elements, systems, devices and methods of the present inventive concepts can be configured to avoid ablating or otherwise adversely affecting certain tissue, termed "non-target tissue" herein. Depending on the location of tissue intended for treatment (i.e. target tissue), different non-target tissue can be applicable. In certain embodiments, non-target tissue can comprise tissue selected from the group consisting of: gastrointestinal adventitia; duodenal adventitia; the tunica serosa; the tunica muscularis; the

outermost partial layer of the submucosa; ampulla of Vater; papilla; pancreas; bile duct; pylorus; and combinations of two or more of these.

[091] In some embodiments, two or more clinical procedures are performed in which one or more volumes of target tissue are treated in each clinical procedure, such as is described in applicant's co-pending United States Patent Application Serial Number 17/568,145 (Attorney Docket No. 41714-708.302; Client Docket No. MCT-009-US-CON1), entitled "Methods, Systems and Devices for Performing Multiple Treatments on a Patient", filed January 4, 2022. For example, a second clinical procedure can be performed at least twenty-four hours after the first clinical procedure, such as a second clinical procedure performed within six months of a first clinical procedure or a clinical procedure performed after at least six months after the first clinical procedure. The first and second clinical procedures can be performed using similar or dissimilar methods, and they can be performed using similar or dissimilar systems and/or devices (e.g. performed with similar or dissimilar treatment and/or other functional elements). The first and second clinical procedures can treat similar or dissimilar volumes of target tissue (e.g. similar or dissimilar amounts of tissue treated and/or locations of tissue treated), and they can deliver energy to similar or dissimilar sets of multiple delivery zones. In some embodiments, the first and second clinical procedures can include treating and/or delivering energy to contiguous and/or overlapping regions of the GI tract either in the circumferential and/or axial dimensions. In other embodiments, the first and second clinical procedures can include the treatment of disparate regions of the GI tract (such as disparate regions of the duodenum, ileum, and/or stomach). The first and second clinical procedures can be performed using similar or dissimilar devices (e.g. catheters). The first and second clinical procedures can comprise similar or dissimilar deliveries of energy to treat the target tissue. The first and second clinical procedures can be performed at similar or dissimilar temperatures. The second clinical procedure can be performed based on diagnostic results collected after the first clinical procedure has been performed, such as when the diagnostic results are based on a biopsy of mucosal tissue.

[092] The functional assemblies (also referred to as treatment assemblies and tissue treatment assemblies), treatment elements and other functional elements of the present inventive concepts can comprise an expandable element or otherwise be configured to automatically and/or manually expand or traverse in at least one radial direction. Typical expandable elements include but are not limited to: an inflatable balloon; a radially expandable cage or stent; one or more radially deployable arms; an expandable helix; an unfurlable compacted coiled structure; an unfurlable sheet; an unfoldable compacted structure; and combinations of two or more of these. In some embodiments, an expandable element can comprise a radially expandable tube,

such as a sheet of material resiliently biased in a radially expanded condition that can be compacted through a furling operation, or a sheet of material resiliently biased in a radially compact condition that can be expanded through an unfurling operation. An expandable element can comprise a foldable sheet, such as a sheet configured to be folded to be radially compacted and/or to be unfolded to radially expand. In some embodiments, an expandable element expands to contact tissue, such as to expand to a diameter similar to the diameter of the luminal wall tissue into which the expandable element has been placed. In some embodiments, an expandable element expands to be closer to wall tissue, but the element remains at a distance (e.g. a fixed or pre-determined distance) from the tissue surface, such as when the tissue is subsequently brought into contact with all or a portion of an expanded functional assembly or functional element (e.g. using insufflation fluid withdrawal techniques). In some embodiments, an expandable element expands to be larger than the diameter of the luminal wall tissue into which the expandable element has been placed, such as to improve the quality of the apposition of the expandable element against the uneven surface of the tissue. In these embodiments, the fully expanded diameter of an expandable element would be configured to avoid a diameter large enough to cause lasting mechanical damage to the apposed tissue and/or to tissue proximate the apposed tissue. In some embodiments, the expansion of an expandable element (e.g. the expansion of an expandable functional assembly) is monitored and/or varied (e.g. decreased and/or increased), such as to accommodate or otherwise compensate for peristalsis or other muscle contractions that occur in the GI tract (e.g. contractions that occur when a foreign body is present in the GI tract) and/or varied to accommodate changes in GI lumen diameter imposed by aspects of the procedure itself.

[093] Any device (e.g. catheter) of the present inventive concepts can include one or more functional elements comprising one or more treatment elements configured to deliver energy to one or more delivery zones, to treat at least a portion of target tissue. Any device can include one or more functional elements comprising one or more fluid delivery elements, such as one or more nozzles or needles configured to deliver fluid toward and/or into tissue. The fluid delivery elements can be constructed and arranged to deliver fluid to perform a function selected from the group consisting of: expanding one or more tissue layers; warming or cooling tissue; removing debris or other substance from a tissue surface; delivering energy to a delivery zone comprising a continuous or segmented surface; treating target tissue; and combinations of two or more of these. Any of the expandable functional assemblies of the present inventive concepts can include one or more other functional elements, such as are described herein. The treatment elements and/or other functional elements (e.g. fluid delivery elements) can be mounted on, within (e.g. within the wall) and/or inside of an expandable element such as a balloon or

expandable cage. In some embodiments, one or more functional elements is not mounted to an expandable element, such as those attached to a shaft or other non-expandable catheter component.

[094] In some embodiments, a catheter comprises at least one functional element configured to deliver energy to a delivery zone such as to ablate target tissue. Examples of ablation-based functional elements include but are not limited to: ablative fluids, such as hot or cold ablative fluids delivered to a balloon and/or directly to target tissue; one or more fluid delivery elements configured to deliver ablative fluid directly to target tissue; a radiofrequency (RF) and/or microwave energy delivery element such as one or more electrodes; an ultrasonic and/or subsonic transducer such as one or more piezo crystals configured to ablate tissue with ultrasonic or subsonic energy, respectively, sound waves; a laser energy delivery element such as one or more optical fibers, laser diodes, prisms and/or lenses; a rotating ablation element; a circumferential array of ablation elements; and combinations of two or more of these.

[095] The expandable elements comprising balloons of the present inventive concepts can be divided into two general categories: those that are composed of a substantially elastic material, such as silicone, latex, low-durometer polyurethane, and the like; and those that are composed of a substantially inelastic material, such as polyethylene terephthalate (PET), nylon, high-durometer polyurethane and the like. A third category includes balloons which include both elastic and inelastic portions. Within the category of elastic balloons, two subcategories exist: a first sub-category wherein a combination of material properties and/or wall thickness can be combined to produce a balloon that exhibits a measurable pressure-threshold for inflation (i.e. the balloon becomes inflated only after a minimum fluidic pressure is applied to the interior of the balloon); and a second sub-category, wherein the balloon expands elastically until an elastic limit is reached which effectively restricts the balloon diameter to a maximum value. The individual properties of the balloons in each of these categories can be applied to one or more advantages in the specific embodiments disclosed herein, these properties integrated singly or in combination. By way of example only, one or more of the following configurations can be employed: a highly elastic balloon can be used to achieve a wide range of operating diameters during treatment (e.g. during operation a desired balloon diameter can be achieved by adjustment of a combination of fluid temperature and pressure); a substantially inelastic balloon or a balloon that reaches its elastic limit within a diameter approximating a target tissue diameter (e.g. a duodenal mucosal diameter) can be used to achieve a relatively constant operating diameter that will be substantially independent of operating pressure and temperature; a balloon with a pressure-threshold for inflation can be used to maintain an uninflated diameter during relatively low pressure conditions of fluid flow and then achieve a larger operating diameter at

higher pressure conditions of flow. Pressure-thresholded balloons can be configured in numerous ways. In one embodiment, a balloon is configured to have a relatively thick wall in its uninflated state, such as to maximize an electrically and/or thermally insulating effect while the balloon is maintained in this uninflated state. The balloon can be further configured such that its wall thickness decreases during radial expansion (e.g. to decrease an electrically and/or thermally insulating effect). In another embodiment, a balloon is configured to have a relatively small diameter in its uninflated state (e.g. a diameter that is small relative to the inner diameter of tubular target tissue such as the diameter of the mucosal layer of duodenal wall tissue), such as to minimize or completely eliminate apposition between the balloon and the surrounding tissue to minimize heat, RF and/or other energy transfer into the surrounding tissue until the balloon is fully inflated. In another embodiment, a balloon and an ablation system or catheter are configured to circulate a flow of fluid through the balloon (e.g. an elastic balloon or an inelastic balloon) at a sufficiently low enough pressure to prevent apposition of the balloon or other catheter component with target tissue, such as to pre-heat one or more surfaces of the ablation system or ablation device that are in fluid communication with the balloon. In this configuration, when the balloon or other ablation element is positioned to deliver energy to target tissue, the temperature of the balloon or other ablation element will be at a desired level or it will rapidly and efficiently reach the desired level for treatment (i.e. minimal heat loss to the fluid path components due to the pre-heating or pre-cooling). These configurations provide a method of delivering energy to tissue with an ablative fluid filled balloon. A “thermal priming” procedure can be performed prior to one or more target tissue treatments, such as to improve thermal response time of one or more portions of the catheter. Ablative fluid filled balloon catheters as well as thermal priming devices and methods can be configured as is described in applicant’s co-pending United States Patent Application Serial Number 17/864,855 (Attorney Docket No. 41714-704.303; Client Docket No. MCT-002-US-CON2), entitled “Heat Ablation Systems, Devices and Methods for the Treatment of Tissue”, filed July 14, 2022.

[096] A fluid evacuation procedure can be performed on one or more internal locations of the catheters, functional assemblies and/or functional elements of the present inventive concepts, such as when a negative pressure is applied to purge or otherwise evacuate fluid from one or more locations. A fluid evacuation procedure can be performed prior to a thermal priming procedure and/or prior to delivering ablative fluid to a treatment element.

[097] At times during target tissue treatment when it is desirable to initiate, increase and/or otherwise modify the treatment of tissue by one or more treatment elements (e.g. a fluid delivery element delivering ablative fluid, a mechanically abrasive element, a hot or cold fluid balloon delivering a thermal energy to tissue and/or an electrode delivering RF energy), the diameter of

the tissue treatment assembly and/or treatment element (e.g. the diameter of a balloon, deployable cage, expandable tube or other expandable assembly) can be increased in situ to move a treatment element closer to target tissue and/or to change the contact force between the treatment element and the target tissue. At times during treatment when it is desirable to stop or otherwise decrease the amount of tissue treatment, the diameter of the tissue treatment assembly and/or treatment element can be reduced in situ, such as to prevent or otherwise reduce delivery of energy or other treatment to the target tissue by eliminating or reducing tissue contact of one or more treatment elements (e.g. electrodes, abrasive surfaces or ablative fluid-filled balloons). For those cases where the native diameter of the target tissue varies substantially within a delivery zone, then a highly elastic or compliant balloon or other expandable element can be employed, such as a balloon or deployable cage which can be adjusted to achieve a wide range of operating diameters.

[098] Alternatively or additionally, to initiate, increase and/or otherwise modify the treatment of tissue by one or more functional elements (e.g. a fluid delivery element delivering ablative fluid, a mechanically abrasive element, a hot or cold fluid balloon delivering thermal energy to or from tissue and/or an electrode delivering RF energy), the diameter of the target tissue can be decreased in situ to move target tissue closer to a treatment element and/or to change the contact force between the target tissue and the treatment element. To stop or otherwise decrease ablation of tissue, the diameter of tissue neighboring a treatment element can be increased in situ, such as to prevent or otherwise reduce delivery of energy or other treatment to the target tissue by eliminating or reducing tissue contact of one or more treatment elements (e.g. electrodes, abrasive surfaces or ablative fluid filled balloons). The diameter of the tissue proximate a functional assembly can be increased or decreased, independent of the functional assembly diameter, by means of delivering and/or withdrawing a fluid, to and/or from a body lumen (e.g. a lumen of a segment of the intestine) surrounded by target tissue, such as by using standard GI insufflation techniques. Typical insufflation fluids include but are not limited to: gases such as carbon dioxide or air; liquids such as water or saline solution; and combinations of two or more of these. The insufflation fluids can be introduced through a catheter, through an endoscope such as an endoscope through which the catheter is inserted, and/or via another device placed proximate the target tissue. Delivery of insufflation fluids can be performed to move target tissue away from one or more functional elements, such as to stop transfer of energy to target tissue at the end of a treatment of target tissue as described herein. Alternatively or additionally, delivery of insufflation fluids can be performed to manipulate tissue, such as to distend and/or elongate tissue. Extraction of these insufflation fluids and/or the application of a vacuum or other negative pressure can be used to decrease the diameter of the target tissue, such

as to bring the target tissue in closer proximity to one or more functional elements and/or to increase the contact force between target tissue and one or more functional elements, also as described herein. In this tissue diameter-controlled approach, a functional assembly including a balloon that can be maintained at a substantially constant diameter can be desirable, such as a substantially inelastic balloon such as a balloon with an elastic-limit.

[099] The systems of the present inventive concepts can include one or more tissue expansion catheters that comprise one or more functional elements configured as fluid delivery elements. In these embodiments, the one or more functional elements can comprise one or more needles, nozzles and/or fluid jets configured to deliver one or more fluids or other injectates to tissue, such as to expand target tissue and/or tissue proximate the target tissue (e.g. safety margin tissue) prior to treatment of target tissue by a tissue treatment element. The expanded tissue layer acts as a safety volume of tissue, reducing the specificity of the treatment (e.g. ablation) required and/or the need to protect the underlying non-target tissue from damage. In some embodiments, a vacuum pressure can be used to manipulate tissue and/or to maintain proximity between a portion of a tissue expansion device and tissue. The vacuum can be provided by one or more vacuum sources, such as via one or more operator adjustable vacuum sources.

[0100] Many patients with type 2 diabetes (T2D) are prescribed insulin therapy, “daily insulin”, in order to treat high blood sugar. While insulin administration is a mainstay of type 2 diabetes therapy, more than half of patients do not achieve glycemic targets. Typically, insulin-treated patients have a higher prevalence of severe comorbidities, such as cardiovascular, renal, and/or hepatic comorbidities, than non-insulin-treated patients. Further, insulin therapy for type 2 diabetes is associated with weight gain (an increase in visceral adiposity), loss of beta-cell function, worsening of insulin resistance, and/or a high frequency of hypoglycemia, which is associated with poorer health outcomes and increased mortality. Moreover, insulin therapy in T2D is a symptomatic treatment of high blood sugar rather than a pharmacotherapy targeting the underlying insulin resistance that leads to the progressive nature of the disease. As such, insulin therapy quickly becomes insufficient and treatment intensification is needed. These factors taken together lead to tremendous dissatisfaction on the part of patients, poor clinical outcomes, and high cost of care. Therapies that reduce the need for insulin enable improved glycemic control with reduced rates of hypoglycemia and reduced rates of weight gain. The systems and methods (e.g. treatments) of the present inventive concepts provide improved glycemic control with reduced rates of hypoglycemia, weight loss, improvements to hepatic disease (such as improved liver fat content), and other benefits. These systems and methods can be configured to not require significant adherence to a drug protocol by the patient (e.g. including minimization or complete avoidance of taking one or more drugs previously part of the patient’s treatment).

Similarly, undesirable side-effects of these drugs can be avoided (e.g. nausea with GLP-1, or increased rates of urologic infections with SGLT2 inhibitors). The systems and methods of the present inventive concepts can be configured to allow an operator to perform a tissue treatment procedure (e.g. a tissue ablation procedure) on one or more segments of the patient's duodenum and/or other portions of the patient's gastrointestinal (GI) tract. The systems and methods of the present inventive concepts can reduce insulin intake by the patient without requiring the patient to adhere to a special diet (e.g. differing from diet-based approaches to insulin reduction). The systems and methods of the present inventive concepts can be configured to provide a reduction in therapeutic complications (e.g. as compared to a previous therapy in which the patient was treated) such as a reduction in microvascular complications (e.g. diabetic kidney disease, diabetic retinopathy) and/or macrovascular complications (e.g. myocardial infarction, stroke). The therapeutic benefits provided by the present inventive concepts can also include improvements in blood pressure, microalbuminuria, glomerular filtration rate, and/or other microvascular and macrovascular risk factors. The therapeutic benefits provided by the present inventive concepts can include a reduction in total body weight. The therapeutic benefits provided by the present inventive concepts can include a reduction in the likelihood of liver disease such as cirrhosis or liver carcinoma.

[0101] The systems, devices, and methods of the present inventive concepts can be configured to treat various duodenal dysfunctions, such as are described herein. Furthermore, and also as described herein, duodenal mucosal hyperplasia is a potential therapeutic target for metabolic diseases related to insulin-resistance. Applicant has demonstrated that treatment of intestinal mucosa (e.g. one or more portions of duodenal mucosa) can correspondingly therapeutically treat intestinal hyperplasia (e.g. duodenal mucosal hyperplasia), such as by reducing at least one of: duodenal mucosal surface area; duodenal mucosal volume; duodenal mucosal weight; duodenal mucosal villous height; quantity of duodenal villi; duodenal mucosal crypt density; duodenal mucosal enteroendocrine cell quantity; and/or duodenum-specific hormone production (e.g. GIP and/or CCK).

[0102] **Referring now to Fig. 1**, a system for treating and/or diagnosing ("treating" herein) gastrointestinal tissue is illustrated, consistent with the present inventive concepts. **System 10** is configured to treat and/or diagnose a patient such as a human or other mammal. System 10 includes one or more treatment devices, **treatment device 100** shown. System 10 and treatment device 100 can be used by an operator (e.g., one or more clinicians) to perform one or more medical procedures, such as a therapeutic procedure and/or a diagnostic procedure. Treatment device 100 can comprise a treatment device that is constructed and arranged to treat and/or

diagnose target tissue, such as tissue of the small intestine (e.g., mucosal tissue of the duodenum and/or jejunum, and/or nerve tissue proximate the duodenum and/or jejunum) and/or other locations within the gastrointestinal (GI) tract. Treatment device 100 can be constructed and arranged to deliver energy to tissue, such as to denature, ablate, remove, and/or otherwise modify the tissue. Alternatively or additionally, treatment device 100 can be constructed and arranged to expand one or more layers of tissue of the GI tract, such as when a submucosal tissue expansion procedure is performed in one axial segment of the GI tract after which an energy delivery to mucosal tissue is performed in that same axial segment. Treatment device 100 can be constructed and arranged to treat multiple relatively contiguous axial segments (“contiguous segments” or “contiguous axial segments” herein) or non-contiguous axial segments of the GI tract. In some embodiments, two or more axial segments of submucosal tissue of intestine are expanded, after which a single ablation procedure is performed (e.g., an ablation of a length of tissue of similar or lesser length as compared to the cumulative length of submucosal tissue expanded, such as when the length treated by a single ablation step is greater than the length expanded in a single tissue expansion step).

[0103] As described herein, system 10 can be configured to deliver one or more therapeutic doses of electromagnetic energy to tissue (e.g., to target tissue), such as a delivery of electromagnetic energy configured to irreversibly alter the target tissue. In some embodiments, the electromagnetic energy can be delivered between two or more energy delivery elements such as two or more electrode-based energy delivery elements of system 10 (e.g., electrodes 112 described herein). For example, electromagnetic energy can be delivered by one or more pairs of electrodes, such as when a first electrode is configured as a cathode and a second electrode is configured as an anode. In some embodiments, a therapeutic dose of electromagnetic energy comprises delivery of energy that causes irreversible electroporation of the target tissue, such as one or more pulses of electromagnetic energy delivered to irreversibly electroporate the tissue, an “IEP” energy delivery herein. As used herein, the delivery of an IEP can comprise the delivery of one or more pulses of electromagnetic energy to tissue that cause the irreversible electroporation of the tissue. The parameters of an IEP energy delivery can be selected such that the resultant electric field (e.g., the electric field generated by the one or more pulses of electromagnetic energy) causes irreversible electroporation of the target tissue. In some embodiments, an IEP energy delivery provided by system 10 does not cause significant thermal damage to tissue (e.g., to target tissue, tissue surrounding the target tissue, and/or non-target tissue).

[0104] System 10 can include one or more consoles that operably attach to treatment device 100, **console 200** shown. Console 200 can include one or more units and/or modules that enable

various functions of system 10 and treatment device 100 described herein, such as one or more modules configured to provide energy to treatment device 100, record one or more signals from treatment device 100, process information (e.g., information recorded from one or more devices of system 10), provide information to and/or receive input from the operator of system 10, and otherwise perform or enable the functions of system 10 described herein. Console 200 can operably attach (e.g., fluidly, electrically, magnetically, mechanically, pneumatically, hydraulically, optically, and/or acoustically attach) to treatment device 100 and/or other devices or assemblies of system 10. System 10 can include one or more cables, conduits, and/or other connection devices, **connection assembly 150** shown. Connection assembly 150 can operably connect treatment device 100 to console 200, as shown.

[0105] Treatment device 100 can include one or more assemblies for providing therapy and/or performing a diagnostic procedure, **treatment assembly 110** shown. In some embodiments, system 10 is configured to deliver energy to target tissue, such as energy configured to electroporate the target tissue (e.g., to reversibly and/or irreversibly electroporate the target tissue) to provide a therapeutic benefit, as described herein. Treatment assembly 110 can comprise one or more arrays of functional elements (e.g., sensors and/or transducers), **electrode array 111**, comprising one, two, or more elements, **electrodes 112**. In some embodiments, treatment assembly 110 can comprise an expandable assembly, such as an assembly configured to transition from a first, compacted geometry, to a second, expanded geometry. For example, treatment assembly 110 can include one or more expandable mechanisms, **expandable structure 113** shown. Expandable structure 113 can include an expandable mechanism such as an inflatable balloon, an expandable cage, an unfurlable sheet, an expandable spiral mechanism, radially deployable arms, and/or other mechanisms (e.g., as described herein) configured to transition between a first, compacted geometry, and a second, expanded geometry, such as to transition treatment assembly 110 between a first, compacted geometry, and a second, expanded geometry.

[0106] In some embodiments, electrodes 112 comprise a length no more than 1cm. In some embodiments, electrodes 112 can comprise a shape selected from the group consisting of: round; square; triangular; an irregular shape; and combinations of these. Electrodes 112 can comprise a surface geometry selected from the group consisting of: flat; pointed; rounded; and combinations of these. In some embodiments, electrodes 112 comprise a material selected from the group consisting of: gold; stainless steel; tungsten; platinum-iridium; titanium; a nickel-titanium alloy such as Nitinol; palladium; silver; and combinations of these. Electrode 112 materials can be chosen to achieve: low impedance; enhanced biocompatibility; improved corrosion resistance;

and/or improved thermal conductivity (e.g., to help dissipate heat generated during energy delivery).

[0107] Electrodes 112 can each have a conductive surface that has a height (e.g., a height above a neighboring surface) of 0 μ m (e.g., the conductive surface is flush with a neighboring surface), and/or a height of at least 100 μ m or 500 μ m. In some embodiments, electrodes 112 are configured to puncture into tissue, such as to puncture into tissue at a puncture distance of at least 100 μ m, 500 μ m, 1000 μ m, and/or 1500 μ m.

[0108] Electrode array 111 can comprise an array of electrodes 112 that comprises a major axis (e.g., an axis that extends along the major axis of treatment device 100) that is at least 2cm, 5cm, 10cm, 20cm, 30cm or 40cm long.

[0109] Electrode array 111 can comprise an array of electrodes 112 that are separated by a distance of approximately 100 μ m, 250 μ m, 500 μ m, 1000 μ m, or 2000 μ m, 2540 μ m, and/or 6350 μ m.

[0110] In some embodiments, treatment assembly 110 comprises one, two, three, or more individual “ribs” (e.g., one or more flexible members) each configured to conform to the variability of the intestinal wall. In some embodiments, each rib can include an array of electrodes, for example when electrode array 111 comprises multiple discrete arrays each positioned on one of the ribs of treatment assembly 110.

[0111] In some embodiments, one or more portions of treatment assembly 110 and/or other portions of treatment device 100 can comprise atraumatic edges, such as tapered edges. For example, one or more portions of electrode array 111 and/or electrodes 112 can comprise tapered edges to limit the likelihood of tissue damage caused by array 111 (e.g., when treatment assembly 110 is being advanced and/or retracted within the patient).

[0112] In some embodiments, electrode array 111 comprises a photo-etched electrode array. Photoetching can comprise a process that is performed by applying a mask to two sides of a thin sheet of metal. The masked sheet is then exposed to an etchant (e.g., an acid etchant) that chemically removes unmasked portions of the sheet. After chemical etching, the mask is removed, such as using a chemical process that removes the mask without affecting the sheet. Typically, the mask is applied to both sides of the sheet, where the reliefs in the mask are aligned such that the etchant removes material through the entire width of the sheet (e.g., where material is removed by the etchant from both sides and “meets in the middle”). In some embodiments, electrode array 111 can comprise a one-sided etched array. For example, an array that is time etched from a single side, such that the depth of the etches can be controlled, and the thickness of the remaining material can be controlled (e.g., based on the duration of the etching process). Electrode array 111 can comprise a “flexibility profile” (e.g., a profile of varying flexibility

across various portions of the array) configured to promote conformance to tissue. In some embodiments, the flexibility is achieved based on the pattern and the depth of the etches of electrode array 111. For example, the etching can be performed to leave a percentage of the thickness of the sheet intact, for example, at least 30%, such as at least 50% of the material can remain in each etch, and/or at least 50%, such as at least 70% of the material can be removed by each etch. In some embodiments, etching results in between 40% and 60% of the material remaining (e.g., in a single pass, or two pass etching process). Etching can be performed on one or two sides of a component to be etched. The etching process can include agitation of the components, and/or increased flow rate, temperature, and/or concentration (e.g., acidity) of the etchant. In some embodiments, a first step is performed in which a first side of a component is completely masked, and a second side of the component is partially masked, and the second side is etched (e.g., to a desired depth). In a second step, the second side can be completely masked, the first side can be partially masked, and the first side can be etched (e.g., to a desired depth). This multi-step process would allow whatever thickness profile is desired, such as 90% from the second side, and 10% from the first side, or 10% from the second side and 90% from the first side, and other applicable desired ratios. In some embodiments, a lower concentration of etchant (e.g., an acid) and a longer etching time would provide greater depth resolution.

[0113] In some embodiments, the etching process is performed at a temperature of at least 15° C, and/or at a temperature of no more than 80°C.

[0114] In some embodiments, one or more parameters of the etch can be selected (e.g., for a manufacturing process) to control the thickness, the sharpness, the shape, and/or other physical parameters of electrode array 111. For example, one or more parameters of the photo-etching process can be selected from the group consisting of: duration of the etching process; temperature of the etching process (e.g., the ambient temperature surrounding the sheet during the etching process and/or the temperature of the acid and/or other etchant fluid); the concentration of the etchant; the speed of materials passing through the etchant; speed and/or vibration magnitude of an agitator used in the etching process; and combinations of these. In some embodiments, electrode array 111 can be manufactured using multiple photoetching processes, such as multiple photoetching processes each comprising various parameters configured to modify various portions of electrode array 111. Alternatively and/or in addition to photoetching, electrode array 111 can be manufactured using stamping, die cutting, laser cutting, and/or other subtractive manufacturing processes configured to form electrode array 111 from a sheet of metal. Alternatively or additionally, at least a portion of electrode array 111 can be manufactured using additive manufacturing processes, such as 3D printing processes, molding processes, sintering processes, and/or laser powder bed fusion (LPBF). In some embodiments, a

photo-etching process can be used to refine electrode array 111, for example a photo-etching process applied to most and/or all of electrode array 111 to remove any sharp edges and/or burrs (e.g., sharp edges and/or burrs created during another manufacturing process, such as die cutting).

[0115] In some embodiments, electrode array 111 can be coated with a material, such as a polymer material, to cover sharp edges and/or burrs (e.g., electrode array 111 can be dip-coated). Additionally or alternatively, one or more portions of electrode array 111 can comprise a rubber, plastic, and/or elastomer lining configured to prevent sharp edges and/or burrs from injuring the tissue.

[0116] In some embodiments, electrode array 111 can be heat-treated, such as during a manufacturing process used to create electrode array 111. In some embodiments, a heat treatment is configured to increase the yield strength and/or reduce the ductility of the material of electrode array 111. In some embodiments, a heat-treating and/or other process is used to create electrode array 111 to increase the ductility of array 111, such as when the electrodes 112 of array 111 are positioned on a balloon and/or other expandable structure. In some embodiments, a heat-treating and/or other process is used to create electrode array 111 and to stiffen (decrease the ductility of) array 111, such as when electrodes 112 are configured as tissue-penetrating electrodes.

[0117] In some embodiments, electrodes 112 comprise 17-7 precipitation-hardened stainless steel, 17-4PH stainless steel, and/or heat-treated martensitic stainless steel.

[0118] In some embodiments, electrode array 111 includes one or more strain relief elements, for example one or more strain reliefs located in portions of electrode array 111 where increased flexibility is desired. In some embodiments, one or more strain reliefs can be located in electrode array 111 to provide a desired flexibility profile, as described herein. In some embodiments, array 111 comprises one or more strain reliefs that are manufactured using a one-sided etch.

[0119] In some embodiments, electrode array 111 comprises a single pair of electrodes 112 (e.g., only a single pair of electrodes). In some embodiments, treatment assembly 110 can comprise a motive element configured to move electrode array 111 to contact different portions of target tissue, for example a track around an expandable balloon on which electrode array 111 travels (e.g., a track comprising a spiral path around a balloon).

[0120] In some embodiments, electrode array 111 comprises a single electrode 112. For example, treatment device 100 can be configured to deliver monopolar electromagnetic energy to treat target tissue (e.g., monopolar electromagnetic energy configured to irreversibly electroporate target tissue, such as a monopolar IEP) via the single electrode 112, such as when a

function element of system 10 (e.g., functional element 99 described herein) comprises a patch electrode configured to provide a monopolar return path. Alternatively, electrode array 111 can comprise at least two electrodes 112, such as one or more pairs of electrodes 112. Treatment device 100 can be configured to deliver bipolar electromagnetic energy to treat target tissue, such as a bipolar IEP delivered by a pair of electrodes 112. In some embodiments, system 10 is configured to assess the efficacy of a treatment procedure, such as is described herein, for example by correlating one or more resistance and/or other impedance measurements to efficacy (e.g., correlating pre and post treatment measurements to a level of tissue damage caused by the treatment).

[0121] In some embodiments, electrode array 111 is located on expandable structure 113. Expandable structure 113 can comprise an array of looping arms (e.g., “petals”) upon which electrodes 112 of electrode array 111 are located. In some embodiments, the petals are at least 10mm in length (e.g., the tip of each petal extends at least 10mm from the base of each petal that is located proximate shaft 102), such as at least 20mm, or at least 30mm. Expandable structure 113 comprising petals can be similar to expandable structure 113 described in reference to Figs. 12A and 12B herein.

[0122] Treatment device 100 can include one or more conduits, **conduits 101** shown, such as one or more electrical conduits (e.g., wires), one or more fluid conduits (e.g., tubes configured to allow the passage of fluid), one or more optical conduits (e.g., optical fibers), one or more linkages (e.g., mechanical linkages configured to transfer longitudinal and/or rotational motion), and/or other conduits configured to operably attach two or more components of system 10.

[0123] In some embodiments, one or more of conduits 101 provide two or more functions, for example when a conduit 101 is configured to transmit one or more electrical signals (e.g., one or more electrical signals from console 200 to treatment assembly 110) and to transfer a force, for example a force transferred via navigation assembly 140 to steer a portion of treatment device 100 (e.g., when conduit 101 comprises a steering cable). In some embodiments, one or more of conduits 101 are in a braided configuration, for example when shaft 102 comprises a braided shaft and one or more of the wires of the braided shaft comprise one or more of the conduits 101. In some embodiments, shaft 102 provides insulation (e.g., electrical and/or thermal insulation) for one or more conduits 101, such as when conduits 101 are located within the walls of shaft 102.

[0124] In some embodiments, treatment device 100 comprises an elongate device, such as when treatment device 100 is configured to be inserted into the patient (e.g., via a natural orifice, such as via the mouth) and to position treatment assembly 110 proximate target tissue, such as target tissue of the small intestine. Treatment device 100 can include one or more shafts, **shaft**

102 shown, such as one or more shafts each extending from a **proximal end 1021** to a **distal end 1029**. Shaft 102 can include **proximal portion 1022** and **distal portion 1028**, which can each include proximal end 1021 and distal end 1029, respectively. Alternatively or additionally, shaft 102 can include a proximal or distal portion that does not include the proximal and/or distal end of the shaft, respectively (e.g., when a distal portion 1028 of shaft 102 is located proximal to distal end 1029 of shaft 102). Shaft 102 can include one or more lumens or other elongated passages, **lumen 1023** shown. In some embodiments, one or more lumens 1023 extend from proximal end 1021 to distal end 1029 of shaft 102. Lumen 1023 can be configured to transport fluid and/or other materials, and/or lumen 1023 can be sized to receive (e.g., slidably receive) one or more separate elongate components of system 10, such as one or more conduits 101.

[0125] In some embodiments, shaft 102 comprises a variable durometer shaft, such as a shaft with two, three, or more sections with varying flexibility (e.g., a tri-flex shaft). In some embodiments, a distal portion 1028 of shaft 102 comprises a stiffness that is greater than a proximal portion 1022 of shaft 102.

[0126] In some embodiments, treatment device 100 includes one or more user control assemblies, **handle 105** shown. Handle 105 can be located at or near proximal end 1021 of shaft 102. Handle 105 can be configured to be grasped by the operator (e.g., held in the operator's hand) such that the operator can manipulate the location and/or the position of one or more portion of treatment device 100 (e.g., such that the operator can position treatment assembly 110 proximate target tissue). Handle 105 can include one or more user manipulatable controls, **control 1051** shown, each configured to allow the user to perform a function, such as to manually perform a function of system 10 and/or to initiate the performance of a function of system 10 that is performed automatically and/or semi-automatically by treatment device 100, console 200, and/or another component of system 10. For example, control 1051 can comprise a button configured to allow the operator to initiate a treatment to be performed by console 200 via treatment device 100. In some embodiments, control 1051 comprises a mechanical mechanism, such as a knob configured to actuate one or more steering cables configured to steer distal portion 1028 of shaft 102, or to actuate one or more linkages configured to transition expandable structure 113 between a compacted geometry and an expanded geometry.

[0127] In some embodiments, expandable structure 113 comprises an inflatable balloon (e.g., a compliant and/or non-compliant balloon). For example, expandable structure 113 can comprise a compliant balloon configured to conform to the tissue wall when expanded. In some embodiments, electrode array 111 is located on the outer surface of expandable structure 113 (e.g., on the outer surface of an expandable balloon). Alternatively or additionally, electrode array 111 can be located on the inner surface of an expandable balloon. The expandable balloon

can comprise one or more openings (e.g., one or more laser cut openings) such that electrodes 112 of electrode array 111 located within the balloon can contact target tissue. Additionally or alternatively, electrodes 112 can permeate the balloon (e.g., penetrate through the wall of the balloon) to deliver electrical energy to target tissue. Electrodes 112 comprising permeated balloon electrodes can be manufactured by blow molding a customized balloon parison (raw material tube), and blow molding it in a cavity with electrodes 112 in the wall of the balloon. The balloon material will blow open and thermally weld against the positioned electrodes 112. Therefore, there would be a balloon with permeated electrodes 112 that still enables inflation of the balloon. In some embodiments, one or more electrodes 112 comprise a rivet-like construction, such as to allow the balloon material to sealingly capture the rivet structure.

[0128] In some embodiments, expandable structure 113 comprises a furled sheet located within an expandable balloon. Electrode array 111 can be located on the furled sheet and can be configured to unfurl within the balloon of expandable structure 113 (e.g., to unfurl due to a bias when the balloon is inflated, or to be unfurled by the operator after the balloon has been inflated).

[0129] In some embodiments, expandable structure 113 comprises a structure configured to transition from a compacted geometry to an expanded geometry when a torsional force is applied. For example, a conduit 101 of treatment device 100 can comprise a torque wire that transfers a torsional force from handle 105 to expandable structure 113. In some embodiments, console 200 is configured to monitor and analyze (e.g., using algorithm 25 described herein) the torsional resistance provided by expandable structure 113 (e.g., via a functional element 199, described herein, configured as a torsional force sensor). Console 200 can analyze the torsional resistance to determine the size of the lumen (e.g., the duodenum) within which expandable structure 113 is positioned. In some embodiments, console 200 is configured to determine one or more treatment parameters based on the size of the lumen of the target tissue (e.g., based on the diameter of the portion of the duodenum to be treated by system 10). For example, the one or more treatment parameters that can be determined (e.g., modified and/or otherwise determined by system 10) can be a selection of a subset of electrodes 112 to deliver energy, where the subset of electrodes is based on the diameter of the lumen to be treated (e.g., such as to avoid energy delivery from one or more electrodes 112 that are not likely to be in contact with tissue).

[0130] In some embodiments, expandable structure 113 is biased in a compacted geometry, such that if a mechanism of treatment device 100 configured to expand and compact expandable structure 113 fails, expandable structure 113 automatically returns to a compacted geometry. For example, expandable structure 113 can comprise a spring mechanism (e.g., a spring

mechanism including a constant force spring), or a shape memory material, such as a nickel-titanium alloy that is biased in a compacted geometry (e.g., biased in a compacted geometry when at body temperature). In some embodiments, expandable structure 113 can comprise an unfurlable structure including a torsion spring configured to bias the structure in a furled, compacted geometry.

[0131] In some embodiments, expandable structure 113 can comprise two or more expandable structures. For example, expandable structure 113 can comprise a first balloon that is positioned by the operator proximal to the most proximal target tissue location (e.g., at or just distal to the papilla), and a second balloon that is positioned by the operator distal to the most distal target tissue location (e.g., at or just proximal to the ligament of Treitz). System 10 can be configured to fill the space between the two balloons with a liquid (e.g., saline and/or other electrically conductive fluid delivered via console 200, such as from fluid delivery unit 230 described herein) to increase efficacy of treatment provided by system 10 (e.g., to provide improved contact between electrodes 112 and the target tissue). Electrode array 111 can be translated between the two balloons of expandable structure 113 to provide treatment to the target tissue therebetween.

[0132] In some embodiments, expandable structure 113 comprises an expandable tube, such as a tube that is configured to expand when the distal end of the tube is retracted proximally. Electrode array 111 can be located on the outside of the tube, such that when the tube is expanded, electrodes 112 are brought into contact with the tissue.

[0133] In some embodiments, expandable structure 113 includes a “mechanical fuse”, such as a portion of expandable structure 113 configured to fail (e.g., such that expandable structure 113 collapses to a compacted geometry) if a force and/or a pressure threshold is exceeded. For example, expandable structure 113 can be configured to prevent the application of a pressure to tissue greater than a threshold level to tissue while transitioning to an expanded geometry, such as a threshold level of at least 0.5psi or 1.0psi, and/or a threshold level of no more than 2.5psi or 5.0psi. Alternatively or additionally, expandable structure 113 (and/or other component of treatment device 100 and/or system 10) can comprise an electrical fuse that is configured to stop delivery of energy to one or more electrodes 112 (e.g., all or a subset of electrodes 112) if a fault condition is encountered (e.g., if too much current is inadvertently applied).

[0134] In some embodiments, expandable structure 113 and/or another component of treatment device 100 includes a mechanical fuse, sensor, and/or other component that is configured to reduce the likelihood of applying a force to a luminal wall of the intestine that might result in ischemia to non-target tissue.

[0135] In some embodiments, expandable structure 113 comprises a balloon expandable structure, such as a furled structure surrounding an inflatable balloon. Electrode array 111 can be located on the outer surface of the furled structure, and the inflatable balloon can be used to control the force applied to tissue by electrode array 111 (e.g., via pressure control of the balloon).

[0136] In some embodiments, expandable structure 113 comprises a contoured multilayer balloon, such as a balloon configured to capture portions of target tissue.

[0137] In some embodiments, expandable structure 113 comprises an inflatable balloon, where electrodes 112 of electrode array 111 are integrated into the balloon. For example, electrodes 112 can comprise copper electrodes integrated onto the outside of the balloon, and/or one or more conductive coatings that are applied to the outside of the balloon (e.g., in a manufacturing process). In some embodiments, electrodes 112 are over-molded onto the balloon.

[0138] In some embodiments, electrode array 111 can comprise a liquid metal thin film circuit that is reinforced with nanowire. The thin film circuit can be applied to expandable structure 113 comprising a balloon (e.g., in a manufacturing process). In some embodiments, electrode array 111 and the balloon are coated with a membrane that has been selectively etched to expose electrodes 112.

[0139] In some embodiments, treatment assembly 110 comprises a ring of electrodes 112. Electrode array 111 can comprise two or more pairs of electrodes 112 positioned on expandable structure 113. Treatment assembly 110 can comprise a subassembly located within expandable structure 113 and configured to operably attach to one or more of the pairs of electrodes 112 to operably connect the pairs of electrodes to console 200 (e.g., such that treatment energy can be delivered via the connected electrodes 112).

[0140] In some embodiments, treatment device 100 comprises **injection assembly 130** which can be configured to deliver one or more materials into the tissue of the patient, such as into the submucosal tissue of the patient. Injection assembly 130 can include one or more needles and/or fluid jets configured to deliver material into the tissue. In some embodiments, injection assembly 130 includes one or more ports configured to capture tissue (e.g., via an applied vacuum), such as to capture tissue prior to the advancement of a needle of injection assembly 130 into the captured tissue. Injection assembly 130 can be of similar construction and arrangement to the corresponding components described in applicant's co-pending United States Patent Application Serial Number 17/721,937 (Attorney Docket No. 41714-720.301; Client Docket No. MCT-050-US), entitled "Systems, Device, and Methods for Performing Medical Procedures in the Intestine", filed April 15, 2022.

[0141] In some embodiments, treatment device 100 comprises **navigation assembly 140** configured to provide information regarding the location and/or position of treatment device 100. For example, navigation assembly 140 can include one or more sensors configured to detect the location and/or position of treatment assembly 110 and/or shaft 102. Navigation assembly 140 can be further configured to manipulate (e.g., to robotically and/or otherwise control the position of, the state of, and/or the location of) one or more portions of treatment device 100, such as to manipulate (e.g., robotically manipulate) one or more portions of treatment device 100. Injection assembly 130 can be of similar construction and arrangement to the corresponding components described in applicant's co-pending United States Patent Application Serial Number 17/863,016 (Attorney Docket No. 41714-722.301; Client Docket No. MCT-051-US), entitled "Automated Tissue Treatment Devices, Systems, and Methods", filed July 12, 2022.

[0142] In some embodiments, treatment device 100 comprises **visualization assembly 180** configured to provide visualization of one or more portions of treatment device 100 and/or of a treatment site, such as visualization of the GI tract when treatment assembly 110 is positioned in the GI tract. Visualization assembly 180 can comprise one or more imaging devices, such as a visual imaging device (e.g., a visual light camera), an ultrasonic imaging device (e.g., an array of ultrasound transducers), a radiation-based imaging device (e.g., an X-ray imager), and/or other imaging devices configured to provide images and/or other visualizable information related to one or more portions of system 10 and/or the tissue of the patient. In some embodiments, treatment device 100 comprises two or more separate devices, for example a first device comprising treatment assembly 110 and a second device comprising visualization assembly 180, where the first and second devices are configured to be inserted alongside each other such that visualization assembly 180 can provide visualization of the first device. In some embodiments, visualization assembly 180 is part of a body introduction device (e.g., introduction device 80 described herein), such as an endoscope inserted alongside treatment device 100.

[0143] In some embodiments, visualization assembly 180 includes one or more visual or other indicators, **marker 1801** shown, such as one or more visual markers located on shaft 102. Visualization assembly 180 can be configured to correlate the location marker 1801 relative to one or more other visualizable landmarks (e.g., anatomic landmarks and/or identifiable portions of other devices of system 10 positioned in the patient) to determine the location of and/or position of one or more portions of treatment device 100.

[0144] In some embodiments, treatment device 100 can include one or more assemblies and/or other components for providing additional therapy and/or performing additional diagnostic procedures, **supplementary treatment assembly 160** shown. In some embodiments,

treatment assembly 110 and supplementary treatment assembly 160 comprise a single assembly configured to provide multiple forms of treatment, as described herein. Supplementary treatment assembly 160 can include an expandable assembly, also as described herein. In some embodiments, supplementary treatment assembly 160 is configured to provide a thermal therapy and/or other thermal treatment to the target tissue, for example, when supplementary treatment assembly 160 comprises a balloon configured to receive a heated and/or a cooled fluid, such as to heat and/or cool, respectively, the target tissue (e.g., to heat and/or cool the target tissue prior to, during, and/or after the delivery of therapy from treatment assembly 110, such as electroporation therapy described herein).

[0145] In some embodiments, treatment device 100 comprises **anchoring assembly 170** configured to temporarily fix the position of one or more portions of treatment device 100 relative to the patient. For example, anchoring assembly 170 can include one or more elements configured to prevent longitudinal translation of treatment assembly 110 within the small intestine (e.g., for example during the delivery of energy to the tissue from treatment assembly 110 and/or between various procedural steps, such as between a first treatment provided by supplementary treatment assembly 160 and a second treatment provided by treatment assembly 110).

[0146] In some embodiments, anchoring assembly 170 anchors a portion of treatment device 100 (e.g., a distal portion of shaft 102) while treatment assembly 110 transitions between the compacted and expanded geometries described herein, such that the relative axial location of treatment assembly 110 does not change unintentionally during the transition. In some embodiments, treatment assembly 110 expands in an asymmetric fashion, for example when expandable structure 113 comprises an unfurlable structure. Anchoring assembly 170 can be configured to anchor a portion of treatment assembly 110 to a first wall portion of the target tissue lumen to allow the unfurlable structure to expand into the lumen (e.g., away from the first wall portion towards a wall portion opposite the first wall portion).

[0147] In some embodiments, at least a portion of shaft 102 comprises a stiffness great enough to provide an anchoring force to a portion of treatment device 100. For example, at least a distal portion of shaft 102 (e.g., a distal portion proximate treatment assembly 110) can comprise a durometer of at least 40D and/or a durometer of no more than 90D.

[0148] In some embodiments, anchoring assembly 170 includes one or more vacuum and/or aspiration ports (e.g., one or more ports operably connected to fluid delivery unit 230 described herein) configured to temporarily attach to tissue to anchor treatment device 100 when a source of vacuum is applied. In some embodiments, treatment assembly 110 comprises one or more aspiration ports of anchoring assembly 170, such as when one or more aspiration ports are

positioned near the center of expandable structure 113. In some embodiments, one or more aspiration ports of anchoring assembly 170 are located proximate one or more of electrodes 112, such as to increase tissue contact between the electrode and the tissue proximate the port.

[0149] In some embodiments, treatment device 100 comprises one or more functional elements, **functional element 199**, such as one or more sensors and/or transducers. Functional element 199 can comprise one, two, or more transducers, and/or one, two, or more sensors (e.g., as described herein). For example, the functional element can comprise a transducer configured to deliver energy and/or to convert one form of energy to another form of energy. In some embodiments, the functional element comprises a sensor configured to measure impedance, such as impedance of tissue between two electrodes according to the present inventive concepts. In some embodiments, the functional element comprises a sensor configured to measure a physiologic parameter of the patient, such as a physiologic parameter of the intestine and/or other location on and/or within the patient. In some embodiments, the functional element comprises a needle and/or other agent delivery component. In some embodiments, the functional element comprises an element configured to apply and/or receive a source of vacuum. In some embodiments, the functional element comprises a component configured to compress and/or expand tissue. In some embodiments, the functional element comprises a component configured to cause another component of system 10 to be robotically manipulated, such as a robotic manipulation that causes a translation, rotation, expansion, and/or compacting of a component of system 10.

[0150] Console 200 can include **energy delivery unit 210** configured to provide energy to treatment device 100 to be delivered to the patient (e.g., via one or more electrodes 112), such as energy delivered to provide a therapeutic treatment. Energy delivery unit 210 can provide electromagnetic energy that is configured to electroporate target tissue, such as to irreversibly electroporate target tissue (e.g., an IEP described herein). In some embodiments, energy delivery unit 210 provides electromagnetic energy that is configured to reversibly electroporate target tissue, such as to enable delivery of one or more agents into the target tissue (e.g., agent 45 comprising hypertonic saline, alcohol, or ethanol). For example, agent 45 can be delivered to target tissue using reversible electroporation to treat the target tissue.

[0151] In some embodiments, energy delivery unit 210 is configured to deliver energy synchronously with the patient's heartbeat, such that energy delivered by treatment device 100 to the patient does not cause unwanted cardiovascular effects. In some embodiments, console 200 is configured to record an ECG signal to synchronize energy delivery, for example when a functional element of system 10 (e.g., functional element 99 described herein) comprises one or more ECG leads.

[0152] In some embodiments, energy delivery unit 210 is configured to measure one or more electrical properties and/or electrical signals (e.g., the impedance between two or more components of system 10) to determine if any mechanical damage has occurred to one or more devices of system 10 (e.g., to treatment device 100). For example, energy delivery unit 210 can measure the resistance and/or other impedance (“impedance” herein) between various electrodes 112 to assess for any shorts or other mechanical failures (e.g., mechanical damage to treatment device 100). In some embodiments, energy delivery unit 210 delivers one or more sub-therapeutic pulses to electrode array 111, for example to measure the resistance between electrodes 112 to ensure proper functionality of each electrode 112 (e.g., to ensure each electrode 112 is properly connected).

[0153] In some embodiments, energy delivery unit 210 alerts the operator if mechanical damage or other non-functionality of treatment device 100 is detected (e.g., alerts the operator via user interface 250 described herein). In some embodiments, energy delivery unit 210 will not provide energy for a treatment procedure if treatment device 100 is damaged or otherwise not functioning properly. Alternatively or additionally, energy delivery unit 210 can be configured to modify one or more energy delivery parameters based on the functionality of treatment device 100 (e.g., if one electrode 112 of electrode array 111 is not functioning properly, treatment energy can be delivered via the functioning electrodes 112). In some embodiments, system 10 is configured to instruct the operator on replacing a malfunctioning portion of system 10 (e.g., treatment assembly 110 of treatment device 100, or treatment device 100), such as via visual instruction provided by user interface 250 described herein.

[0154] In some embodiments, energy delivery unit 210 delivers electromagnetic energy configured to irreversibly electroporate the target tissue, where the energy is at and/or above a power threshold that may cause bubble formation, as bubbles formed in the intestine do not cause an adverse event (e.g., as opposed to bubble formation in locations containing systemically flowing blood).

[0155] Console 200, via energy delivery unit 210, can be configured to provide (e.g., generate and deliver) several types of signals to the electrodes 112 of treatment device 100, these signal types including, but not limited to: AC current; square wave AC current; sine wave AC current; AC current interrupted at predetermined time intervals; multiple profile current pulse trains of various power intensities; direct current (DC) impulses; stimulus range impulses; hybrid electrical impulses; and combinations of one, two, or more of these. For example, energy delivery unit 210 can be configured to provide monophasic (DC) pulses, biphasic (DC and AC) pulses, or both. In some embodiments, energy delivery unit 210 is configured to generate signals of at least 1V and/or no more than 3,000V, such as when providing a current of at least

1A and/or no more than 200A. The generated signals can comprise a frequency of at least 50kHz and/or no more than 950kHz, and can be delivered into a circuit (e.g., including electrodes 112 and neighboring tissue) with an impedance of at least 2Ω and/or no more than 30Ω .

[0156] System 10 can be configured (e.g., treatment device 100 and console 200 with energy delivery unit 210 can be configured) to provide electroporation energy (e.g., an IEP) at a level of at least 1,000V/cm, such as at least 1,500V/cm and/or no more than 4,500V/cm, such as no more than 2,500V/cm, such as to induce electric fields across cell membranes of at least 0.5V in the duodenum. In some embodiments, the maximum continuous on-time (100% duty cycle of alternating polarity pulses) can be about 10msec (e.g., to avoid undesired temperature elevation in the tissue). In some embodiments, the pulse waveform provided by energy delivery unit 210 can comprise pairs of unipolar pulses of about 1 μ s. Pairs of unipolar pulses can be provided in groups of at least 5 and/or no more than 500, with a delay between each group. In some embodiments, a series of these groups can be repetitively applied with increasingly longer delays between series. In some embodiments, a sequence of series may be applied with longer delays between sequences. In some embodiments, at least 5 milliseconds and/or no more than 50 milliseconds of cumulative ON time may be distributed across a period of at least 5 seconds and/or no more than 15 seconds.

[0157] In some embodiments, energy delivery unit 210 can be configured to generate current, voltage, and power in the pulsed or modulated electric field spectrum with one, two, or more of the following energy delivery parameters: a frequency of at least 250kHz and/or no more than 950MHz; a pulse width of at least 0.5 μ s and/or no more than 4 μ s; a voltage applied by electrodes 112 of at least 100V and/or no more than 2kV; and/or a current density of at least 0.6A; and/or no more than 100A from the electrodes 112 per square centimeter of tissue. In some embodiments, energy delivery unit 210 can be configured to drive into tissue resistance of at least 5 ohms and/or no more than 30 ohms of load. For example, the current density can be at least 0.6A and/or no more than 100A from the electrodes 112 per square centimeter of tissue. In some embodiments, the pulse waveform provided by energy delivery unit 210 can comprise a pulse group of at least 1 group and/or no more than 50 groups with at least 1 pulse and/or no more than 100 pulses per group. In some of these embodiments, the pulse waveform provided by energy delivery unit 210 can comprise a group delay of at least 10 μ s and/or no more than 4000 μ s, and/or a replenish rate of at least 50ms and/or no more than 4000ms. For example, a balanced bipolar pulse waveform (e.g., within 10%) can be provided by energy delivery unit 210 to reduce sympathetic nerve excitation, which may reduce perceived pain and spontaneous

muscle contraction. Energy delivery unit 210 can be configured to provide pulsing of at least $1\mu\text{s}$ and/or no more than $10\mu\text{s}$, such as to generate cell lysis while minimizing nerve stimulation.

[0158] In some embodiments, energy delivery unit 210 is configured to provide to the electrodes 112 of treatment device 100 a set of bipolar pulses that are divided into bursts of bipolar pairs with a time delay between the bursts. This signal can be configured to cause the dispersion of the heat generated at the cell membranes, allowing more treatment before the transition from cell lysis to necrosis.

[0159] Energy delivery unit 210 can be configured to deliver a pulse waveform to electrodes 112 to generate a pulsed and/or modulated electric field configured to generate cell lysis while limiting thermal heating of tissue to less than 13°C up to a tissue depth of about 1.5mm.

[0160] Energy delivery unit 210 can be configured to generate a pulse waveform configured to generate a pulsed and/or modulated electric field comprising a power of at least 16,200W and/or no more than 96,800W.

[0161] Energy delivery unit 210 can be configured to deliver a pulse waveform to electrodes 112 to generate a pulsed and/or modulated electric field with a magnitude that is substantially uniform at a predetermined distance from the electrode array. For example, the predetermined distance can comprise a distance of at least 0.5mm and/or no more than 1.5mm. The electric field magnitude can be below a therapeutic threshold at a distance beyond the predetermined distance.

[0162] In some embodiments, energy delivery unit 210 is configured to detect tissue apposition (e.g., to assess the contact between one or more electrodes 112 and the tissue), for example by measuring impedance. Energy delivery unit 210 can adjust one or more energy delivery parameters based on the determined tissue apposition (e.g., based on the tissue contact surface area).

[0163] In some embodiments, console 200 is configured to provide one or more fluids and/or other materials to be injected or otherwise delivered to the patient via treatment device 100. Additionally or alternatively, console 200 can be configured to provide and/or remove one or more fluid and/or other materials to and/or from a device of system 10 (e.g., treatment device 100) and/or a portion of the GI tract (e.g., a portion of the GI tract surrounding a portion of treatment device 100, such as treatment assembly 110). For example, console 200 can include **fluid delivery unit 230** configured to provide the fluid and/or other materials described herein. Additionally or alternatively, fluid delivery unit 230 can be configured to remove one or more fluids and/or other materials, such as when fluid delivery unit 230 comprises a source of vacuum and/or a pump configured to draw fluid from the source (e.g., to remove fluid from a patient via treatment device 100). In some embodiments, fluid delivery unit 230 is configured provide

insufflation and/or desufflation of the GI tract, such as by providing and/or removing a fluid via a lumen 1023 of shaft 102. Fluid delivery unit 230 can be configured to recirculate a fluid (e.g., continuously and/or semi-continuously recirculate), such as to recirculate a hot and/or a cold fluid through supplementary treatment assembly 160. For example, supplementary treatment assembly 160 can comprise a balloon configured to receive a fluid, such as an expandable balloon configured to expand via the pressure differential between fluid received from fluid delivery unit 230 and the fluid removed from fluid delivery unit 230.

[0164] In some embodiments, fluid delivery unit 230 provides one or more fluids and/or other materials to the patient via injection assembly 130 of treatment device 100. For example, fluid delivery unit 230 can provide a fluid (e.g., injectate 40 described herein) to injection assembly 130 for injection into the submucosa of the small intestine, such as to perform a submucosal lift procedure.

[0165] Console 200 can include **diagnostic unit 240** configured to perform one or more diagnostic procedures, such as one or more procedures configured to diagnose the patient, to assess the status of a treatment procedure, to assess the efficacy of a treatment procedure, to gather information used to plan a treatment procedure, and/or to otherwise record and/or analyze information collected by system 10 to provide diagnostic data to the operator.

[0166] In some embodiments, diagnostic unit 240 is configured to measure the impedance of tissue (e.g., via electrodes 112) to differentiate tissue that has been treated and tissue that has not been treated. For example, diagnostic unit 240 can be configured to perform electrical impedance tomography to differentiate tissue (e.g., electrical impedance tomography performed utilizing multiple frequencies).

[0167] In some embodiments, diagnostic unit 240 is configured to measure differentiation of scarred and/or retreated tissue, such as to avoid damage to tissue (e.g., unwanted damage that may be caused by the application of electromagnetic energy). Scarred and/or otherwise damaged tissue (e.g., tissue that has previously been treated using system 10) can have different properties (e.g., different impedance) than that of healthy or untreated tissue. Diagnostic unit 240 can be configured to measure one or more properties (e.g., impedance and/or other properties) of tissue to be treated, such that energy delivery by electrodes 112 can be adjusted based on the measured properties. In some embodiments, system 10, via tissue property information received from diagnostic unit 240, can be configured to avoid treatment of certain tissue (e.g., avoid treatment of scarred and/or previously treated tissue).

[0168] In some embodiments, diagnostic unit 240 is configured to perform baseline measurements (e.g., prior to the delivery of therapy by system 10) to identify any tissue abnormalities, lesions, and/or diverticula.

[0169] In some embodiments, diagnostic unit 240 is configured to measure bile salt and/or other salt content (e.g., salt content of tissue and/or locations proximate tissue to be treated). In some embodiments, diagnostic unit 240 is configured to measure salt content and/or conductivity of tissue of and/or material within the intestine of a patient such that system 10 can determine proximity of that measured location to the papilla (e.g., based on locations proximate the papilla have higher concentrations of bile). In these embodiments, treatment assembly 110 (e.g., including electrodes 112 or otherwise) can be positioned at a location with lower conductivity than those associated with locations proximate the papilla. In some embodiments, diagnostic unit 240 is configured to measure salt content and/or conductivity of tissue of and/or material within a gastrointestinal segment of a patient to ensure a sufficient conductivity is present prior to a tissue treatment (e.g., to lead to more efficacious treatment via electrodes 112). In some embodiments, diagnostic unit 240 comprises an assembly configured to measure salt content and/or conductivity selected from the group consisting of: a refractometer, such as a refractometer that is used to measure salinity by measuring how much light refracts when entering a liquid; a conductivity meter, such as a conductivity meter that emits an electric charge via a conductivity probe positioned within a lumen and correlates a level of dissolved ions to a level of electrical charge; and combinations of these.

[0170] In some embodiments, diagnostic unit 240 is configured to measure the impedance of tissue prior to the delivery of electromagnetic energy. Diagnostic unit 240 can be configured to identify target and/or non-target tissue (e.g., the papilla) based on the measured impedance of the tissue, and to prevent the delivery of energy to non-target tissue, such as by preventing the delivery of energy until treatment assembly 110 is moved to a location where non-target tissue is not detected via the impedance measurement performed by diagnostic unit 240.

[0171] In some embodiments, one or more treatment parameters can be adjusted by console 200 (e.g., using algorithm 25) based on results of a diagnostic test performed by diagnostic unit 240. For example, diagnostic unit 240 can be configured to measure the thickness, the length of villi, and/or the crypt density of a portion target tissue to be treated, and console 200 can determine a dose (e.g., an amount of energy) to be delivered to treat that portion of target tissue based on that measurement. For example, measured tissue thickness, villi length, and/or crypt density can correlate to the electric field delivered by electrodes 112 (e.g., confirmation of thicker target tissue), longer villi length (e.g., length above 1mm, such as at or above 1.2mm, 1.5mm and/or 2mm), and/or higher crypt density (e.g., crypt density above 30 per cm, or above 50, 60, or 70 per cm, and/or crypt density above a normal crypt density, such as at least 10% or 20% above a normal crypt density) can result in higher electric field strength delivered, more pulses delivered, faster pulses delivered, less time between pulses delivered, higher voltage of

pulses delivered, and/or higher current of pulses delivered. In some embodiments, villi length and crypt density are measured via visual images (e.g., to be used to adjust energy delivery settings and/or as a surrogate assessment of mucosal thickness determination). In some embodiments, diagnostic unit 240 produces data that is analyzed by algorithm 25 (e.g., an AI algorithm) to predict mucosal thickness. In some embodiments, diagnostic unit 240 comprises ultrasound-based sensors that measure mucosal thickness.

[0172] In some embodiments, energy delivery by treatment assembly 110 (e.g., electroporation delivery by electrodes 112), can be configured to ablate a minimum number of cells (e.g., at least 50%, 60%, and/or 70% of cells) that are positioned at 0.6mm depth of the intestinal wall, and assembly 110 can be further configured to limit death of cells at 1mm depth to a maximum level (e.g., no more than 20%, or 10%). In a patient with more severe disease, these minimum and maximum levels can be applied to deeper locations, such as 1mm/1.5mm, 1.5mm/2mm, and/or 2mm/2.5mm depths. In some embodiments, energy delivery by treatment assembly 110 (e.g., irreversible electroporation delivery) at depths at the layer of intestinal muscle, is avoided (e.g., maintained below 5%, 2%, or 1% cell death rate).

[0173] In some embodiments, diagnostic unit 240 is configured to measure conductivity and/or perform a “pulse check” (e.g., energy delivery) comprising a tissue status check performed before and/or after a tissue treatment. For example, diagnostic unit 240 can be configured to measure the difference in impedance between non-treated tissue (e.g., fully intact cell membrane tissue) and treated tissue (e.g., electroporated cell membranes) such as to determine if treatment assembly 110 is positioned in a treated region of tissue, or not. Diagnostic unit 240 can be configured to deliver a pulse check comprising an energy delivery at a non-ablative level (e.g., single pulse, lower voltage, benign waveform, and/or other non-ablative level) in order to accomplish a tissue assessment. In some embodiments, diagnostic unit 240 performs such a tissue assessment after one or more ablative tissue treatments, such as to determine if each treatment was satisfactory or if additional treatments are warranted at that location. In some embodiments, algorithm 25 comprises an AI algorithm that is based on (e.g., trained using) data collected by diagnostic unit 240 (data collected prior to and/or after successful tissue ablations and/or other tissue ablations).

[0174] Console 200 can include **processing unit 220** that can be configured to perform and/or facilitate one or more of the functions of system 10, such as one or more processes, energy deliveries (e.g., light, RF and/or other electromagnetic energy deliveries), data collections, data analyses, data transfers, signal processing, and/or other functions of system 10 (“**functions of system 10**” or “**system functions**” herein). Processing unit 220 can include **processor 221** and **memory 222**, each shown. Memory 222 can be coupled to processor 221,

and memory 222 can store instructions used by processor 221 to perform one or more algorithms of system 10. For example, system 10 can comprise one or more algorithms, **algorithm 25** shown. Algorithm 25 can comprise one or more machine learning, neural net, and/or other artificial intelligence algorithms (“AI algorithm” herein). Algorithm 25 can be performed by one or more processors of system 10 (e.g., a processor of a system component, such as processor 221 of processing unit 220). The processor of a component of system 10 can perform an algorithm 25 using instructions stored in memory of that component, that is coupled to the processor (e.g., instructions for algorithm 25 stored in memory 222 of processing unit 220). All or a portion of algorithm 25 can be integrated (e.g., stored in the memory of) into one, two, or more of the various components of system 10, such as a server (e.g., server 300 described herein), a device comprising a processor (e.g., treatment device 100, introduction device 80, and/or imaging device 60), and/or a console of system 10 (e.g., console 200).

[0175] System 10 can include an interface, **user interface 250**, for providing and/or receiving information, to and/or from an operator of system 10. User interface 250 can be integrated into console 200 as shown. In some embodiments, user interface 250 comprises a component (e.g., a hand-held component) that is separate from a main portion (e.g., a console portion) of console 200, such as a display that is separate from, but operably attached to, the main portion of console 200. User interface 250 can include one, two, or more user input and/or user output components. For example, user interface 250 can comprise a joystick, keyboard, mouse, touchscreen, and/or another human interface device, **user input device 251** shown. In some embodiments, user interface 250 comprises a display (e.g., a touchscreen display), such as **display 252**, also shown. In some embodiments, processor 221 can provide a graphical user interface, **GUI 253**, to be presented on and/or provided by display 252. User interface 250 can include an input and/or output device selected from the group consisting of: a speaker; an indicator light, such as an LED indicator; a haptic feedback device; a foot pedal; a switch such as a momentary switch; a microphone; a camera (e.g., when processor 221 enables eye tracking and/or other input via image processing of an image of an operator); and combinations of these.

[0176] In some embodiments, system 10 requires one or more affirmative operator inputs (e.g., inputs provided by the operator via user input device 251) before a treatment procedure, such as a treatment procedure including an energy delivery, can be performed. For example, system 10 can require the operator to confirm that treatment assembly 110 is positioned away from non-target tissue (e.g., positioned distal to the papilla) prior to enabling the user to initiate a therapeutic energy delivery (e.g., a delivery of electromagnetic energy configured to irreversibly electroporate the target tissue).

[0177] In some embodiments, system 10 includes a data storage and processing device, **server 300**. Server 300 can comprise an “off-site” server (e.g., outside of the clinical site in which patient image data is recorded and/or other system 10 function is performed on a patient), such as a server owned, maintained, and/or otherwise provided by the manufacturer of system 10. Alternatively or additionally, server 300 can comprise a cloud-based server. Server 300 can include **processing unit 310** shown, which can be configured to perform one or more functions of system 10, such as one or more system functions described herein. Processing unit 310 can be configured to perform one or more algorithms of system 10, such as algorithm 25 described herein. For example, processing unit 310 can comprise a memory (not shown) that stores instructions for algorithm 25 such that a processing unit 310 can perform algorithm 25. Server 300 can be configured to receive and store various forms of data, such as: image data, diagnostic data, treatment planning data and/or treatment outcome data, **data 320** shown and described herein. In some embodiments, data 320 can comprise data collected from multiple patients (e.g., multiple patients treated with system 10), such as data collected during and/or after clinical procedures performed on the multiple patients. In some embodiments, console 200 and server 300 are configured to communicate over a network, **network 50**, for example, a wide area network such as the Internet. Alternatively or additionally, network 50 can include a virtual private network (VPN), such as a VPN through which various devices of system 10 can transfer data. As described herein, the one or more functions of system 10 performed by processing unit 220 and/or 310 can be performed by either or both processing units.

[0178] In some embodiments, console 200 comprises one or more functional elements, **functional element 299**, such as one or more sensors and/or transducers. Functional element 299 can comprise one, two, or more transducers, and/or one, two, or more sensors (e.g., as described herein). For example, the functional element can comprise a transducer configured to deliver energy and/or to convert one form of energy to another form of energy. In some embodiments, the functional element comprises a sensor configured to measure impedance, such as impedance of tissue between two electrodes according to the present inventive concepts. In some embodiments, the functional element comprises a sensor configured to measure a physiologic parameter of the patient, such as a physiologic parameter of the intestine and/or other location on and/or within the patient. In some embodiments, the functional element comprises a needle and/or other agent delivery component. In some embodiments, the functional element comprises an element configured to apply and/or receive a source of vacuum. In some embodiments, the functional element comprises a component configured to compress and/or expand tissue. In some embodiments, the functional element comprises a component configured to cause another component of system 10 to be robotically manipulated, such as a

robotic manipulation that causes a translation, rotation, expansion, and/or compacting of a component of system 10.

[0179] As described herein, treatment device 100 can be introduced into the patient via the patient's mouth. In some embodiments, system 10 includes one or more patient access devices, **introduction device 80** shown. Introduction device 80 can comprise one, two, or more body access devices selected from the group consisting of: an endoscope; an introducer; a sheath such as an endoscope-attached sheath; laparoscopic port; another body access device; and combinations of these. Introduction device 80 can include an elongate body, **shaft 82**. Introduction device 80 can include **handle 81** located at the proximal end of shaft 82. Introduction device 80 can include one or more working channels, **working channel 8203** shown, extending the length of shaft 82, such as from handle 81 to **distal portion 8208** and/or exiting **distal end 8209** of shaft 82. Working channel 8203 can slidably receive a portion of treatment device 100, for example shaft 102 can be slidably received within working channel 8203 to introduce treatment assembly 110 into the patient (e.g., after distal portion 8208 of shaft 82 has been positioned proximate a target location). In some embodiments, introduction device 80 and treatment device 100 are each introduced through the patient's mouth. In these embodiments, treatment device 100 can be introduced through working channel 8203 and/or alongside introduction device 80.

[0180] In some embodiments, treatment device 100 comprises a device configured to attach to distal portion 8208 of shaft 82 (e.g., when at least a portion of treatment device 100 including treatment assembly 110 comprises a "cap" that is positioned on the distal end of an endoscope). One or more conduits 101 can be configured to extend from treatment assembly 110, through a working channel 8203 to operably connect to console 200 (e.g., via connection assembly 150). In some embodiments, expandable structure 113 comprises one or more flexible arms that extend from the treatment device 100 attached to distal portion 8208 of shaft 82.

[0181] In some embodiments, introduction device 80 comprises a telescoping mechanism that is positioned distal to the papilla (e.g., distal to but within at least 0.5cm or at least 1cm, but not more than 5cm or 10cm from the papilla). The telescoping mechanism can be configured to extend distally, such that treatment device 100 can be tracked through the telescoping mechanism to access distal target tissue. The telescoping mechanism can comprise a collar or other endoscope-surround component that is configured to function as a backstop positioned distal to the papilla, such that treatment device 100 is limited to retract only to the location of the backstop, avoiding inadvertent positioning of treatment assembly 110 at the papilla. In some embodiments, introduction device 80 comprises a sheath that is configured to anchor (e.g., to tissue) to enhance one-to-one translation of treatment device 100 in the intestine. In some

embodiments, a working channel of device 80 (e.g., a working channel of an endoscope) is configured to anchor (e.g., to tissue) to enhance one-to-one translation of treatment device 100 in the intestine.

[0182] In some embodiments, system 10 comprises one, two, three, or more guidewires, **guidewire 85** shown. In some embodiments, treatment device 100 is configured for over-the-wire manipulation (e.g., advancement and retraction) using guidewire 85. In these embodiments, guidewire 85 can comprise a guidewire with a construction comprising: a shaft with a relatively stiff material, such as stainless steel or L605 cobalt-chromium; a shaft diameter of no more than 0.038", 0.035" and/or 0.032"; a lubricious coating; an atraumatic distal portion, such as a distal portion constructed of nickel titanium alloy and/or a distal portion comprising a centerless-grinding steep tapering; a shaft length of at least 300cm, or at least 340cm; a shaft length of no more than 450cm, no more than 400cm, and/or no more than 380cm; and combinations of these. In some embodiments, guidewire 85 comprises a proximal portion (e.g., a portion that is repeatedly grasped by an operator of system 10) that is void of a lubricious coating (e.g., on its outer surface), while the more distal portion of guidewire 85 comprises a lubricious coating, such as to improve fine control of guidewire 85 by the operator. In some embodiments, guidewire 85 comprises a distal portion that is configured to transition from a straight geometry (e.g., a relatively straight geometry), to an expandable coil geometry, such as a coil with sufficient hoop strength to resist motion of guidewire 85 when the expandable coil is positioned in the intestine (e.g., in the jejunum or other location of the small intestine), and treatment device 100, introduction device 80, and/or another component of system 10 is being advanced and/or retracted over guidewire 85. In some embodiments, the distal end of guidewire 85 comprises a greater flexibility than the proximal end of guidewire 85, such as to enable better push-ability of the proximal end and greater tracking of the distal end. In some embodiments, guidewire 85 comprises at least a 50GPa, such as a stainless-steel guidewire with approximately 175GPa.

[0183] In some embodiments, system 10 comprises one or more tissue markers, **marker 30** shown, which can comprise a dye or other visualizable media configured to mark tissue (e.g., using a needle-based tool), and/or a visualizable implant (e.g., a temporary implant) used to mark tissue, such as a small, temporary anchor configured to be attached to tissue and removed at the end of the procedure or otherwise passed by the natural digestive process of the patient shortly after procedure completion. One or more markers 30 can be deposited or deployed in reference to non-target tissue and/or target tissue. The markers 30 can be identified by an operator of system 10 (e.g., visually via a camera-based sensor of system 10), and/or by system 10 (e.g., via a camera, material-detector, and/or other sensor of system 10). Use of markers 30

can be included to avoid damage to non-target tissue (e.g., the papilla and/or tissue proximate the ampulla of Vater), and/or to cause sufficient ablation of target tissue (e.g., a sufficient amount of duodenal mucosa and/or other duodenal tissue proximate yet distal to the papilla and/or the ampulla of Vater). In some embodiments, marker 30 is deposited or deployed in reference to tissue selected from the group consisting of: gastrointestinal adventitia; duodenal adventitia; the tunica serosa; the tunica muscularis; the outermost partial layer of the submucosa; papilla; ampulla of Vater; pancreas; bile duct; pylorus; and combinations of one or more of these. In some embodiments, marker 30 is positioned in tissue and/or removed from tissue by a robotically manipulatable component of system 10. In some embodiments, marker 30 includes one or more functional elements (e.g., one or more sensors and/or transducers), **functional element 39** shown. For example, marker 30 can include a transducer configured to transmit a signal that another component of system 10 is configured to receive and to determine the location of marker 30 based on the received signal.

[0184] In some embodiments, functional element 39 can be configured to prevent the delivery of treatment energy (e.g., electromagnetic energy configured to irreversibly electroporate target tissue) proximate marker 30, for example when marker 30 is positioned by an operator proximate non-target tissue, such as the papilla. For example, functional element 39 can be configured to create an electrical short or other electrical connection (e.g., when a conduit extends from functional element 39 to console 200) configured to prevent the delivery of electromagnetic energy from console 200 (e.g., when energy delivery unit 210 is configured to only deliver energy if the short is not detected).

[0185] System 10 can include one or more materials to be injected into the patient, **injectate 40** shown, such as an injectate that is injected via injection assembly 130 into the tissue of the patient. Injectate 40 can comprise one or more liquids, gels, and/or other flowable materials for injecting into tissue, such as to expand one or more layers of tissue (e.g., submucosal tissue expanded prior to a mucosal ablation procedure) and/or to narrow a lumen of the intestine and/or other axial segment of the GI tract (e.g., to create a therapeutic restriction). Alternatively or additionally, injectate 40 can comprise an agent configured to cause tissue necrosis. In some embodiments, injectate 40 comprises a warming and/or cooling fluid delivered onto and/or into tissue (e.g., a neutralizing fluid that is configured to limit, stop and/or at least reduce the progression of a tissue modification procedure of system 10). In some embodiments, injectate 40 comprises one, two, or more materials selected from the group consisting of: a peptide polymer (e.g., a peptide polymer configured to stimulate fibroblasts to produce collagen); polylactic acid; polymethylmethacrylate (PMMA); a hydrogel; ethylene vinyl alcohol (EVOH); a material configured to polymerize EVOH; dimethyl sulfoxide (DMSO); saline; a material

harvested from a mammalian body; autologous material; fat cells; collagen; autologous collagen; bovine collagen; porcine collagen; bioengineered human collagen; dermis; a dermal filler; hyaluronic acid; conjugated hyaluronic acid; calcium hydroxyapatite; fibroblasts; a sclerosant; an adhesive; cyanoacrylate; a pharmaceutical agent; a visualizable material; a radiopaque material; a visible dye; ultrasonically reflective material; a combination of materials configured to cause an endothermic reaction when mixed (e.g., when mixed in tissue); a combination of materials configured to cause an exothermic reaction when mixed (e.g., when mixed in tissue); a combination of materials configured to expand when mixed (e.g., when mixed in tissue); and combinations of one or more of these. In some embodiments, injectate 40 comprises beads (e.g., pyrolytic carbon-coated beads) suspended in a carrier (e.g., a water-based carrier gel). In some embodiments, injectate 40 comprises a solid silicone elastomer (e.g., heat-vulcanized polydimethylsiloxane) suspended in a carrier, such as a bio-excretable polyvinylpyrrolidone (PVP) carrier gel. In some embodiments, injectate 40 has an adjustable degradation rate, such as an injectate 40 comprising one or more cross linkers in combination with polyalkyleneimines at specific concentrations that result in hydrogels with adjustable degradation properties. In some embodiments, injectate 40 (or agent 45 described herein), comprises living cells, such as living cells injected into the mucosa or submucosa of the intestine to provide a therapeutic benefit.

[0186] In some embodiments, injectate 40 comprises a visualizable and/or otherwise detectable (e.g., magnetic) material (e.g., in addition to one or more materials of above) selected from the group consisting of: a dye; a visible dye; indigo carmine; methylene blue; India ink; SPOTTM dye; a visualizable media; radiopaque material; radiopaque powder; tantalum; tantalum powder; ultrasonically reflective material; magnetic material; ferrous material; and combinations of one or more of these. In some embodiments, console 200 is configured to perform a robotic manipulation of a treatment device 100 and/or other system 10 component based on a measurement of injectate 40 (e.g., a measurement made by a camera or other visualization device of system 10, such as imaging device 60 described herein). For example, robotic manipulation performed by console 200 can be initiated, maintained, terminated, and/or prevented based on a measurement of the presence of injectate 40 (e.g., a sufficient amount of injectate 40) within and/or on tissue.

[0187] In some embodiments, injectate 40 comprises a fluorescent-labeled material and/or other biomarker configured to identify the presence of a biological substance, such as to identify diseased tissue and/or other tissue to be treated by treatment device 100 (e.g., to identify target tissue). For example, injectate 40 can comprise a material configured to be identified by one or more imaging devices (e.g., imaging device 60 described herein), such as to identify a visualizable change to injectate 40 that occurs after contacting one or more biological

substances. In these embodiments, imaging device 60 can comprise a molecular imaging device, such as when imaging device 60 comprises a molecular imaging probe and injectate 40 comprises an associated molecular imaging contrast agent. In these embodiments, injectate 40 can be configured to identify diseased tissue and/or to identify a particular level of one or more of pH, tissue oxygenation, blood flow, and the like. Injectate 40 can be configured to be delivered onto the inner surface of intestinal or other tissue, and/or to be delivered into tissue (i.e. beneath the surface).

[0188] In some embodiments, injectate 40 comprises a conductive material, such as a conductive material configured to be injected into the submucosal tissue proximate target tissue to be treated by system 10. In some embodiments, electrode array 111 comprises at least one electrode 112 configured to extend into the expanded submucosal space (e.g., after expansion with injectate 40 comprising a conductive material). System 10 can be configured to provide treatment energy, such as electromagnetic energy configured to irreversibly electroporate target tissue, between injectate 40 (e.g., when injectate 40 is electrically connected to an electrode 112) and at least one other electrode 112 of electrode array 111 positioned on the mucosal wall within the GI tract. In some embodiments, electrode 112 positioned on the mucosal wall comprises a coating, such as a conductive coating located on the surface of expandable structure 113 comprising an expandable balloon. The conductive coating can comprise a metallic coating; a barium sulfate plastic infusion; and/or a coating deposited via a dip-coating process performed using conductive material.

[0189] In some embodiments, injectate 40 comprises a dielectric material, such as a material configured to at least partially electrically insulate the mucosal layer from the muscularis when injectate 40 is injected into the submucosa between the mucosal layer and the muscularis. For example, injectate 40 can comprise CO₂.

[0190] In some embodiments, injectate 40 comprises a chilled material (e.g., a material at a temperature lower than body temperature), or a heated material (e.g., a material at a temperature higher than body temperature). For example, injectate 40 can comprise a material at a temperature lower than body temperature, such as to offset heating but without degrading an irreversible electroporation (IRE) delivery by treatment assembly 110.

[0191] In some embodiments, injectate 40 comprises a material configured to undergo a physical change when a sufficient dose of electrical energy has been applied to the material (e.g., when the material has been exposed to an electric field sufficient to cause irreversible electroporation of tissue). Injectate 40 can be injected submucosally, as described herein, and can be used to titrate the dosage of electromagnetic energy delivered to the target tissue positioned between treatment assembly 110 and injectate 40. For example, injectate 40 can

comprise a fluid or a gel configured to become luminescent when exposed to a sufficient electrical field. A sensor of system 10, such as visualization assembly 180, can be configured to monitor for luminescence from injectate 40 while electromagnetic energy is applied to the target tissue. In some embodiments, once luminescence has been detected, the energy delivery is stopped.

[0192] In some embodiments, system 10 further comprises one or more agents, **agent 45** shown. Agent 45 can be delivered by one or more components of system 10, such as by injection assembly 130 of treatment device 100. Agent 45 can comprise a material selected from the group consisting of: anti-peristaltic agent, such as L-menthol (i.e. oil of peppermint); glucagon; buscopan; hyoscine; somatostatin; a diabetic medication; an analgesic agent; an opioid agent; a chemotherapeutic agent; a hormone; and combinations of one or more of these. In some embodiments, agent 45 comprises a mucolytic agent configured to remove mucus from a tissue surface.

[0193] In some embodiments, system 10 further comprises one or more imaging devices, **imaging device 60** shown, which can comprise an imaging device constructed and arranged to provide image data that can comprise an image of the patient's anatomy (e.g., inner wall or any part of the intestine of the patient) and/or an image of all or part of treatment device 100 and/or other portion of system 10, as described in detail herein. In some embodiments, imaging device 60 is configured to be robotically manipulated by console 200, such as to change the orientation of imaging device 60 relative to the patient and/or a system 10 component prior to and/or during imaging. Imaging device 60 can comprise an imaging device selected from the group consisting of: endoscope camera; visible light camera; infrared camera; X-ray imager; fluoroscope; CT Scanner; MRI; PET Scanner; ultrasound imaging device; molecular imaging device; and combinations of one or more of these. In some embodiments, image data provided by imaging device 60 comprising a patient image and/or an image of treatment device 100 is used to set, confirm, and/or adjust one or more system 10 parameters, such as when imaging device 60 comprises a sensor of the present inventive concepts configured to produce a signal. In some embodiments, treatment device 100 comprises imaging device 60 (e.g., treatment device 100 includes one or more integrated imaging devices, such as an imaging device of visualization assembly 180). In some embodiments, console 200 is configured to robotically manipulate treatment device 100 and/or other system 10 component based on image data provided by imaging device 60 (e.g., a robotic manipulation based on anatomical position and/or geometric configuration of the component being robotically manipulated).

[0194] In some embodiments, console 200 is configured to analyze image data provided by imaging device 60 (e.g., fluoroscopy image data) to ensure treatment energy is not delivered

while treatment assembly 110 is positioned proximate non-target tissue, such as the papilla (e.g., when non-target tissue has been previously identified and marked, such as with marker 30 comprising a radiopaque marker).

[0195] In some embodiments, system 10 comprises one or more functional elements, **functional element 99**, such as one or more sensors and/or transducers. Functional element 99 can comprise one, two, or more transducers, and/or one, two, or more sensors (e.g., as described herein). For example, the functional element can comprise a transducer configured to deliver energy and/or to convert one form of energy to another form of energy. In some embodiments, the functional element comprises a sensor configured to measure impedance, such as impedance of tissue between two electrodes according to the present inventive concepts. In some embodiments, the functional element comprises a sensor configured to measure a physiologic parameter of the patient, such as a physiologic parameter of the intestine and/or other location on and/or within the patient. In some embodiments, the functional element comprises a needle and/or other agent delivery component. In some embodiments, the functional element comprises an element configured to apply and/or receive a source of vacuum. In some embodiments, the functional element comprises a component configured to compress and/or expand tissue. In some embodiments, the functional element comprises a component configured to cause another component of system 10 to be robotically manipulated, such as a robotic manipulation that causes a translation, rotation, expansion, and/or compacting of a component of system 10.

[0196] In some embodiments, functional element 99 comprises an insulating cover configured to protect non-target tissue from electromagnetic energy delivered by treatment assembly 110. For example, functional element 99 can comprise an insulating cover that protects the papilla or other non-target tissue. An insulating cover can include a stent, a balloon, a graft, a gel, or other device or material configured to electrically insulate all or a portion of non-target tissue (e.g., the papilla). In some embodiments, for example when the papilla (e.g., the exposed surface of the papilla) is covered and electrically insulated by functional element 99, system 10 can be configured to treat a proximal portion of the duodenum (e.g., the D1 region, including tissue proximate the papilla), without damaging the papilla or other non-target tissue surrounding the papilla (e.g., the pancreatic duct).

[0197] In some embodiments, functional element 99 comprises a sizing device configured to size the target tissue lumen (e.g., the duodenum). For example, functional element 99 can comprise a balloon sizing device configured to be inserted into the patient prior to treatment device 100, such as via working channel 8203 of introduction device 80. The balloon sizing device can use pressure (e.g., fluid pressure provided by and monitored by console 200) to determine the diameter of the lumen.

[0198] In some embodiments, treatment device 100 includes a rotary member that is anchored at the distal end of the treatment location (e.g., distal to the most distal treatment location), and anchored at the proximal end of the treatment location (e.g., proximal to the most proximal treatment location). The rotary member can be anchored using endoscopic visualization (e.g., when introduction device 80 comprises visualization assembly 180 as described herein). Treatment device 100 can include a guide rail that extends from the distal anchor location to a location outside of the patient. Treatment assembly 110 can be delivered over the guide rail to the treatment location. Electrode array 111 can comprise a pad of electrodes 112 operably attached to conduits 101. Conduits 101 can comprise a torque cable and/or can be positioned within a torque cable. Treatment assembly 110 can be positioned proximate the distal anchor location, and electromagnetic energy (e.g., energy pulses configured to irreversibly electroporate target tissue) can be continuously or semi-continuously delivered as treatment assembly 110 is rotated about the guide rail (e.g., via the torque cable) and retracted, such that energy is delivered in a helical pattern to the target tissue between the distal anchor and the proximal anchor.

[0199] In some embodiments, treatment assembly 110 can be positioned on a distal portion of introduction device 80, such as on distal portion 8208 of shaft 82. For example, in some embodiments, treatment assembly 110 comprises an expandable structure 113 that can be positioned on distal portion 8208 of shaft 82. Expandable structure 113 of treatment assembly 110 can include an array of longitudinal members in a circumferential arrangement, configured to be positioned around a shaft, such as distal portion 8208 of shaft 82. Alternatively, expandable structure 113 can be positioned around distal portion 1028 of shaft 102, and/or can extend from distal end 1029 of shaft 102. Electrodes 112 of electrode array 111 can be located on the longitudinal members. In some embodiments, expandable structure 113 comprises an expandable basket comprising the longitudinal members.

[0200] Expandable structure 113 can be configured to transition to an expanded geometry when the distal end of expandable structure 113 is brought closer to its proximal end, and to transition to a compact geometry when the distal end of expandable structure 113 is moved away from its proximal end (e.g., such that the longitudinal members are caused to bow outward and straighten, respectively). Conduit 101 can comprise a linkage that is configured to move the distal end of expandable structure 113 relative to its proximal end, such as when the proximal end is fixedly attached to a shaft (e.g., temporarily fixedly attached to shaft 82). Conduit 101 can be translated (e.g., manually by an operator of system 10 and/or automatically by system 10) to expand and/or contract expandable structure 113. Expandable structure 113 can be biased in an expanded geometry, or in a compact geometry, for example when the longitudinal members

of expandable assembly 113 comprise a set shape, such as a relatively bowed shape to bias expandable structure 113 in an expanded geometry, or a relatively straight shape to bias expandable structure 113 in a compact geometry.

[0201] In some embodiments, treatment assembly 110 includes an electrode deployment mechanism that is magnetically activated. For example, electrode array 111 can comprise one or more electrodes 112 that are configured to be radially extended from and/or retracted into a housing of treatment assembly 110 via application of a magnetic force. Additionally, or alternatively, treatment assembly 110 can comprise expandable structure 113 that is configured to transition between a compact geometry and an expanded geometry via the application of a magnetic force. In some embodiments, treatment assembly 110 comprises a magnetic coil (e.g., an electromagnet) that attracts and/or repels electrodes 112 to retract and/or deploy electrodes 112, respectively.

[0202] In some embodiments, treatment assembly 110 comprises an elongate anchoring device, such as anchoring assembly 170, that provides a scaffolding of the lumen in which it is inserted (e.g. lumen of the small intestine) from within which treatment assembly 110 can provide treatment, such as IEP treatment, to the target tissue (e.g. mucosal tissue, submucosal tissue, and/or nerve tissue of the duodenum or intestinal location). In some embodiments, anchoring assembly 170 comprises an elongate scaffold that is positioned in an axial segment of the small intestine during a treatment procedure (e.g., placed by a clinician using a device of system 10). For example, anchoring assembly 170 can comprise an expandable stent-like structure, such as an expandable structure that is configured to be deployed into the small intestine via working channel 8203 of introduction device 80. In some embodiments, introduction device 80 is positioned in a distal portion of the small intestine (e.g., proximate the ligament of Treitz), and anchoring assembly 170 is deployed from working channel 8203 as shaft 82 of introduction device 80 is retracted proximally through the small intestine. Once deployed, anchoring assembly 170 can extend from the distal location proximate the ligament of Treitz to a proximal location, such as a location within 5mm of the papilla (e.g., proximal to and/or distal to the papilla), such as a location at least 1mm, or 2mm distal to the papilla.

[0203] In some embodiments, anchoring assembly 170 includes a central member, such as a central guidewire or other tracking component that treatment assembly 110 can translate along. Treatment assembly 110 can translate along the track of anchoring assembly 170 to reach various target tissue treatment locations. In some embodiments, electrode array 111 includes a rotary array configured to rotate within anchoring assembly 170, such as to rotate and translate along the central track of anchoring assembly 170, such as to treat an axial segment of the intestine (e.g., such that a helical portion of the axial segment is treated).

[0204] In some embodiments, anchoring assembly 170 comprises an expandable structure (e.g., expandable structure 113) such as an expandable balloon. The expandable balloon can include a plurality of conductors (e.g., conductors configurable as electrodes), such as one or more ring electrodes positioned on the outer surface of the balloon. Treatment assembly 110 can include a translating element configured to selectively connect to a subset of the plurality of conductors, such that an IEP can be delivered to the target tissue via the conductors of anchoring assembly 170 connected to the translating element of treatment assembly 110. For example, the translating element can be configured to translate and/or rotate within anchoring assembly 170 to selectively connect to the conductors positioned on the outer (e.g., tissue facing) surface of anchoring assembly 170.

[0205] In some embodiments, treatment assembly 110 is configured to insert at least a portion of at least a first electrode 112 of a pair of electrodes 112 into the tissue, such as an insertion into the submucosal tissue, to deliver an IEP from one side of the target tissue (e.g., from inside the lumen of the small intestine) to the other side of target tissue (e.g., to inside the submucosal tissue).

[0206] In some embodiments, treatment assembly 110 is configured to inject a conductive material (e.g., a conductive fluid such as a highly concentrated saline solution) into the submucosal tissue. For example, at least one first electrode 112 can be inserted into the submucosal tissue (e.g., when a first electrode 112 is located on a needle or other device configured to be inserted into tissue), such that the conductive material and the first electrode collectively form a first electrode from which an IEP can be delivered to the target tissue (e.g. an IEP delivered between this first electrode 112 and a second electrode 112, as described herein). In some embodiments, the at least one first electrode 112 can include a proximal first electrode 112 inserted at a proximal end of an axial segment of target tissue to be treated, and a distal first electrode 112 inserted at a distal end of the axial segment of target tissue to be treated. In some embodiments, the conductive material is injected into the submucosal tissue at a first location (e.g. the proximal or distal location) via one of the two needles and drawn towards and potentially extracted from the submucosal tissue at a second location (e.g. the distal or proximal location, respectively) via the other needle, such that the conductive material can be positioned in (e.g. and circulated through) the submucosal tissue, for example while one or more IEP energy deliveries are being performed by system 10. In these embodiments, the conductive material can be positioned in the submucosal tissue to form a hollow tubular structure, such that the conductive material and the associated one or more needles described herein can collectively form a hollow tubular shaped electrode that surrounds a hollow tubular shaped portion of

mucosal tissue as well as treatment assembly 110 (e.g. a treatment assembly 110 also comprising a hollow tubular shaped electrode as described immediately herebelow).

[0207] In some embodiments, treatment assembly 110 includes at least one second electrode 112, such as when system 10 is configured to deliver the IEP between the first electrode 112 (e.g. a first electrode 112 comprising one or more needles as well as conductive fluid positioned in the submucosal tissue in a hollow tubular geometry) and a second electrode 112. In some embodiments, the second electrode 112 comprises a conductive coating located on the outer surface of expandable structure 113, such as expandable structure 113 comprising an inflatable balloon, where the second electrode 112 comprises a hollow tubular geometry that is concentric with the hollow tubular geometry of the first electrode 112 (e.g. including the conductive material in the submucosal tissue). In these embodiments, delivery of the IEP treatment is limited to the mucosal tissue between the two hollow tubular shaped electrodes, significantly limiting the likelihood of damaging any non-target tissue.

[0208] In some embodiments, treatment assembly 110 comprises a first set of needles including a first set of electrodes 112, and a second set of needles including a second set of electrodes 112. The first set of needles can extend a first depth into the tissue (e.g., into the submucosal tissue to position the first set of electrodes 112 in the submucosal tissue) and the second set of needles can extend a second depth into tissue, where the second depth is more shallow than the first depth (e.g., when the second set of needles only extends into the mucosal layer, and/or positions the second set of electrodes 112 in contact with the mucosal layer).

[0209] In some embodiments, treatment assembly 110 includes expandable structure 113 that comprises a multilayer balloon. Expandable structure 113 can include an inner layer comprising an expandable balloon, and an outer layer comprising electrode array 111 positioned on a porous substrate. Expandable structure 113 can include a middle layer, which can be located between the inner balloon layer and the outer electrode layer. The middle layer can comprise a porous membrane configured to allow a vacuum to be applied between the inner layer and the outer layer, such that the vacuum is also applied to the porous portions of the outer layer. The applied vacuum can suction tissue to the outer layer of expandable structure 113, such that the tissue is held by the vacuum against electrodes 112 of electrode array 111. In some embodiments, the middle layer of expandable structure 113 is fluidly connected to a vacuum lumen, such as lumen 1023 of shaft 102 and/or working channel 8203 of introduction device 80, either comprising a vacuum channel fluidly attached to a source of vacuum (e.g., to a source of vacuum supplied by console 200).

[0210] In some embodiments, treatment assembly 110 comprises a ring of electrodes 112. Treatment assembly 110 can include a subassembly located within expandable structure 113 that

is configured to rotate within the ring of electrodes 112. The subassembly can be configured to operably connect one or more pairs of electrodes 112, such as to electrically connect the one or more pairs of electrodes to console 200. For example, the subassembly can operably connect two or more electrodes 112 to console 200 such that an IEP can be delivered from console 200 to tissue via the connected electrodes 112.

[0211] **Referring now to Fig. 1A**, a flow chart of a method of treating target tissue of a patient is illustrated, consistent with the present inventive concepts. In some embodiments, **Method 1000** of Fig. 1A is performed using system 10 described in reference to Fig. 1 and/or otherwise herein. In **Step 1100**, a patient is selected for treatment, such as a patient selected to treat and/or diagnose a patient disease or disorder selected from the group consisting of: Type 2 diabetes; Type 1 diabetes; "Double Diabetes"; gestational diabetes; hyperglycemia; pre-diabetes; impaired glucose tolerance; insulin resistance; non-alcoholic fatty liver disease (NAFLD); non-alcoholic steatohepatitis (NASH); obesity; obesity-related disorder; polycystic ovarian syndrome (PCOS); hypertriglyceridemia; hypercholesterolemia; psoriasis; GERD; coronary artery disease (e.g., as a secondary prevention); stroke; TIA; cognitive decline; dementia; Alzheimer's Disease; neuropathy; diabetic nephropathy; retinopathy; heart disease; diabetic heart disease; heart failure; diabetic heart failure; metabolic dysfunction-associated steatotic liver disease (MASLD); and combinations of these. In some embodiments, the patient is selected to treat two or more of the above diseases or disorders, such as a patient selected to treat two or more of diabetes, insulin resistance, NAFLD, NASH, and/or PCOS.

[0212] The patient selected can be taking one or more medicines to treat their diabetes. The patient selected can have an HbA1c level between 7.5% and 12.0%, between 7.5% and 10%, or between 7.5% and 9.0%. In some embodiments, the patient selected can have an HbA1c level between 6.0% and 12.0%. In some embodiments, patients with higher HbA1c levels and/or other higher disease burden can receive more aggressive treatments (e.g., more tissue treated and/or higher number of repeated treatments over time).

[0213] Patient selection can be based on the current level of one or more parameters representing one or more various biomarkers or other representative values of physiologic conditions (e.g., as compared to an average among diabetic and/or non-diabetic patients), such as a level of a parameter selected from the group consisting of: body mass index (BMI) level; waist circumference; HbA1c level; fasting glucose; insulin resistance; liver fibrosis; cholesterol or triglyceride level; duration of years exhibiting type 2 diabetes; fasting insulin, fasting C-peptide or C-Peptide stimulation in response to a meal; age; and combinations of these.

[0214] Prior to placing one or more devices into the patient (e.g., treatment device 100), or at any time thereafter (e.g., during or after the procedure), one or more agents can be introduced into the patient, such as agent 45 described in reference to Fig. 1 and otherwise herein. In some embodiments, one or more agents are introduced into the GI tract directly. In some embodiments, agent 45 comprises L-menthol (i.e. oil of peppermint) or other agent configured to provide an anti-peristalsis effect. In these embodiments, a few drops of agent 45 can be placed in an irrigation or other lumen of a device inserted into the patient (e.g., treatment device 100 and/or introduction device 80). In some embodiments, approximately 8mL of L-menthol is mixed with approximately 0.2mL of Tween 80 (polysorbate 80) in approximately 500mL of distilled water (i.e. to create an approximately 1.6% solution). Approximately 20mL of this mixture can be sprayed through a working channel of treatment device 100, or more as required to dampen peristalsis. In some embodiments, the solution can vary between approximately 1.6% and 3.2%. Tween and/or sorbitan monostearate can be used as an emulsifier.

[0215] One or more agents 45 can be delivered once treatment device 100 or any other agent delivery device of system 10 enters the small intestine (e.g., the duodenum). In some embodiments, agent 45 comprises one or more agents that are delivered intravenously, and can include glucagon and/or buscopan.

[0216] As described herein, in some embodiments, an endoscope-based introduction device 80 is inserted into the patient. In these embodiments, subsequently inserted devices can be placed through a working channel of introduction device 80 and/or alongside introduction device 80. In some embodiments, introduction device 80 and an attachable sheath are both inserted into the patient, and subsequently inserted devices (e.g., treatment device 100) can be placed through a working channel of introduction device 80, through the attachable sheath, and/or alongside introduction device 80. In some embodiments, treatment device 100 is inserted into the patient without introduction device 80 (e.g., after introduction device 80 has been inserted and subsequently removed from the patient, such as when introduction device 80 has been used to position guidewire 85 within the patient). In some embodiments, one or more patient-inserted devices can be inserted over a guidewire (e.g., guidewire 85 placed by introduction device 80). In some embodiments, an elongate stiffening device is used (e.g., inserted into treatment device 100), such as an endoscope stiffening system provided by Zutron Medical of Lenexa, Kansas, USA.

[0217] In some embodiments, non-target tissue is identified (e.g., identified by the operator and/or automatically by system 10, such as by algorithm 25 described herein). Non-target tissue can be identified using image information produced by a visualization device, such as by imaging device 60 and/or an imaging component of treatment device 100, visualization

assembly 180. The non-target tissue can comprise the papilla, tissue proximate the ampulla of Vater, the pancreas, and/or other tissue to which treatment (e.g., the denaturing of tissue) may adversely affect the patient. Marking of the non-target tissue (or tissue proximate the non-target tissue) can be performed, such as with a tattoo, ink, or other visualizable substance, such as a visual agent or clip placed in and/or on the mucosa and/or submucosa in or proximate the papilla and/or the ampulla of Vater. In some embodiments, one or more markers similar to marker 30 described in reference to Fig. 1 and otherwise herein are positioned in the patient, such as to provide a reference location relative to non-target tissue. The marking of the tissue can be performed manually by an operator, automatically by system 10 (e.g., using algorithm 25), or semi-automatically (e.g., marking performed with both operator input and system 10 automation). Tissue treatment performed in subsequent steps of Method 1000 can avoid treating (e.g., avoid delivering energy to) the non-target tissue identified and potentially marked (e.g., with one or more markers 30). The tissue treatment can also be performed manually by an operator, automatically by system 10 (e.g., via robotic control provided by console 200), and/or semi-automatically. For example, manual and/or automatic detection of one or more markers can be performed, and the results used in manual and/or automatic selection of one or more treatment locations, and/or positioning of treatment assembly 110 at the one or more treatment locations (e.g., positioning provided via robotic control of treatment device 100 by console 200). In some embodiments, system 10 (e.g., console 200) automatically prevents treatment at an undesired location, such as when system 10 prevents an operator from (manually) treating tissue proximate a non-target location identified by algorithm 25 (e.g., a non-target location identified by one or more markers 30).

[0218] In Step 1200, treatment device 100 is inserted through the patient's mouth and advanced through the stomach and into the small intestine (if not already in place). Step 1200 can include selecting a particular model of treatment device 100, such as a particular size (e.g., treatment assembly length and/or diameter) or other configuration of treatment device 100. Treatment device 100 can be inserted over guidewire 85, such as is described herein. Guidewire 85 can be advanced such that its distal end is in the jejunum or a more distal location. During advancement of treatment device 100 (e.g., manually by an operator or automatically by system 10), guidewire 85 can be held taut (e.g., via robotic manipulation via console 200) in order to prevent treatment device 100 from forming a loop in the stomach. As described herein, treatment device 100 can be inserted through a working channel of introduction device 80 and/or alongside introduction device 80. In some embodiments, treatment device 100 includes both endoscopic components (e.g., steering, integrated camera, and the like) as well as a treatment assembly 110 and its associated fluid pathways (conduits) and other associated componentry.

[0219] Treatment device 100 can be advanced (e.g., over guidewire 85 or not, via an operator, or robotically via console 200) such that treatment assembly 110 is positioned in the duodenum (or another GI location) comprising target tissue to be treated. Treatment assembly 110 can be positioned at the first target tissue location in the intestine. The first location can be a most-proximal target location to be treated, such as a location in the duodenum at least 0.5cm or at least 1cm, but not more than 5cm or 10cm from the papilla and/or the ampulla of Vater. Alternatively, the first location can be a most-distal target location to be treated. For example, treatment device 100 can be configured to treat target tissue in a distal to proximal manner, such as when treatment assembly 110 is positioned in a distal portion of the duodenum (e.g., proximate a most distal target tissue location such as a location at or proximate to the ligament of Treitz), and the most distal target tissue is treated first (e.g., as described herein), followed by more proximal target tissue as treatment assembly 110 is retracted proximally (e.g., retracted between treatment steps). In some embodiments, distal to proximal treatment enables direct visualization of treated tissue, for example when visualization assembly 180 comprises a forward-facing camera that captures image data of the treated tissue as treatment device 100 is retracted. In some embodiments, treatment assembly 110 is positioned based on the location of a previously placed marker, such as marker 30 described herein. Prior to and/or during insertion of treatment device 100, a stiffening wire can be inserted within treatment device 100.

[0220] In some embodiments, system 10 is configured to insufflate a portion of the GI tract (e.g., with a fluid provided by fluid delivery unit 230 and delivered via a lumen 1023 of shaft 102 and/or working channel 8203 of introduction device 80). In some embodiments, system 10 is configured to insufflate a portion of the GI tract while treatment assembly 110 is translated, such as to prevent or at least limit the likelihood of one or more portions of treatment device 100 catching on the tissue of the GI tract (e.g., to prevent a portion of electrode array 111 from catching on the tissue).

[0221] In **Step 1300**, an optional pre-treatment procedure can be performed, such as a when supplementary treatment assembly 160 is positioned at the first target tissue location, and a pre-treatment tissue modification is performed via supplementary treatment assembly 160. Alternatively or additionally, a pre-treatment procedure can be performed via treatment assembly 110. In some embodiments, a pre-treatment procedure includes a tissue modification procedure, such as a procedure selected from the group consisting of: a tissue expansion procedure; a tissue cooling procedure, such as a procedure configured to cool the tissue to increase the efficacy of a subsequent treatment procedure and/or to reduce damage to non-target tissue during a subsequent treatment procedure; a tissue warming procedure, such as a procedure

configured to heat the tissue to increase the efficacy of a subsequent treatment procedure; and combinations of these.

[0222] In some embodiments, a pre-treatment procedure includes a tissue warming procedure configured to enable better electromagnetic energy delivery. For example, target tissue can be heated to at least 45°C prior to a treatment procedure comprising the delivery of electromagnetic energy to irreversibly electroporate the target tissue. In some embodiments, a pre-treatment procedure includes a tissue cooling procedure, such as a tissue cooling procedure using fluids at temperature of no more than 35°C, 25°C, and/or 15°C for durations of at least 10 seconds, 20 seconds, 40 seconds, and/or 60 seconds (e.g., to prevent undesired deep tissue heating caused by IRE or other energy delivery via treatment assembly 110). In some embodiments, tissue cooling is performed using a cryogenic fluid, such as fluid at a temperature below -30°C.

[0223] In **Step 1400**, a tissue treatment procedure is performed. For example, target tissue of an axial segment of the gastrointestinal tract can be electroporated by delivering electromagnetic energy via electrodes 112 of electrode array 111 positioned proximate the target tissue. Energy delivered via electrodes 112 can be configured to irreversibly electroporate the target tissue, such as to irreversibly electroporate at least a portion of the mucosal layer of the axial segment of the duodenum or other portion of the GI tract. In some embodiments, the energy delivery of the tissue treatment procedure causes ablation of the full thickness of the mucosal layer of the axial segment (e.g., and a portion of the submucosal layer). A tissue treatment procedure can comprise a tissue treatment procedure described herein.

[0224] In **Step 1500**, an optional post-treatment procedure can be performed, such as when supplementary treatment assembly 160 is positioned at the location where the treatment procedure was performed, and a post-treatment tissue modification is performed via supplementary treatment assembly 160. Alternatively or additionally, a post-treatment procedure can be performed via treatment assembly 110. In some embodiments, a post-treatment procedure can be performed to limit, stop and/or at least reduce the progression of a tissue modification caused by the tissue treatment procedure.

[0225] In some embodiments, a pre-treatment and/or a post-treatment procedure includes a tissue cooling procedure configured to prevent undesirable treatment (e.g., to prevent undesirable expansion of irreversible electroporation treatment delivered by treatment assembly 110). In some embodiments, a tissue cooling procedure can be performed during a treatment procedure comprising the delivery of electromagnetic energy configured to irreversibly electroporate the target tissue. For example, in some embodiments, a tissue cooling procedure can be performed to enable the delivery of increased electromagnetic energy (e.g., to create a

stronger electric field configured to irreversibly electroporate the target tissue) without causing thermal damage to tissue (e.g., not causing thermal damage to tissue proximate the target tissue). In some embodiments, cooling is performed using fluid at room temperature, and/or fluid at a temperature less than 41°C. In some embodiments, fluid used to perform a tissue cooling procedure is provided at a temperature of no more than 45°C, 35°C, 25°C, and/or 15°C (e.g., sufficient to suppress thermal ablation that can be caused by electroporation and/or other electrical energy delivery). In some embodiments, tissue cooling is performed using cryogenic fluids, such as a fluid at or below -30°C. Cooling fluid can be provided to tissue for a minimum time period (e.g., prior to and/or after electrical energy delivery), such as for a time period of at least 10s, 20s, 40s, and/or 60s.

[0226] In **Step 1600**, the operator of system 10 and/or an algorithm (e.g., algorithm 25) of system 10 can determine if additional target tissue is to be treated prior to concluding the procedure (e.g., a determination made using data provided by diagnostic unit 240, such as when diagnostic unit 240 applies a voltage and/or current and measures impedance or other electrical property to differentiate treated versus non-treated tissue, and/or to assess level of treatment of treated tissue). If additional target tissue is to be treated, Method 1000 can return to Step 1200 where the treatment assembly 110 is repositioned proximate the next target tissue to be treated (e.g., an axial segment of the duodenum or other segment of the gastrointestinal tract), and Method 1000 repeats. If no additional tissue is to be treated, Method 1000 continues to Step 1700.

[0227] In some embodiments, prior to, during, and/or after a tissue treatment procedure is performed at a target tissue location, system 10 is configured to mark the treated and/or to-be treated tissue to identify the location of the treatment. For example, system 10 can be configured to “brand” the tissue, such as by applying electromagnetic energy (e.g., RF energy configured to heat the tissue) to create a visualizable lesion on the tissue (e.g., a burn). In some embodiments, electromagnetic energy delivered to brand the tissue can be delivered via electrode array 111 before, during, and/or after electromagnetic energy is applied via electrode array 111 to irreversibly electroporate the target tissue.

[0228] In some embodiments, to reposition treatment assembly 110 for subsequent target tissue treatment, the operator can align a marker 1801 located on shaft 102 with a tissue brand or other tissue identifier indicating the location of previous treatment. Marker 1801 can be positioned on shaft 102 proximal to treatment assembly 110 such that subsequent tissue treatments are appropriately spaced when marker 1801 is aligned with the tissue brand (e.g., such that tissue treatments do not overlap).

[0229] In **Step 1700**, treatment device 100 is removed from the patient. Other devices of system 10, such as introduction device 80, can also be removed from the patient. In some embodiments, one or more components of system 10 can remain within the patient, for example when marker 30 comprises a bioabsorbable device and/or a device configured to be passed naturally by the body.

[0230] **Referring now to Figs. 2A and 2B**, schematic views of a treatment device inserted into a patient and that device shown in an anatomical shape (e.g., a shape the device assumes when inserted into a patient) are illustrated, respectively, consistent with the present inventive concepts. As described herein, treatment device 100 is configured to be inserted into a patient's GI tract via the mouth. In Fig. 2A, treatment device 100 is shown inserted through introduction device 80, such as an introduction device comprising a bite block. Treatment device 100 can be configured to track within the anatomy of the patient (e.g., follow a natural anatomic path, such as the GI tract) to reach one, two, or more locations to perform a treatment procedure (e.g., a mucosal or other tissue treatment procedure described herein). In some embodiments, treatment device 100 is configured to be advanced over a guidewire (e.g., guidewire 85 not shown but described herein), such as when the distal portion of a guidewire has been positioned within the small intestine of the patient prior to the introduction of treatment device 100 into the small intestine. In Fig. 2A, treatment device 100 is shown inserted into the patient with functional treatment assembly 110 positioned within the patient's duodenum, specifically with treatment assembly 110 positioned distal to the pylorus and the ampulla of Vater. For example, treatment device 100 can be advanced (e.g., autonomously or otherwise automatically by system 10) through the mouth of the patient, through the esophagus, and into the patient's stomach. Once in the stomach, treatment device 100 can be further advanced, such that the distal end of treatment device 100 tracks through the pylorus and enters the small intestine. In Fig. 2A, treatment assembly 110 is shown advanced through the pylorus, into the duodenum, and positioned at a treatment location (e.g., in contact with target tissue) distal to the papilla. The trajectory of treatment device 100 in the stomach is shown in both a "long position" and a "short position", depicted with long and short dashes, respectively. The long position is achieved when a portion of shaft 102 is pressing against a wall of the stomach, following the curvature of the stomach from the end of the esophagus to the pylorus. The short position is achieved when shaft 102 follows a shorter path between the end of the esophagus and the pylorus. In Fig. 2B, treatment device 100 is shown in the long position.

[0231] As described herein, treatment device 100 can be advanced into the small intestine of a patient, where at least one tissue treatment can be performed, such as are described herein.

After a first treatment has been performed, treatment device 100 can be advanced (e.g., robotically advanced), and a subsequent tissue treatment can be performed. In some embodiments, an operator first places guidewire 85 (not shown) into the small intestine of the patient following the long position illustrated (e.g., using an introduction device comprising an endoscope, not shown). In some embodiments, two or more devices of system 10 are configured to be inserted into the patient simultaneously, for example treatment device 100 and an introduction device, such as introduction device 80 comprising an endoscope. In some embodiments, introduction device 80 comprising an endoscope can be positioned next to (e.g., parallel to) treatment device 100 (e.g., after treatment device 100 has been advanced into the patient over guidewire 85), such that the proximal end of treatment assembly 110 of treatment device 100 is visible via a visualization assembly of introduction device 80 (e.g., by visualization assembly 180 integrated into introduction device 80, as described herein). In some embodiments, at least the distal portion of introduction device 80 is positioned next to treatment device 100 (e.g., in the small intestine of the patient), and at least a proximal portion of introduction device 80 is next to at least a proximal portion of treatment device 100 (e.g., in the esophagus of the patient). Once both introduction device 80 and treatment device 100 are positioned at least through the pylorus, introduction device 80 and treatment device 100 can be advanced (e.g., robotically advanced) simultaneously into the duodenum, such that treatment assembly 110 is positioned distal to the papilla. In some embodiments, introduction device 80 and treatment device 100 are advanced (e.g., robotically advanced) simultaneously to reduce friction between the two devices and/or to limit the force required to advance either or both of the two devices. After each treatment procedure, introduction device 80 and treatment device 100 can be advanced such that treatment assembly 110 is distal to a previous treatment site using visualization (e.g., via a visualization assembly 180), such as to prevent treatment of the same tissue twice.

[0232] Shaft 102 of treatment device 100 can comprise one, two, or more discrete, contiguous axial sections (“sections” herein), where each section can comprise a different hardness and/or stiffness (“stiffness” herein). Alternatively or additionally, shaft 102 and/or a section of shaft 102 can comprise a continuously variable stiffness. A stiffness profile for shaft 102 can be selected to enhance the pushability, rotation, and/or trackability (“trackability” herein) of treatment device 100 (e.g., the ease at which treatment device 100 is advanced through and/or retracted within the anatomy of the patient). Stiffness of each section of shaft 102 is determined by the properties (e.g., hardness) of the materials used to manufacture (e.g., extrude) the particular section of shaft 102, the geometry of that section of shaft 102 (e.g., geometry of

lumens, wall thicknesses, and the like), as well as the properties of the components positioned within one or more lumens of that section of shaft 102.

[0233] Shaft 102 can comprise multiple sections, each with a different stiffness (e.g., a minimally varying stiffness along the length of the section), and/or it can include one or more sections with a varying (e.g., continuously varying) stiffness. In some embodiments, shaft 102 of treatment device 100 comprises three sections, sections S_P , S_M , and S_D , shown in Fig. 2B, each with a different stiffness. Treatment device 100 can comprise a distal tip (e.g., a portion of shaft 102 that extends distally beyond treatment assembly 110) such as a tip with a tapered shape as shown. In some embodiments, shaft 102 terminates at the distal end of treatment assembly 110, and the distal tip of treatment device 100 comprises a shaft that extends from distal end 1029 of shaft 102. Alternatively or additionally, the distal tip can comprise the distal portion (e.g., distal portion 1028) of shaft 102, such as a tapered portion of shaft 102 extending beyond the distal end of treatment assembly 110. Section S_P can comprise the proximal portion of shaft 102, extending distally from handle 105; section S_M can comprise a middle section of shaft 102, adjacent and distal to section S_P ; and section S_D can comprise a distal section of shaft 102 adjacent and distal to section S_M (e.g., the portion of shaft 102 immediately proximal to treatment assembly 110), each as shown. In some embodiments, treatment device 100 comprises a fourth section, section S_T , comprising at least the distal tip of treatment device 100, also as shown. Sections S_P , S_M , and/or S_D can each comprise a discrete length of shaft 102.

[0234] Each section S_P , S_M , S_D , and/or S_T can comprise a stiffness similar or dissimilar from the stiffness of an adjacent section. In some embodiments, section S_P comprises a first stiffness, section S_M comprises a second stiffness, section S_D comprises a third stiffness, and section S_T comprises a fourth stiffness, where two, three, or four (all) of these sections comprise different stiffnesses. In some embodiments, the stiffness of section S_P can comprise the highest stiffness, the stiffness of section S_M can comprise the second highest stiffness, the stiffness of section S_D can comprise the third highest stiffness, and/or the stiffness of section S_T can comprise the lowest stiffness (e.g., each successive section of treatment device 100 has a lower stiffness than the adjacent proximal section). In some embodiments, section S_P of shaft 102 comprises a higher stiffness (e.g., higher relative to the other sections of treatment device 100), such as a stiffness configured to aid in the trackability of treatment device 100 (e.g., the ability to advance treatment device 100 into the anatomy of the patient without kinking or other undesired deformation). Section S_D of shaft 102 can comprise a relatively flexible section (e.g., lower stiffness than sections S_P and/or S_M), such as a stiffness configured to enable a smaller bend radius than the more proximal sections, enhancing the trackability of treatment device 100 (e.g., the trackability of the distal portion of treatment device 100 through tortuous portions of the

anatomy). Section S_M can comprise a relatively medium stiffness (e.g., a stiffness at a level between that of sections S_P and S_D), configured to maintain an adequate pushability of treatment device 100 while being flexible enough to follow section S_D through anatomical bends in the patient, such as the path through the stomach, pylorus, and into the duodenum.

[0235] The change in stiffness between two adjacent sections of shaft 102 can comprise a relatively short stiffness transition (e.g., an abrupt transition), or it can comprise a relatively long transition of stiffness. For example, a short stiffness transition can comprise a distance of less than 2.5", less than 1.5", or less than 1", while a long stiffness transition can comprise a distance of at least 6", at least 12", or at least 18". Stiffness transitions between two adjacent sections of shaft 102 can be created during a manufacturing process of shaft 102. For example, a butt-welding of the two sections can include a reflow of the materials of the two sections (e.g., a reflow of two materials of different hardness). Alternatively or additionally, an extrusion process used to create at least the two sections of shaft 102 can be configured to controllably vary the stiffness of the manufactured extrusion (e.g., the resultant extrusion can include a material change at the transition that includes mixing of two or more materials). Long transitions in stiffness can be included to prevent or at least limit kinking of shaft 102 (e.g., to limit kinking in the transition regions of shaft 102).

[0236] In some embodiments, shaft 102 comprises an extrusion that gradually transitions from a first stiffness at the proximal end of shaft 102 to a second, lesser stiffness at the distal end of shaft 102 (e.g., via an extrusion process as described herein). In these embodiments, the stiffness transition can be uniform along the length of shaft 102. Alternatively, as described herein, the transition can be varied, such that the sections of shaft 102 maintain a near constant stiffness and the stiffness transitions gradually (e.g., over at least 2.5") between sections S_P , S_M , S_D , and/or S_T .

[0237] Section S_P can comprise at least a first S_P material, such as a material with a durometer of at least 63D or 70D, such as a material with a durometer of approximately 63D, or 80D. In some embodiments, section S_P comprises this first S_P material (e.g., polyether block amide) and one or more additives such as a lubricant, a plasticizer, and/or a radiopaque additive (e.g., barium sulfate at a 20% concentration), where the inclusion of these one or more additives can change (e.g., increase) the durometer of the section. Section S_M can comprise at least a first S_M material, such as a material with a durometer of approximately 55D. Similar to section S_P , section S_M can comprise this first S_M material (e.g., polyether block amide) and one or more additives such as a lubricant, a plasticizer, and/or a radiopaque additive (e.g., barium sulfate at a 20% concentration), where the inclusion of these one or more additives can change (e.g., increase) the durometer of the section. Section S_D can comprise at least a first S_D material, such

as a material with a durometer of approximately 40D. Similar to sections S_P and/or S_M , section S_D can comprise this first S_D material (e.g., polyether block amide) and one or more additives such as a lubricant, a plasticizer, and/or a radiopaque additive (e.g., barium sulfate at a 20% concentration), where the inclusion of these one or more additives can change (e.g., increase) the durometer of the section. In some embodiments, at least one section of shaft 102 comprises a mixture of at least 5% of a radiopaque material, such as at least 10%, such as at least 20%, such as at least 30%, such as at least 40%. Section S_T can comprise at least a first S_T material, such as a material with a durometer of approximately 35D. Similar to sections S_P , S_M , and/or S_D , section S_T can comprise this first S_T material (e.g., polyether block amide) and one or more additives such as a lubricant, a plasticizer, and/or a radiopaque additive (e.g., barium sulfate at a 20% concentration), where the inclusion of these one or more additives can change (e.g., increase) the durometer of the section. The distal tip of treatment device 100 can comprise a taper (e.g., a taper such that the distal portion of the distal tip comprises a smaller diameter than the proximal portion of the distal tip). In some embodiments, the taper and/or other geometric feature (e.g., wall thickness variation) of the distal tip is configured such that the proximal portion of the tip comprises a stiffness greater than guidewire 85, and the distal portion of the tip comprises a stiffness less than guidewire 85 (e.g., a guidewire 85 which can be slidingly positioned within treatment device 100, exiting the distal portion of the distal tip of treatment device 100). In some embodiments, the proximal end of the distal tip comprises a stiffness approximately equal to the stiffness of the distal end of section S_D . In some embodiments, section S_D and/or S_T comprises at least one material (e.g., polyether block amide) with a durometer of less than 40D, such as less than 30D, such as less than 20D, such as approximately 10D.

[0238] Section S_P can comprise a length long enough to reach the pylorus of the patient when treatment device 100 is fully inserted into the patient. In some embodiments, the length of sections S_P , S_M , and/or S_D are selected to enable treatment device 100 to be advanced into the patient such that treatment assembly 110 can be positioned at least 15" into the duodenum, such as at least 18" into the duodenum. In some embodiments, section S_P comprises a length of at least 32", such as at least 49", such as no more than 72", such as approximately 57". Section S_M can comprise a length of at least 10", such as approximately 17". Section S_D can comprise a length of at least 2", such as approximately 5".

[0239] Shaft 102 of Fig. 2A and 2B has been described in terms of a shaft with at least a portion with a continuously varying stiffness (e.g., lower stiffness at distal locations), or a shaft with three or four sections with different stiffnesses (e.g., successively lower stiffnesses in each more distal section). In some embodiments, shaft 102 comprises two sections with different stiffnesses, such as a proximal section with a greater stiffness than a distal section, such as to

improve trackability as described herein. In some embodiments, shaft 102 comprises four, five, six or more sections with different stiffnesses (e.g., successively lower stiffnesses in each more distal section), such as to improve trackability as described herein.

[0240] In some embodiments, sections S_P , S_M , and/or S_D each comprise a stiffness as defined by a stiffness test performed by a test fixture, such as described in applicant's co-pending United States Patent Application Serial Number 17/863,016 (Attorney Docket No. 41714-722.301; Client Docket No. MCT-051-US), entitled "Automated Tissue Treatment Devices, Systems, and Methods", filed July 12, 2022. The "required bending force" is defined by the force required to cause the midpoint of a two-inch span of the section of shaft 102 to deflect approximately 0.125". In some embodiments, section S_P of shaft 102 comprises a stiffness with a required bending force of at least 10lbf, such as at least 13lbf, such as 16lbf. Section S_M of shaft 102 can comprise a stiffness with a required bending force of at least 8lbf, such as at least 10lbf, such as 11lbf. Section S_D of shaft 102 can comprise a stiffness with a required bending force of no more than 14lbf, such as no more than 11lbf, such as no more than 8lbf, such as no more than 5lbf. In some embodiments, section S_M comprises a required bending force of at least 3lbf more than the required bending force of section S_D . In some embodiments, section S_P comprises a required bending force of at least 4lbf more than the required bending force of section S_M . In some embodiments, section S_P comprises a required bending force of at least 7lbf more than the required bending force of section S_D .

[0241] **Referring now to Figs. 3A and 3B**, various views of a treatment assembly comprising a cap positioned on the distal end of an introduction device are illustrated, consistent with the present inventive concepts. Treatment device 100 and/or other components of system 10 of Figs. 3A and 3B can be of similar construction and arrangement as the similar components described in reference to Fig. 1 and otherwise herein. In some embodiments, treatment assembly 110 comprises a cap-like structure that can be positioned on a distal portion of introduction device 80, such as distal portion 8208 of shaft 82. Treatment assembly 110 can include one or more housings, **housing 114** shown, that surround one or more portions of treatment assembly 110. For example, electrode array 111 can be positioned on and/or within housing 114, for example as shown in Fig. 3A and can be configured to be advanced from within housing 114, such as to be advanced and subsequently radially expanded to contact tissue, for example as shown in Fig. 3B. Housing 114 can be positioned (e.g., removably positioned) on distal portion 8208 of shaft 82, for example when positioned by an operator of system 10 before introduction device 80 is introduced into the patient. In some embodiments, one or more conduits 101 each include a slack portion that allows electrode array 111 to extend from housing 114 (e.g., conduit

101 shown with slack in Fig. 3A, and without slack in Fig. 3B, with electrode array 111 extended). In some embodiments, conduit 101 is configured to loop around a portion of shaft 82, for example to prevent and/or limit unintended tangling of slack portions of the conduit. In some embodiments, electrode array 111 is configured to rotate about the central axis of shaft 82 while advancing, such as to unwind conduit 101, as shown in Fig. 3B.

[0242] In some embodiments, housing 114 includes a securing mechanism, **collar 1141** shown, that fixedly attaches housing 114 to shaft 82. In some embodiments, electrode array 111 can be advanced from within housing 114, as shown in Fig. 3B and described herein.

Alternatively, or additionally, housing 114 can be retracted along shaft 82 relative to electrode array 111, for example such that electrode array 111 remains in a position surrounding shaft 82 (e.g., as shown in Fig. 3A) while housing 114 is retracted, allowing expandable structure 113 to expand, as described herein. In some embodiments, collar 1141 is slidably attached to shaft 82, such that the position of housing 114 along the length of shaft 82 can be adjusted by the operator, such as via a linkage extending along shaft 82 to collar 1141 (e.g., conduit 101).

[0243] Expandable structure 113 of treatment assembly 110 can include one or more projections, such as **arms 1131** shown. Electrode array 111 can be positioned about a portion of arms 1131, for example when electrode array 111 comprises a circular array surrounding a portion of arms 1131, as shown (e.g., a furled array looped about arms 1131). In some embodiments, arms 1131 can be electrically connected to electrodes 112 of electrode array 111, such as when a first arm 1131 is electrically connected to a first set of electrodes 112, a second arm 1131 is electrically connected to a second set of electrodes 112, and an IEP can be delivered to the target tissue between the first set of electrodes 112 and the second set of electrodes 112. One or more conduits 101 can electrically connect arms 1131 to console 200 (not shown), such as electrically connect to energy delivery unit 210 of console 200. Alternatively, or additionally, a set of conductors of conduit 101 can extend to one or more sets of electrodes 112 (e.g., arms 1131 do not form a portion of the circuit connecting conduits 101 to electrode array 111).

[0244] In some embodiments, arms 1131 and electrode array 111 are configured to transition to an expanded geometry when extended from within housing 114, for example when arms 1131 are biased in an expanded state and configured to transition to an expanded geometry when transitioning from a constrained state to an unconstrained state (e.g., when not constrained by housing 114). Arms 1131 and electrode array 111 can be configured to transition to a compact geometry when retracted into housing 114 (e.g., when housing 114 applies a compacting force to arms 1131 as it is retracted). In some embodiments, system 10 is configured to perform aspiration (e.g., via working channel 8203), such as to pull tissue into contact with electrodes 112 of electrode array 111. In some embodiments, arms 1131 do not transition from a first

geometry to a second geometry (e.g., arms 1131 do not deploy radially outward), and system 10 is configured to perform aspiration and/or insufflation to cause tissue to move toward and/or away from electrode array 111, respectively.

[0245] In some embodiments, electrode array 111 comprises an array that is furled about arms 1131, such that array 111 can be unfurled to contact tissue, and/or furls to transition to a compact geometry (e.g., to move away from tissue), for example such that treatment assembly 110 can be moved (e.g., moved to a new treatment location) and/or retracted into housing 114. In some embodiments, treatment assembly 110 comprises a motor, such as when functional element 199 comprises a motor configured to provide a rotation that furls and/or unfurls array 111. For example, a functional element 199 comprising a motor can be located within an arm 1131, and the motor can be configured to furl and/or unfurl array 111. Alternatively, or additionally, one or more linkages, such as conduit 101a shown, can be fixedly attached to a portion of expandable structure 113, such as to arm 1131 as shown, and can be configured to control the advancement and/or expansion of expandable structure 113. Conduit 101a can be slidably received within a working channel 8203 and extend to the proximal end of introduction device 80 and can be actuated by an operator of system 10 to control the position and/or geometry of expandable structure 113. In some embodiments, expandable structure 113 comprises a malecot-like configuration, for example where retraction of the distal end of expandable structure 113 toward the proximal end (e.g., via retraction of a linkage such as conduit 101a) causes expansion of expandable structure 113.

[0246] In some embodiments, housing 114 can include a deployment assembly configured to control and/or assist the deployment of expandable structure 113 from housing 114. For example, a deployment assembly can comprise one or more pulleys that redirect the force applied to expandable structure 113 by one or more linkages, such as conduit 101a comprising two or more pull wires (e.g., a first pull wire configured to advance expandable structure 113 from housing 114 when pulled, and a second pull wire configured to retract expandable structure 113 into housing 114 when pulled). In some embodiments, one or more pull wires (e.g., conduits 101a) can extend along shaft 82 to housing 114 or through one or more working channels 8203. Pull wires can engage various pulleys of a deployment assembly and/or attach to different longitudinal locations of expandable structure 113 such that the pulling of the pull wire causes the intended motion (e.g., advancement and/or retraction) of expandable structure 113.

[0247] In some embodiments, an expandable array of electrodes 112 described herein, for example electrode array 111 shown, can be configured to expand to an expanded **diameter DE**. The expandable array can expand from a collapsed **diameter DC**. Electrode array 111 can comprise **length AL** comprising the distance from the proximal most to the distal most electrode

112 of array 111. In some embodiments, diameter DE comprises a diameter of at least 24cm, such as least 27cm, or 30cm. In some embodiments, diameter DE comprises a diameter of no more than 35mm, such as no more than 31mm or 27mm. In some embodiments, expandable structure 113 is configured to expand with **force FE**. Force FE can comprise a force sufficient to expand electrode array 111 into contact with surrounding tissue (e.g., to expand to a diameter up to a maximum diameter DC), such as a force of at least 0.7psi, such as at least 0.9psi or 1.3psi. Force FE can comprise a force of no more than 6psi, such as no more than 4psi or 2 psi, for example such as to prevent injury to tissue that may be caused by overexpanding electrode array 111. Diameter DC can comprise a diameter of less than 18mm, such as less than 16mm, 14mm, or 12mm. In some embodiments, diameter DC comprises a diameter that is smaller than the inner diameter of housing 114, such that electrode array 111 can be positioned within housing 114, as shown in Fig. 3A. Housing 114 can comprise an outer diameter of less than 18mm, such as less than 16mm, 14mm, or 12mm. In some embodiments, length AL comprises a length of at least 1cm, such as at least 1.5cm or 2cm.

[0248] **Referring now to Figs. 4A-4D**, various views of a treatment assembly comprising a cap positioned on the distal end of an introduction device and a rotatory electrode are illustrated, consistent with the present inventive concepts. Treatment device 100 and/or other components of system 10 of Figs. 4A-4D can be of similar construction and arrangement as the similar components described in reference to Fig. 1 and otherwise herein. Fig. 4A shows a side view of a treatment assembly 110 positioned on a distal portion of an introduction device 80. Fig. 4D shows a sectional view of a tissue treatment assembly 110 positioned on an introduction device 80, positioned within a body lumen, such as a portion of the GI tract. In some embodiments, treatment assembly 110 comprises a cap-like structure, housing 114, that can be positioned on a distal portion of an introduction device 80, such as a distal portion 8208 of shaft 82. For example, housing 114 of treatment assembly 110 can be positioned on distal portion 8208 of shaft 82 as shown. In some embodiments, housing 114 comprises a clam shell design configured to fit (e.g., “snap fit”) onto distal portion 8208. Housing 114 can be secured to shaft 82 with a clamp (e.g., a clamp with a rotatable securing mechanism configured to tighten the clamp) and/or with a compression fit, such as when housing 114 comprises a compressible O-ring configured to secure housing 114 to shaft 82 when compressed.

[0249] Electrode array 111 can be positioned on a portion of a carrier assembly that is located within a circumferential channel of housing 114. Fig. 4B shows a side view of the carrier assembly including electrode array 111, and Fig. 4C shows a sectional end view of treatment assembly 110 including electrode array 111 positioned on the carrier assembly withing

housing 114. The carrier assembly can be configured to traverse about the circumference of housing 114 within the channel (e.g., to orbit about the longitudinal axis of shaft 82), for example when the carrier assembly is connected to a conduit 101 configured to apply a rotating force (also referred to as a “torsional force”). Electrodes 112 of electrode array 111 can extend through the channel (e.g., when at least a segment of the channel extends through the wall of housing 114) to contact tissue. In some embodiments, system 10 is configured to perform aspiration and/or insufflation to cause tissue to move toward and/or away from electrode array 111 (e.g., and housing 114), respectively. In some embodiments, the distal end of conduit 101 is located within a circumferential channel of housing 114, such that a rotational force applied to conduit 101 (e.g., a rotational force applied by an operator of system 10 and/or by a functional element of system 10 comprising a motive element) causes conduit 101 and the carrier assembly (e.g., including electrode array 111) to translate circumferentially within housing 114 as described herein. Alternatively, electrode array 111 can comprise a circumferential array located within a circumferential channel of housing 114 (e.g., such that electrode array 111 does not need to be rotated to treat a circumferential portion of tissue).

[0250] **Referring now to Figs. 5A-5C**, various views of a treatment assembly comprising a pad-like electrode array are illustrated, consistent with the present inventive concepts.

Treatment device 100 and/or other components of system 10 of Figs. 5A-5C can be of similar construction and arrangement as the similar components described in reference to Fig. 1 and otherwise herein. Figs. 5A-5C show top, side, and bottom views of treatment assembly 110 positioned on a distal portion of introduction device 80.

[0251] In some embodiments, treatment assembly 110 comprises a cap-like structure that can be positioned on a distal portion of introduction device 80, such as distal portion 8208 of shaft 82. For example, as described herein, housing 114 of treatment assembly 110 can be positioned on distal portion 8208 of shaft 82 as shown. Treatment assembly 110 can attach to introduction device 80 without preventing or otherwise adversely affecting the functionality of the introduction device (e.g., without affecting steering, visualization, aspiration, and/or other functions of an endoscope or other introduction device 80 to which treatment assembly 110 may be attached). In some embodiments, housing 114 includes one or more passageways or other openings, such as **opening 1142** shown, that align with one or more channels and/or functional components of introduction device 80, such as when opening 1142 aligns with working channel 8203 of introduction device 80, for example such that the functionality of working channel 8203 is not limited when housing 114 is positioned on shaft 82 as shown. In some embodiments, introduction device 80 comprises an imaging assembly, such as when introduction device 80

comprises imaging device 60, not shown but described herein. Opening 1142 can be configured to align with an imaging assembly of introduction device 80, such as to not impede imaging from introduction device 80.

[0252] In some embodiments, housing 114 of treatment assembly 110 is configured to rotate about the longitudinal axis of introduction device 80. For example, housing 114 can be rotated to reposition electrode array 111 about a circumferential portion of the GI tract (e.g., to treat a circumferential portion of target tissue). One or more linkages, conduits 101, can be attached to housing 114 and extend proximally, along shaft 82 of introduction device 80 (as shown) and/or through working channel 8203 of introduction device 80. Conduits 101 can provide a securing force (e.g., a lateral pulling force) that prevents housing 114 from detaching from and/or otherwise extending from introduction device 80. Additionally or alternatively, conduits 101 can provide a torque or other rotational force, for example a rotational force configured to rotate housing 114 about the longitudinal axis of introduction device 80.

[0253] Electrode array 111 of treatment assembly 110 can comprise an array of two or more electrodes 112 located on one side of housing 114 as shown. For example, electrode array 111 can comprise an array of at least 50 electrodes 112, such as at least 75 or 100. Electrode array 111 can comprise a pad-like structure, such as a pad of electrodes 112 configured to be positioned in contact with tissue. In some embodiments, introduction device 80 applies a lateral force to treatment assembly 110 to force electrode array 111 to contact the tissue (e.g., make contact with target tissue of a luminal wall of the intestine). For example, distal portion 8208 can be steered by the operator of system 10 toward the target tissue in the direction of electrode array 111, such as to bring electrodes 112 into contact with target tissue. In some embodiments, after an IEP has been delivered, introduction device 80 can be steered to a neutral position (e.g., such that no lateral force is applied to treatment assembly 110), housing 114 can be rotated, and introduction device 80 can be steered toward the new direction of electrode array 111 to bring electrodes 112 into contact with additional target tissue. In some embodiments, treatment assembly 110 comprises one or more sensors, such as a pressure sensor, such as a functional element 199 configured as a pressure sensor. System 10 can monitor signals recorded from a pressure sensor positioned and otherwise configured to measure the pressure between electrode array 111 and the tissue. In some embodiments, one or more conduits 101 can comprise one or more linkages configured to articulate housing 114, for example to move electrode array 111 into contact with target tissue.

[0254] In some embodiments, one or more conduits 101 comprising one or more fluid conduits (e.g., tubes) can extend to electrode array 111, for example such that the distal end of the tubes are located on the outward face (e.g., the tissue facing surface) of electrode array 111.

For example, conduits 101 can fluidly attach to functional elements 199 of treatment assembly 110 comprising fluid ports through the bottom surface of housing 114. System 10 can be configured to perform aspiration, irrigation, and/or insufflation via one or more of the fluid conduits. In some embodiments, one or more conduits 101 comprising fluid conduits can be fluidly attached to one or more fluid conduits of introduction device 80, such as a working channel 8203 configured as a fluid conduit (e.g., a fluid conduit configured to provide aspiration, irrigation, and/or insufflation). In some embodiments, system 10 provides aspiration to cause target tissue to pull toward electrodes 112 of electrode array 111.

[0255] In some embodiments, the electrode array 111 comprises a convex outer surface (e.g., the bottom surface of housing 114 comprises a convex surface), such as a convex surface that approximates the curvature of the target tissue (e.g., the curvature of the inner wall of the duodenum). In some embodiments, electrode array 111 comprises one, two, three or more rows of electrodes 112 (e.g., rows that each extend across the width of housing 114). Each row of electrode array 111 can include one, two, three, or more pairs of electrodes 112. In some embodiments, electrode array 111 comprises a single row of electrodes 112, and housing 114 can comprise a relatively short length, such as a length approximating the width of the single row of electrodes 112. Treatment assembly 110 can be configured to treat a narrow axial section of the small intestine (e.g., configured to treat a single narrow axial section per IEP delivery), for example such that contact between electrodes 112 and the wall of the small intestine can be more accurately controlled (e.g., more accurately controlled than a longer electrode array 111 that may not lie flat on the axially variable mucosal tissue). Array 111 can comprise **length AL**, **width AW**, and a **surface area AS**. Length AL can comprise a length of at least 0.75cm, such as at least 1.0cm or 1.5cm, and/or no more than 3.0cm, such as no more than 2.5cm or 2.0cm. Width AW can comprise a width of at least 6mm, such as at least 8mm or 10mm, and/or no more than 26mm, such as no more than 23mm or 20mm. In some embodiments, surface area AS of array 111 can comprise an area of at least 4.5cm², such as at least 8cm² or 10.5cm².

[0256] In some embodiments, system 10 is configured to perform a tissue treatment procedure, such as is described herein, without the use of fluoroscopic imaging. For example, treatment assembly 110 of Figs. 5A-5C can be positioned relative to target tissue and can provide treatment to target tissue using endoscopic and/or other visualization techniques without fluoroscopic imaging (e.g., such that the tissue treatment procedure can be performed in an endoscopy suite without a fluoroscope).

[0257] In some embodiments, system 10 includes an elongate device for assisting in aspiration of a body lumen, such as when functional element 99 comprises an aspiration assist device, **aspirator 990** shown. Aspirator 990 can comprise **shaft 991** that is configured to be

slidingly received within a lumen of a device of system 10, such as working channel 8203 of introduction device 80. Aspirator 990 can include one or more lumens, such as **lumen 992**, extending through shaft 991, and one or more fluid ports, **ports 993** shown, that are positioned on a distal portion of shaft 991. The distal portion of shaft 991 can comprise a fenestrated portion of the shaft, such as a fenestrated portion comprising a set of ports 993, such as at least 5 ports, such as at least 10, 20, 30, or 50 ports. The fenestrated length of shaft 991 can comprise **length FL**. Length FL can comprise a length of at least 1cm, such as at least 2cm, 3cm, 4cm, or 5cm, and/or can comprise a length of no more than 10cm, such as no more than 9cm, 8cm, 7cm, or 6cm.

[0258] Lumen 992 can fluidly attach to a source of vacuum and/or to air (e.g., pressurized air and/or atmospheric air), such that aspirator 990 can provide aspiration, insufflation, and/or can provide a fluid pathway to atmospheric air (e.g., to relieve a negative pressure within an aspirated body lumen). Aspirator 990 can be used as an alternative method of aspiration (e.g., without endoscopic and/or other aspiration) and/or in conjunction with aspiration provided by another device of system 10, such as introduction device 80.

[0259] **Referring now to Figs. 6A-6F**, various views of a treatment assembly comprising a pad-like electrode array are illustrated, consistent with the present inventive concepts. Treatment device 100 and/or other components of system 10 of Figs. 6A-6F can be of similar construction and arrangement as the similar components described in reference to Fig. 1 and otherwise herein. Fig. 6A shows a perspective view of treatment assembly 110 positioned and oriented to slidingly receive the distal portion of introduction device 80, and Fig. 6B shows treatment assembly 110 positioned on the distal portion of introduction device 80 (e.g., after the distal portion of introduction device 80 has been inserted into treatment assembly 110, such as into a recess of housing 114, as described herein). In some embodiments, treatment assembly 110 comprises a cap-like structure that can be positioned on a distal portion of introduction device 80, such as distal portion 8208 of shaft 82. For example, as described herein, housing 114 of treatment assembly 110 can be positioned on distal portion 8208 of shaft 82 as shown in Fig. 6B. Treatment assembly 110 can attach to introduction device 80 without preventing or otherwise adversely affecting the functionality of the introduction device (e.g., without affecting steering, visualization, aspiration, or other functions of an endoscope or other introduction device treatment assembly 110 may be attached to). In some embodiments, housing 114 includes an opening (e.g., a window), such as opening 1142 shown, that is sized and positioned to allow unimpeded visualization from introduction device 80, for example when introduction

device 80 comprises a side viewing endoscope, and housing 114 includes a window allowing for side viewing from introduction device 80 through housing 114.

[0260] In some embodiments, treatment assembly 110 is attached (e.g., via a clinician or other operator of system 10) to introduction device 80 prior to insertion into the patient. In some embodiments, one or more conduits 101 of treatment device 100 extend from treatment assembly 110, through working channel 8203 to the proximal end of introduction device 80. Alternatively, or additionally, one or more shafts of treatment device 100 (e.g., shaft 102, not shown but described herein, that can comprise one or more lumens therethrough) can extend proximally from housing 114, such as through working channel 8203 and/or along shaft 82 of introduction device 80. Introduction device 80 can be used to navigate treatment assembly 110 to target tissue, such as when introduction device 80 and treatment assembly 110 are advanced through the mouth and into the GI tract simultaneously.

[0261] Figs. 6C and 6D show sectional end views of a portion of treatment assembly 110. Treatment assembly 110 can include an expandable assembly configured to advance at least a portion of electrode array 111 towards target tissue. For example, housing 114 can include an expandable portion, such as expandable structure 113 shown. Expandable structure 113 can be positioned between a first portion of housing 114, **fixed portion 114a**, and a second portion of housing 114, **extending portion 114b**, each shown. Expandable structure 113 of treatment assembly 110 can include an expansion mechanism, such as an expansion mechanism configured to laterally extend portion 114b, including electrode array 111, from portion 114a of housing 114, as shown in Fig. 6D. In some embodiments, when in a compacted geometry, as shown in Fig. 6C, treatment assembly 110 can comprise a major diameter DC of approximately 10mm (e.g., the diameter of housing 114 with electrode array 111 positioned on the side of housing 114, as shown). When in an expanded geometry, treatment assembly 110 can comprise a major diameter DE of up to approximately 24mm (e.g., the diameter of housing 114 and electrode array 111, when expandable structure 113 is fully expanded). Expandable structure 113 can comprise an expandable chamber, **bladder 1132** shown, such as a chamber that is configured to be expanded and/or contracted via filling and/or removing, respectively, fluid from the chamber. In some embodiments, expandable structure 113 is biased in a compacted geometry, for example when bladder 1132 comprises a biased configuration, such as a compliant balloon-type configuration that expands to extend portion 114b (e.g., including electrode array 111) from portion 114a of housing 114 when a pressurized fluid is delivered to bladder 1132. Bladder 1132 can be configured to contract when the pressurized fluid is no longer pressurized (e.g., when a source of pressure, such as a pump, is disengaged, bladder 1132 can contract forcing the fluid out of bladder 1132). In some embodiments, bladder 1132 can be deflated,

such as when system 10 is configured to remove the fluid from bladder 1132 (e.g., via a pump or a negative pressure source fluidly attached to bladder 1132). In some embodiments, system 10 is configured to control the pressure of fluid within bladder 1132, such as to control the pressure exerted on tissue by electrode array 111 (e.g., to control the contact pressure between electrode array 111 and tissue). In some embodiments, the pressure of fluid within bladder 1132 is limited to a pressure of no more than 6psi, such as no more than 4psi or 2psi. Additionally, or alternatively, the maximum pressure that can be exerted by electrode array 111 on tissue (or the maximum pressure that can be exerted by housing portion 114a on tissue opposite electrode array 111, for example when treatment assembly 110 is positioned within a body lumen, as described herein) can be limited to a pressure of no more than 6psi, such as no more than 4psi or 2psi (e.g., the pressure within bladder 1132 is limited such that the maximum pressure exerted by electrode array 111 is limited).

[0262] In some embodiments, expandable structure 113 comprises a non-inflatable expansion mechanism, such as an elastic mechanism or non-biased mechanism, such as an electromechanically powered or user powered expansion mechanism, or combinations of these. For example, expansion mechanism 113 can comprise an elastically collapsible foam structure (e.g., biased in an expanded geometry as shown in Fig. 6D). In some embodiments, a linkage, such as conduit 101, can be configured to retract housing portion 114b towards portion 114a, to the configuration shown in Fig. 6C. The linkage can be released to allow the foam structure to elastically expand to deploy electrode array 111 as described herein. In other embodiments, expandable structure 113 can comprise a scaffold-like expansion mechanism, for example a mechanism comprising a series of connected parallelograms with hinged pivot-point intersections (e.g., a scissor lift-type mechanism) that can be manually and/or electromechanically actuated, such as via a linkage comprising a torque transfer linkage. The various mechanisms described herein can each be configured to limit the force exerted by treatment assembly 110 on tissue, such as to the limits described hereabove.

[0263] In some embodiments, treatment assembly 110 comprises two, three, or more expandable mechanisms, for example two, three, or more mechanisms similar to expandable structure 113 and extendable portion 114b shown, where the multiple expandable structures 113 are distributed radially about the axis of treatment assembly 110 (e.g., about the longitudinal axis of introduction device 80) and/or are distributed longitudinally, such that multiple target tissue locations that are radially and/or longitudinally distributed (e.g., within a lumen of the patient, such as within a portion of the GI tract) can be treated by treatment assembly 110 without repositioning the assembly. In some embodiments, the multiple expandable structures 113 are independently expandable, such that one, two, or more, of the two, three, or more mechanisms

can each be expanded and/or collapsed independently (e.g., simultaneously, or not). Each expandable structure 113 can comprise an electrode array 111, such as an independently activatable (e.g., activatable to deliver therapy to tissue, such as IEP therapy described herein) electrode array 111. Alternatively, or additionally, one or more expandable mechanisms may not include an electrode array 111, such as when an expandable structure 113 is configured to expand to provide a balancing force to housing 114 (e.g., to keep housing 114 centered within a lumen during treatment). For example, two expandable structures 113 can be oriented 180° apart (e.g., about the longitudinal axis of housing 114), such that a first expandable structure 113 comprising electrode array 111 can be extended toward target tissue, and a second expandable structure 113 not comprising electrode array 111 can be extended in the opposite direction, providing an opposing force to tissue (e.g., luminal tissue) opposite the target tissue. Fig. 6E shows an end sectional view of an example of treatment assembly 110 comprising two expandable structures 113.

[0264] Fig. 6F shows a sectional view of a portion of a treatment assembly 110. Treatment assembly 110 can comprise electrode array 111 located on a portion of housing 114. In some embodiments, housing 114 includes one or more openings, **ports 1143** shown, that are configured to engage with target tissue (e.g., when a vacuum, for example as provided by console 200, not shown, is applied to the inside of housing 114, such as via a working channel 8203 comprising an aspiration tube). In some embodiments, housing 114 comprises a multi-layer construction, such as, for example, when housing 114 comprises outer layer 1144a, distribution layer 1144b, central layer 1144c, and inner layer 1144d, as shown in Fig. 6F. Variations of this multi-layer concept shown should be considered within the scope of the present inventive concepts. In the example shown, outer layer 1144a can include ports 1143 shown. Central layer 1144c can include one or more openings, **channels 1145** shown, that fluidly attach a space, **chamber 1146** that is formed between central layer 1144c and inner layer 1144d, to distribution layer 1144b. Distribution layer 1144b can be configured to fluidly attach chambers 1146 to ports 1143. In some embodiments, housing 114 comprises a greater quantity of ports 1143 than channels 1145, for example at least two, three, or four times as many ports 1143 as channels 1145. Distribution layer 1144b can provide a fluid connection between the mismatched number of ports 1143 and channels 1145. In some embodiments, distribution layer 1144b comprises a porous membrane, such as a porous membrane that is configured to allow air or other gas to pass through ports 1143 but prevent tissue from entering channels 1145 and/or chamber 1146. In some embodiments, electrodes 112 of electrode array 111 are located between ports 1143, such that tissue (e.g., target tissue) can be drawn toward the outer surface of layer 1144a (e.g., by aspiration applied by system 10) around electrodes 112 (e.g., such that target

tissue is held against electrodes 112 by the applied vacuum force). In some embodiments, housing 114 comprises one or more lumens, such as **lumen 1147**, a portion of which is shown extending through inner layer 1144d, that is configured to fluidly attach to a source of vacuum, such as a conduit 101 that is attached to a source of vacuum, to chamber 1146.

[0265] In some embodiments, electrode array 111 is sized and/or positioned to treat a portion of target tissue that is visualizable by introduction device 80. For example, a visualization assembly of introduction device 80 (e.g., when imaging device 60, not shown but described herein, is integral to introduction device 80) can comprise a field of view (e.g., at least a 90° or at least a 110° field of view), and electrode array 111 can be sized and/or positioned on housing 114 relative to the field of view of introduction device 80 to treat the target tissue within the field of view. Treatment assembly 110 and/or introduction device 80 can be rotated to treat a greater portion of target tissue (e.g., target tissue at a single circumferential location), such as a relatively full circumferential (e.g., 270° to 360°) portion of target tissue at an axial location in the small intestine.

[0266] **Referring now to Figs. 7A-7D**, various views of a treatment assembly comprising a deployable electrode positioned on a needle are illustrated, consistent with the present inventive concepts. Treatment device 100 and/or other components of system 10 of Figs. 7A-7D can be of similar construction and arrangement as the similar components described in reference to Fig. 1 and otherwise herein. Fig. 7A shows a cross-sectional view of a needle deployment mechanism in an undeployed position (left) where a needle comprising an electrode is in a retracted position, and a deployed position (right) where the needle is in an advanced position. Fig. 7B shows a side view of treatment assembly 110 comprising an electrode located on, and/or comprising, a deployable needle, such as a needle that is deployed with a mechanism similar to the mechanism shown in Fig. 7A. Electrode 112 can comprise an electrode that is configured to be inserted into tissue, such as an electrode that is positioned on and/or integral to a deployable needle, **needle 1121** shown. In some embodiments, needle 1121 is slidably positioned within a portion of housing 114. Housing 114 can comprise a ramp-like shape that is configured to change the advancement trajectory of needle 1121, for example to redirect longitudinal advancement of needle 1121 to a radial direction, as shown in Fig. 7A.

[0267] In some embodiments, treatment assembly 110 is configured to deliver therapy, such as an IEP (e.g., one, two, or more deliveries of irreversible electroporation energy), between two electrodes 112, where at least one of the two electrodes 112 is located on and/or comprises needle 1121 that has been inserted proximate to the target tissue (e.g., needle 1121 is configured to be inserted into tissue prior to delivery of an IEP). For example, electrode array 111 can

include a first electrode, electrode 112a located on a distal portion of a needle 1121 configured to be inserted through the mucosal tissue and into submucosal tissue (e.g., such that electrode 112a is positioned within the submucosal tissue). In some embodiments, electrode array 111 includes a second electrode, such as electrode 112b shown, that is located on expandable structure 113. Expandable structure 113 can be configured to hold the second electrode against the target tissue. In some embodiments, treatment assembly 110 comprises two, three, or more needles 1121, for example multiple deployable needles 1121 each including an electrode 112a. Electrode 112a can be integral to needle 1121, such as when needle 1121 comprises a conductive material. In some embodiments, needle 1121 includes an insulative coating, such as a coating that covers a proximal portion of the needle (e.g., when the distal portion of needle 1121 remains exposed to function as electrode 112a that can electrically contact the tissue).

[0268] In some embodiments, expandable structure 113 comprises a balloon or other expandable structure, such as **balloon 1133** shown. In some embodiments, balloon 1133 comprises a contiguous outer surface (e.g., the surface of balloon 1133 is configured to oppose a contiguous portion of tissue, such as a full circumferential axial segment of luminal tissue). In some embodiments, second electrode 112b comprises a coating on the outer surface of balloon 1133, for example such that electrode 112a contacts a circumferential portion of tissue (e.g., a circumferential portion of an axial segment of duodenal and/or other tissue of the gastrointestinal tract) when balloon 1133 is expanded to contact a circumferential portion of tissue, for example as shown in Figs. 7C and 7D.

[0269] In some embodiments, system 10 is configured to inject a conductive material (e.g., a conductive fluid such as a highly concentrated saline solution, such as agent 45) into the submucosa (e.g., via needle 1121 on which electrode 112a is located), such that electrode 112a and the injected conductive material, agent 45, collectively form an electrode with a geometry approximating a hollow tube, or at least a portion of a hollow tube (e.g., depending on the extent to which the conductive fluid permeates the submucosa). Since electrode 112b can also comprise a geometry approximating a hollow tube (e.g., when electrode 112b comprises a coating of balloon 1133), an IEP pulse can be delivered by treatment device 100 between the two (concentric) hollow tube electrodes, creating an electric field that is limited to the mucosal tissue between the two electrodes (e.g., to effectively ablate the mucosal tissue and avoid damage to non-target tissue), for example as shown in Figs. 7C and 7D. Figs. 7C and 7D show a sectional end view and a sectional side view, respectively, of a treatment assembly 110 and target tissue positioned between two concentric hollow-tube-shaped electrodes, such as an electrode 112a comprising agent 45 that has been injected into the submucosal tissue, and electrode 112b comprising a coating on balloon 1133.

[0270] In some embodiments, in addition to and/or alternatively to one or more advanceable needles 1121, treatment assembly 110 can comprise an array of one or more fixed needles 1121 (e.g., fixed needles that extend laterally toward tissue from the center of treatment assembly 110), where needles 1121 can be configured to puncture tissue when aspiration is applied by system 10 (e.g., aspiration that causes tissue to be drawn onto needles 1121). In some embodiments, the one or more fixed needles 1121 are located within a port or other protective portion of housing 114 that prevents the needles from unintentionally puncturing or otherwise damaging the tissue (e.g., while treatment assembly 110 is translated through the patient to target tissue). In some embodiments, a vacuum is applied to the ports to cause target tissue to be drawn toward the needles (e.g., such that the needles puncture the target tissue within the ports when the vacuum is applied to the ports).

[0271] In some embodiments, one or more needles 1121 (e.g., one or more needles 1121 including an electrode 112) of treatment assembly 110 are positioned radially about expandable structure 113. For example, treatment assembly 110 can include a radial array of needles 1121 including one, two, three, or more rows of radial rings of needles, for example, where each ring includes two, three, four, or more circumferential needles, for example as shown in Fig. 10B.

[0272] **Referring now to Figs. 8A-8C**, side sectional anatomic views and an end sectional anatomic view of a treatment assembly comprising a folded expandable structure is illustrated, consistent with the present inventive concepts. Treatment device 100 and/or other components of system 10 of Figs. 8A-8C can be of similar construction and arrangement as the similar components described in reference to Fig. 1 and otherwise herein. Figs. 8A and 8B show side sectional views of treatment assembly 110 including an electrode deployment mechanism (e.g., expandable structure 113) comprising an accordion-like structure. Fig. 8C shows an end sectional view of treatment assembly 110. In Figs. 8A-8C, treatment assembly 110 is shown positioned within a segment of luminal tissue, such as a segment of the GI tract to be treated by treatment device 100, as described herein. Figs. 8A and 8C show expandable structure 113 in a radially contracted geometry (e.g., a linearly elongated geometry). Fig. 8B shows expandable structure 113 is a radially expanded geometry (e.g., a linearly contracted geometry), with electrodes 112 in contact with the tissue. Expandable structure 113 can be positioned on a distal portion of shaft 82 of introduction device 80, as shown. In some embodiments, treatment assembly 110 is configured to be inserted into the patient without introduction device 80, such as when expandable structure 113 is positioned on the distal end of a shaft of treatment device 100, such as shaft 102, not shown, but described herein. The various embodiments of treatment assembly 110 described herein that are described as being positioned on and/or otherwise

function in combination with an introduction device 80 should be understood to also comprise use without an introduction device (e.g., without an endoscope). For example, treatment device 100 can comprise a shaft that can be translated within the GI tract of the patient (e.g., with or without a separate introduction device). Similarly, various embodiments of treatment assembly 110 described herein that are described as being positioned on a shaft of treatment device 100 (e.g., shaft 102) should be understood to also include the treatment assembly 110 being positioned on and/or otherwise functioning with a body introduction device, such as introduction device 80.

[0273] In some embodiments, expandable structure 113 of treatment assembly 110 can comprise a folding, accordion-like structure configured to expand and contract when the ends (e.g., proximal and distal ends) of expandable structure 113 are brought together and/or moved apart, respectively. For example, to expand expandable structure 113 (e.g., to transition to a radially expanded geometry), the proximal end of expandable structure 113 can be advanced toward the distal end of expandable structure 113, such as when the distal end is maintained in a fixed position relative to the proximal end. In some embodiments, the distal end can be fixedly attached to introduction device 80 with a temporary attachment mechanism, such as collar 1141 shown. Expandable structure 113 can be transitioned to a collapsed geometry by retracting the proximal end relative to the fixed distal end. Alternatively, or additionally, the proximal end of expandable structure 113 can be maintained in a fixed position relative to the distal end, and the distal end can be advanced and/or retracted to collapse and/or expand, respectively, expandable structure 113.

[0274] In some embodiments, conduit 101 comprises a linkage that is configured to fixedly attach to an end of expandable structure 113 (e.g., the unfixed end, such as the proximal end when the distal end is fixed to introduction device 80 via collar 1141, as shown). Conduit 101 can extend through working channel 8203 and can be advanced and/or retracted to collapse and/or expand, respectively, expandable structure 113. In some embodiments, expandable structure 113 is biased in the elongated, radially collapsed configuration shown in Fig. 8A. Conduit 101 can be configured to “pull” the proximal end of expandable structure 113 distally (e.g., to pull against a biasing force, such as an elastic biasing force), such as to expand the structure. Conduit 101 can be released (e.g., allowed to extend from working channel 8203) to allow the biased structure to return to its resting, extended/collapsed geometry. In some embodiments, as shown only in Fig. 8B, treatment assembly 110 includes a second collar, collar 1141a, that fixedly attaches to a proximal portion of shaft 82 of introduction device 80, and treatment assembly 110 can further include a biasing member, **linkage 1134** shown, that

provides a biasing force to bias expandable structure 113 (e.g., to bias the assembly in the extended/collapsed geometry of Fig. 8A).

[0275] Electrodes 112 can be positioned on the outermost portions of the folds of expandable structure 113, such that when expandable structure 113 is configured in an expanded geometry, electrodes 112 are positioned in contact with the tissue. In some embodiments, expandable structure 113 comprises a cylindrical structure (e.g., an “accordion lantern” structure), where electrode array 111 can comprise one, two, or more, full and/or partial circumferential rings of electrodes 112 positioned on the expanding portions of the accordion structure, for example as shown in Fig. 8C. In Fig. 8C, expandable structure 113 is shown in a collapsed geometry.

[0276] **Referring now to Figs. 9A and 9B**, side views of various embodiments of a treatment assembly comprising an expandable balloon and an array of electrodes are illustrated, consistent with the present inventive concepts. Treatment device 100 and/or other components of system 10 of Figs. 9A and 9B can be of similar construction and arrangement as the similar components described in reference to Fig. 1 and otherwise herein. Fig. 9A shows a side view of a treatment assembly 110 with an expandable structure 113 including an expandable balloon, balloon 1133. Balloon 1133 can be located on distal portion 1028 of shaft 102. Shaft 102 can include one, two, or more lumens 1023, such as one or more lumens through which one or more conduits 101 extend, the one or more lumens 1023 extending proximally from treatment assembly 110. Lumens 1023 can comprise one or more guidewire lumens, and/or one or more fluid lumens configured to provide fluid to inflate and/or deflate balloon 1133.

[0277] Electrode array 111 can comprise one or more wires or other electrical conduits, **traces 1111** shown, that each electrically connect one or more of electrodes 112 to conduit 101, such as to connect electrodes 112 to console 200, not shown but described herein. Conduits 101 and/or traces 1111 can each comprise a set of individual conductors (e.g., individually electrically isolated wires) such that each electrode 112 and/or sets of electrodes 112 are individually addressable by console 200. In some embodiments, multiplexing circuitry, such as **circuitry 1112** shown in Fig. 9B, is located proximate electrode array 111 (e.g., at the distal portion of treatment device 100), such that conduit 101 can comprise fewer individual conductors than the number of individually addressable sets (e.g., sets of one or more) of electrodes 112. Additionally, or alternatively, each electrode 112 can comprise a “smart electrode”, such as an electrode comprising a control circuit that is configured to receive a set of signals from console 200 (e.g., from one or more shared conductors configured to provide the set

of signals to two or more smart electrodes), and to only allow signals intended for delivery from the smart electrode to be delivered from that electrode.

[0278] Electrode array 111 can comprise a “finger-like” pattern, as shown in Fig. 9A, of traces 1111 connecting sets of electrodes 112. In some embodiments, electrode array 111 comprises a flex circuit or other flexible structure of conductive elements connecting electrodes 112 (e.g., traces 1111 comprise traces of a flex circuit positioned on, within the walls of, and/or within balloon 1133). In some embodiments, electrode array 111 comprises two sets of electrodes 112, a first set of electrodes 112a (e.g., a set of electrodes 112 that can be configured as cathodes) and a second set of electrodes 112b (e.g. a set of electrodes 112 that can be configured as anodes). An IEP can be delivered by system 10 between the two sets of electrodes 112. In some embodiments, electrodes 112 configured as cathodes and anodes alternate around the circumference of expandable structure 113, as shown in Fig. 9A. In some embodiments, the first set of electrodes 112 (electrodes 112a) and the second set of electrodes 112 (electrodes 112b) are each connected to a common trace, such as a first and second “ring” trace, rings 1113a and 1113b shown, respectively, where each ring trace 1113 is connected to a conduit 101 (e.g., such that each of the first set of electrodes 112a is electrically coupled to a first conduit 101a via ring 1113a, and each of the second set of electrodes 112b is electrically coupled to a second conduit 101b via ring 1113b).

[0279] The finger-like pattern of electrode array 111 shown in Fig. 9A can be constructed and arranged to allow expandable structure 113 (e.g., an expandable structure comprising balloon 1133) to collapse (e.g., deflate), for example by folding in on itself, by folding in an accordion-like manner, and/or by folding in a “puzzle-piece” manner. In some embodiments, for example as shown in Fig. 9B, electrodes 112 can be positioned in a spiral-like pattern on balloon 1133, such as when traces 1111 spiral over at least a portion of the length of expandable structure 113. In some embodiments, conduit 101 electrically connects circuitry 1112 to console 200, and circuitry 1112 operably connects to each electrode 112, such as via traces 1111 shown. In some embodiments, traces 1111 comprise one, two, or more individual traces extending from circuitry 1112 to each electrode 112, or to each set of two or more individually addressable electrodes 112. Electrode arrays 111 of Figs. 9A and/or 9B can each comprise two or more individually addressable sets of one or more electrodes 112 (e.g., at least a cathode and at least an anode electrode for delivery of an IEP). For example, array 111 can comprise at least two sets of electrodes, such as at least three, four, five, or six sets of individually addressable electrodes. Each set of individually addressable electrodes 112 can comprise at least one electrode 112, such as at least 2, 10, 20, or 40 electrodes 112.

[0280] Referring now to Figs. 10A-10E, various views of a treatment assembly comprising tissue capture ports are illustrated, consistent with the present inventive concepts. Treatment device 100 and/or other components of system 10 of Figs. 10A-10E can be of similar construction and arrangement as the similar components described in reference to Fig. 1 and otherwise herein. Fig. 10A shows a side sectional view of a housing 114 of a treatment assembly 110 comprising a tissue capture port, **capture port 1148**. For example, treatment assembly 110 can include one or more housings, such as one or more housings 114, each constructed and arranged to capture a portion of tissue within a capture port 1148 to be treated by system 10 (e.g., at least a portion of target tissue and/or tissue proximate target tissue). Fig. 10B shows a side view of a treatment assembly 110 including multiple housings 114 located on an expandable structure 113 that are arranged in a circumferential pattern. For example, treatment assembly 110 can include at least 3 housings 114, such as at least 6, at least 12, or at least 18, such as 20 housings 114 arranged circumferentially about expandable structure 113. In some embodiments, capture ports 1148 are aligned laterally, as shown, such as to capture and treat target tissue in a relatively similar longitudinal position within the lumen of the small intestine (e.g., the tissue to be treated in a single IEP delivery treatment step, or without repositioning treatment assembly 110, is longitudinally aligned). Alternatively, capture ports 1148 can be longitudinally staggered (e.g., housings 114 can comprise varying configurations and/or housings 114 can be longitudinally staggered on expandable structure 113), such that, for example in a single IEP delivery treatment step, target tissue from a longer longitudinal portion of the small intestine can be treated. In some embodiments, expandable structure 113 comprises a balloon, such as balloon 1133 configured to inflate to bring housing 114 into contact with target tissue of a luminal wall. Expandable structure 113 can be located on distal portion 1028 of shaft 102. Shaft 102 can include one or more “breakout shafts” (e.g., shaft 102 can separate into multiple shafts) each breakout shaft comprising one or more lumens 1023, and each breakout shaft extending from a central portion of shaft 102 to a housing 114, as shown.

[0281] Each housing 114 can include an opening into which a portion of target tissue can be received, such as capture port 1148 described herein. Each capture port 1148 can be fluidly attached to a vacuum lumen (e.g., a lumen 1023 of shaft 102 that extends to housing 114), such that when vacuum is applied to capture port 1148, tissue is pulled into the port (e.g., mucosal tissue comprising target tissue to be treated by system 10 is pulled into the port). In some embodiments, capture port 1148 is constructed (e.g., sized) and arranged to allow at least mucosal tissue into the opening. In these embodiments, capture port 1148 can also allow a certain amount of submucosal tissue to enter the opening (e.g., to capture a full layer of mucosal tissue), but prevent muscularis tissue or other non-target tissue to be pulled into the opening by

the applied vacuum. Capture port 1148 can comprise **width WCP**, **length LCP**, and **depth DCP**. Width WCP can comprise width of at least 1.5mm, such as at least 2.0mm or 2.5mm, and/or a width of no more than 3.0mm, such as no more than 2.5mm or 2mm. Length LCP can comprise length of at least 0.5cm, such as at least 0.7cm, 1cm, 1.5cm, or 2cm, and/or a length of no more than 5cm, such as no more than 4cm, 3cm, or 2cm. Depth DCP can comprise a depth of at least 1.5mm, such as at least 2.0mm, 2.5mm, or 3mm, and/or a depth of no more than 8mm, such as no more than 7mm, 6mm, or 5mm.

[0282] In some embodiments, two or more electrodes 112 of electrode array 111 are located within each capture port 1148. For example, a first electrode 112a can be located on the inner-most wall (e.g., opposite the opening) of capture port 1148, such that when target tissue is pulled into the port, contact is made with the first electrode 112a. In some embodiments, a second electrode 112b can be located on a translating element (e.g., a translatable needle), such as needle 1121, that can be configured to be advanced into capture port 1148 after the tissue has entered the opening, for example such that the second electrode 112b is positioned within the tissue (e.g., within the submucosal tissue) after the translating element has been advanced, as shown in Fig. 10A. Alternatively, or additionally, a second electrode 112b (and/or additional electrodes 112n) can be located proximate the edges of the opening, for example when a second electrode 112b comprises a ring electrode through which tissue is pulled when the tissue is pulled into capture port 1148 (e.g., the opening is lined with a conductive ring configured as an electrode 112b). In some embodiments, electrodes 112 are located on the inward sides of capture port 1148, such that tissue within each port is positioned between pairs of first and second electrodes 112. For example, Fig. 10C shows an end sectional view of target tissue positioned within capture port 1148 between a first and second electrode 112. Fig. 10D and Fig. 10E show top views of a capture port 1148 with a single pair of first and second electrodes 112, and multiple pairs of first and second electrodes 112, respectively, positioned within the port.

[0283] Treatment assembly 110 can “deliver an IEP” (e.g., deliver one, two, or more irreversible electroporation energy deliveries) to target tissue while the target tissue is positioned within capture port 1148 as described herein. For example, treatment assembly 110 can be positioned relative to a first portion of target tissue, and expandable structure 113 can be expanded to bring housings 114 into contact with the target tissue. Vacuum can be applied to capture ports 1148 (e.g., via console 200, not shown) such that target tissue is pulled into the ports (e.g., such that the target tissue is in contact with the first electrodes 112a, each positioned on the inner-most wall of capture port 1148). In some embodiments, a translating element of treatment device 100 and/or introduction device 80 is advanced, such as needle 1121, positioning second electrodes 112b in contact with the target tissue that is positioned within

capture port 1148. System 10 can then deliver an IEP treatment to the captured target tissue, needle 1121 can be retracted, and the vacuum can be removed, thus releasing the target tissue from capture port 1148. In some embodiments, treatment assembly 110 is then repositioned (e.g., rotated and/or translated proximally or distally within the small intestine) to capture and treat an additional axial segment of target tissue.

[0284] In some embodiments, housings 114 do not comprise openings for target tissue to be drawn into, but housings 114 do include vacuum openings configured to pull tissue onto the outer surface of the housing, for example when electrodes 112 are positioned on the outer surface of housing 114, such as when each electrode 112 is positioned between two vacuum openings configured to hold the tissue in contact with the electrode 112.

[0285] **Referring now to Figs. 11A-11C**, various views of a treatment assembly comprising a vacuum channel are illustrated, consistent with the present inventive concepts. Treatment device 100 and/or other components of system 10 of Figs. 11A-11C can be of similar construction and arrangement as the similar components described in reference to Fig. 1 and otherwise herein. Fig. 11A shows a side view of a treatment assembly 110 comprising a housing 114 constructed and arranged to capture tissue within an elongate channel, **channel 1149**.

Expandable structure 113 can comprise one, two, three or more flexible members, arms 1135 shown, each configured to bow outward, as shown, to contact luminal tissue of the small intestine. In some embodiments, arms 1135 comprise at least a portion of housing 114, such as when each channel 1149 extends along at least a portion of the length of an arm 1135, as shown. In some embodiments a conduit 101 comprises a linkage that is attached to the proximal end of expandable structure 113. Conduit 101 can be retracted (e.g., manually by an operator and/or automatically by a robotic controller of system 10) to position arms 1135 into an outwardly bowed geometry and/or advanced to compact expandable structure 113 (e.g., to straighten arms 1135). In some embodiments, arms 1135 can comprise a biased geometry, such as a bias in the outwardly bowed geometry shown in Fig. 11A, and conduit 101 can be advanced to compact expandable structure 113, or vice versa.

[0286] In some embodiments, each channel 1149 comprises a c-shaped geometry, where the opening in the channel is outward facing toward the tissue. Within each channel 1149, one or more pairs of electrodes 112 of electrode array 111 can be positioned on either side of the channel 1149 (e.g., each pair comprising an electrode 112 on opposite sides). Fig. 11B shows a magnified view of electrodes 112 within the channel 1149 of housing 114. Each channel 1149 can be configured to capture a portion of target tissue (e.g. mucosal tissue) to be treated within the channel between the pairs of electrodes 112, such that an IEP treatment can be delivered to

the tissue within the channel. For example, as shown in Fig. 11C, a sectional view of tissue is shown positioned within channel 1149 of a housing 114. Each channel 1149 can be fluidly attached to a vacuum source that pulls (i.e. draws) tissue into the channel. In some embodiments, each channel 1149 has a series of vacuum openings along the innermost surface of the channel (e.g., openings in a vacuum lumen extending through the inner wall of housing 114) such that vacuum applied to the openings draws tissue into the channel along the length of the channel (e.g. along a majority or other portion of the length of the channel). In some embodiments, channels 1149 of housing 114 are constructed and arranged to allow at least mucosal tissue (e.g. at least the full depth of mucosal tissue) into the channel, while allowing some portion of the submucosal tissue layer into the channel but avoiding capture of muscularis tissue or other non-target tissue to be drawn into the channel by the applied vacuum. In some embodiments, the depth of each channel 1149 of housing 114 is constructed and arranged to set the depth of the treatment. For example, the width and/or depth of the channel can determine the depth of the treatment delivered to the target tissue (e.g., by limiting the amount of target tissue that can be drawn into the channel during energy delivery).

[0287] In some embodiments, channels 1149 of housing 114 comprise a “pac-man-like” geometry configured to grasp a portion of target tissue. For example, arms 1135 can be configured to radially expand, as described herein, to contact tissue. In some embodiments, channels 1149 of housing 114 are configured to expand (e.g., to open laterally) when expandable structure 113 is fully expanded (e.g., such that channels 1149 are relatively open and the target tissue is forced into the channels), and to close (e.g., to revert to the biased c-shaped configuration shown in Fig. 11C) when expandable structure 113 is at least partially collapsed from the most expanded geometry. For example, after expandable structure 113 has been expanded (e.g., fully expanded) and target tissue is positioned within the open channels 1149 of housing 114, expandable structure 113 can be at least partially collapsed, and channels 1149 of housings 114 can close (e.g. partially close) around the captured tissue, such that IEP therapy can be delivered to the target tissue within channels 1149.

[0288] **Referring now to Figs. 12A and 12B**, side views of a treatment assembly with an expandable structure comprising one or more expandable petals are illustrated, consistent with the present inventive concepts. Treatment device 100 and/or other components of system 10 of Figs. 12A and 12B can be of similar construction and arrangement as the similar components described in reference to Fig. 1 and otherwise herein. Fig. 12A shows a side view of a treatment assembly 110 including expandable structure 113. Expandable structure 113 can include one or more flexible sheets, **petals 1136** shown. Petals 1136 can be configured to transition between an

undeployed, back-swept geometry shown in Fig. 12A and an expanded, forward-swept geometry shown in Fig. 12B. In some embodiments, petals 1136 are located on the distal portion of a shaft of treatment device 100, such as shaft 102 (not shown). Alternatively, or additionally, as shown, treatment assembly 110 can be configured to be attached to the distal portion of an introduction device, such as to the distal end of shaft 82 of introduction device 80, as shown. Petals 1136 can be positioned extending proximally along shaft 82 from a distal connection point (e.g., in a back-swept geometry), such as by collar 1141 that is configured to removably attach treatment assembly 110 to shaft 82, as shown in Fig. 12A. In some embodiments, petals 1136 can be maintained in the back-swept geometry shown in Fig. 12A while treatment assembly 110 is tracked distally through the small intestine, such as when petals 1136 are biased in the back-swept geometry, when forward (distal) motion of shaft 82 relative to tissue causes the tissue to apply a force to maintain the back-swept geometry, and/or when a retention mechanism, such as collar 1141a shown, surrounds a portion of petals 1136 and shaft 82 to maintain the geometry. In some embodiments, treatment assembly 110 is configured to be advanced to a most distal treatment location, and treatment assembly 110 can be retracted, such that petals 1136 of expandable structure 113 open (e.g., open and flip relative to shaft 102) to the forward-swept geometry shown in Fig. 12B. Electrodes 112 of electrode array 111 can be located on the underside of petals 1136, such that electrodes 112 are positioned in contact with the tissue when petals 1136 are arranged in the expanded, forward swept geometry shown. In some embodiments, petals 1136 are biased in an expanded geometry, such that when treatment assembly 110 is retracted within the small intestine, interference (e.g., contact) between petals 1136 and the tissue causes the inversion of the petals shown. In some embodiments, before retracting treatment assembly 110, collar 1141a can be removed from petals 1136, for example when a linkage, such as conduit 101a, is used to translate collar 1141a (e.g., to translate collar 1141a distally to allow petals 1136 to expand).

[0289] Treatment assembly 110 can be configured to treat intestinal and/or other luminal tissue comprising a luminal diameter of up to 35mm. Expandable structure 113 can be configured to expand to an expanded diameter of at least 5mm, such as up to 30mm, for example when the petals comprise a length of at least 10mm, such as at least 20mm, at least 30mm, or no more than 60mm. In some embodiments, petals 1136 of expandable structure 113 comprise a width of at least 5mm, such as a width of no more than 50mm. In some embodiments, expandable structure 113 comprises two or more petals 1136, such as at least three, four, or five petals 1136 that are radially positioned about a shaft, such as shaft 82 and/or shaft 102.

[0290] **Referring now to Figs. 13A-13C**, various views of an embodiment of a treatment element comprising an “offset spatula” configuration are illustrated, consistent with the present inventive concepts. Treatment device 100 and/or other components of system 10 of Figs. 13A-13C can be of similar construction and arrangement as the similar components described in reference to Fig. 1 and otherwise herein. Fig. 13A shows a side view of a treatment device 100 comprising an offset geometry, such that electrode array 111 is offset from the central axis of shaft 102 and/or the central axis of shaft 82 of introduction device 80. Treatment device 100 can be configured to be advanced through a working channel of introduction device 80, such as working channel 8203. Treatment device 100 can be configured to transition between a compact geometry that is configured to allow treatment device 100 to be slidably received within working channel 8203 (e.g., as shown in Fig. 13C), and an expanded and/or offset geometry where electrode array 111 is positioned proximate target tissue, as shown in Figs. 13A and 13B.

[0291] Treatment device 100 can include expandable structure 113 that is positioned on distal portion 1028 of shaft 102, as shown. Expandable structure 113 can comprise a furlable substrate, with electrode array 111 positioned on the outward facing surface of the substrate. Expandable structure 113 can be configured to furl (e.g., roll up), such as to furl about the central axis of shaft 102, for example as shown in Fig. 13C. Distal portion 1028 of shaft 102 can be configured to transition from a relatively straight geometry (e.g., when shaft 102 is advanced through working channel 8203), to an “offset” geometry. For example, shaft 102 can comprise two deflection points, deflection point 1025a and 1025b shown, that deflect to position expandable structure 113 proximate target tissue, as shown in Figs. 13A and 13B.

[0292] Fig. 13B shows shaft 102 in an offset geometry, with expandable structure 113 unfurled, such that electrode array 111 is positioned in contact with tissue. In some embodiments, treatment assembly 110 can be rotated (e.g., via rotation of shaft 102), such as to align electrode array 111 with different circumferential portions of tissue (e.g., to change the direction shaft 102 deflects). Additionally, or alternatively, shaft 102 can be advanced and/or retracted from working channel 8203 to reposition electrode array 111, such as to align electrode array 111 with different longitudinal portions of tissue. Using this translation and/or rotation of shaft 102, electrode array 111 can be used to treat a full and/or partial circumferential portion of target tissue with a length greater than the length of electrode array 111, for example without repositioning introduction device 80.

[0293] Fig. 13C shows expandable structure 113 in a furled geometry, relative to a working channel 8203 of introduction device 80. In some embodiments, treatment assembly 110 is configured to be introduced through a working channel with a diameter of no more than 6.0mm, such as no more than 4.5mm, 3.2mm, or 2.8mm. In some embodiments, distal portion 1028 of

shaft 102 and/or expandable structure 113 comprise a shape memory material, for example a nickel-titanium alloy, that is configured to change the shape of distal portion 1028 and/or expandable structure 113, as described herein. Additionally, or alternatively, shaft 102 can comprise an articulatable shaft, such as when treatment device 100 comprises one or more steering wires or other steering mechanisms. In some embodiments, expandable structure 113 is biased in the unfurled geometry shown in Fig. 13B. Expandable structure 113 can be configured to furl (e.g., to overcome an unfurled bias) when retracted into working channel 8203. For example, expandable structure 113 can comprise a tapered proximal end that is configured to convert an axial force from the front edge of working channel 8203 (e.g., as expandable structure 113 is retracted into working channel 8203) to a force that causes the furling of expandable structure 113.

[0294] While the preferred embodiments of the devices and methods have been described in reference to the environment in which they were developed, they are merely illustrative of the principles of the inventions. Modification or combinations of the above-described assemblies, other embodiments, configurations, and methods for carrying out the invention, and variations of aspects of the invention that are obvious to those of skill in the art are intended to be within the scope of the claims. In addition, where this application has listed the steps of a method or procedure in a specific order, it may be possible, or even expedient in certain circumstances, to change the order in which some steps are performed, and it is intended that the particular steps of the method or procedure claim set forth below not be construed as being order-specific unless such order specificity is expressly stated in the claim.

WHAT IS CLAIMED IS:

1. A system for treating a medical condition of a patient, the system comprising:

a device comprising a first elongate shaft for insertion into the small intestine, the first elongate shaft comprising a distal portion; and

a treatment assembly configured to be positioned on the distal portion of the first elongate shaft and comprising an electrode array of one or more electrodes,

wherein the at least one treatment assembly is configured to treat target tissue located in the small intestine of the patient by delivering electrical energy to the target tissue via the electrode array;

wherein the delivery of the electrical energy electroporates cells of the target tissue, and

wherein the system is configured to treat the medical condition of the patient.
2. The system according to claim 1 and/or any one or more other claims herein, wherein the delivery of the electrical energy irreversibly electroporates the cells of the target tissue.
3. The system according to claim 1 and/or any one or more other claims herein, wherein the target tissue comprises duodenal tissue.
4. The system according to claim 3 and/or any one or more other claims herein, wherein the target tissue comprises tissue selected from the group consisting of: mucosal tissue; submucosal tissue; nerve tissue; and combinations thereof.
5. The system according to claim 1 and/or any one or more other claims herein, wherein the medical condition comprises a metabolic condition.
6. The system according to claim 5 and/or any one or more other claims herein, wherein the metabolic condition comprises insulin resistance.
7. The system according to claim 5 and/or any one or more other claims herein, wherein the metabolic condition comprises Type 2 diabetes.
8. The system according to claim 1 and/or any one or more other claims herein, wherein the medical condition is selected from the group consisting of: Type 2 diabetes; Type 1 diabetes; "Double diabetes"; gestational diabetes; hyperglycemia; pre-diabetes; impaired glucose tolerance; insulin resistance; non-alcoholic fatty liver disease (NAFLD); non-alcoholic steatohepatitis (NASH); obesity; obesity-related disorder; polycystic ovarian syndrome; hypertriglyceridemia; hypercholesterolemia; psoriasis;

GERD; coronary artery disease; stroke/TIA; cognitive decline or dementia; diabetic nephropathy; neuropathy; retinopathy; diabetic heart disease and/or heart failure; metabolic dysfunction-associated steatotic liver disease (MASLD); and combinations thereof.

9. The system according to claim 1 and/or any one or more other claims herein,

wherein the treatment assembly further comprises at least one needle for penetrating submucosal tissue of the small intestine,

wherein at least one of the electrodes of the electrode array comprises a hollow tubular shaped electrode,

wherein the system further comprises conductive fluid,

wherein the at least one needle is configured to deliver the conductive fluid to the submucosal tissue, such that the delivered conductive fluid within the submucosal tissue collectively forms a hollow tubular shape that is concentric with the hollow tubular shaped electrode of the functional assembly, and

wherein the system is configured to deliver the electrical energy between the hollow tubular shaped electrode of the functional assembly and the hollow tubular shaped conductive fluid in the submucosal tissue to electroporate the tissue between the hollow tubular shaped electrode of the functional assembly and the hollow tubular shaped conductive fluid in the submucosal tissue.
10. The system according to claim 9 and/or any one or more other claims herein, wherein the treatment assembly is configured to removably attach to the distal portion of the first elongate shaft without adversely affecting the functionality of the endoscope.
11. The system according to claim 10 and/or any one or more other claims herein, wherein the treatment assembly includes a housing configured to attach to the distal portion of the first elongate shaft, wherein the endoscope comprises a working channel, and wherein the housing includes an opening configured to align with the working channel while the housing is attached to the first elongate shaft.
12. The system according to claim 1 and/or any one or more other claims herein, further comprising an endoscope comprising a second elongate shaft and one or more working channels.
13. The system according to claim 12 and/or any one or more other claims herein, wherein the first elongate shaft is configured to be inserted into the small intestine alongside the second elongate shaft.

14. The system according to claim 12 and/or any one or more other claims herein, wherein the first elongate shaft is configured to be inserted into the small intestine through one of the one or more working channels of the endoscope, and wherein the working channel comprises an inner diameter.
15. The system according to claim 14 and/or any one or more other claims herein, wherein the treatment assembly comprises an expandable assembly comprising a compact diameter and an expanded diameter, wherein the compact diameter comprises a diameter smaller than the inner diameter of the working channel and the expanded diameter approximates the diameter of the small intestine.
16. The system according to claim 1 and/or any one or more other claims herein, wherein the treatment assembly further comprises an expandable assembly configured to transition between a compact geometry and an expanded geometry.
17. The system according to claim 16 and/or any one or more other claims herein, wherein the treatment assembly further comprises a housing configured to surround the expandable assembly.
18. The system according to claim 17 and/or any one or more other claims herein, wherein the expandable assembly is configured to deploy from the housing and transition from the compact geometry to the expanded geometry.
19. The system according to claim 16 and/or any one or more other claims herein, wherein the expandable assembly comprises one or more radially expandable arms.
20. The system according to claim 19 and/or any one or more other claims herein, wherein the electrode array is furled about the one or more radially expandable arms.
21. The system according to claim 1 and/or any one or more other claims herein, wherein the treatment assembly further comprises a housing configured to be positioned on the distal portion of the first elongate shaft.
22. The system according to claim 21 and/or any one or more other claims herein, wherein the housing comprises a circumferential channel, and the electrode array is configured to traverse about the circumferential channel.
23. The system according to claim 21 and/or any one or more other claims herein, wherein the electrode array is positioned on a portion of the housing.
24. The system according to claim 23 and/or any one or more other claims herein, wherein the housing is configured to rotate about the distal portion of the first elongate shaft.

25. The system according to claim 23 and/or any one or more other claims herein, wherein the treatment assembly comprises one or more fluid ports proximate the electrode array, and wherein the system is configured to apply a vacuum to the one or more fluid ports to pull tissue toward the electrode array.
26. The system according to claim 21 and/or any one or more other claims herein, wherein the housing comprises a first portion and a second portion, wherein the first portion is configured to attach to the first elongate shaft and the second portion is configured to extend from the first portion toward tissue, and wherein the electrode array is positioned on the second portion.
27. The system according to claim 26 and/or any one or more other claims herein, wherein the housing further comprises a third portion configured to extend from the first portion and opposite the second portion.
28. The system according to claim 1 and/or any one or more other claims herein, further comprising an aspiration assist device comprising a third elongate shaft with a fluid lumen therethrough and one or more aspiration ports positioned on the distal end of the third elongate shaft and fluidly attached to the fluid lumen, wherein the fluid lumen is configured to attach to a source of vacuum.
29. The system according to claim 28 and/or any one or more other claims herein, wherein the device comprises an endoscope including a working channel, and wherein the aspiration assist device is configured to be inserted through the working channel.
30. The system according to claim 29 and/or any one or more other claims herein, wherein the aspiration assist device and the endoscope are configured to provide aspiration.
31. The system according to claim 28 and/or any one or more other claims herein, wherein the third shaft is configured to be inserted into the small intestine alongside the first elongate shaft.
32. The system according to claim 1 and/or any one or more other claims herein, wherein the treatment assembly comprises a radially expandable structure configured to transition between a radially compact and a radially expanded geometry, and wherein the radially expandable structure is configured transition to the radially expanded geometry when the structure is compacted linearly.
33. The system according to claim 32 and/or any one or more other claims herein, wherein the expandable structure comprises an accordion-like structure.

34. The system according to claim 32 and/or any one or more other claims herein, wherein the expandable structure is biased in the radially compact geometry.
35. The system according to claim 34 and/or any one or more other claims herein, further comprising a linkage configured to linearly contract and/or extend the expandable structure to radially extend and/or collapse the expandable structure.
36. The system according to claim 1 and/or any one or more other claims herein, wherein the treatment assembly comprises an expandable balloon and the electrode array is positioned on the expandable balloon.
37. The system according to claim 36 and/or any one or more other claims herein, wherein the electrode array comprises two or more sets of electrodes, and wherein each set of electrodes comprise two or more electrodes.
38. The system according to claim 37 and/or any one or more other claims herein, wherein the two or more sets of electrodes are configured in an alternating pattern about the expandable balloon.
39. The system according to claim 1 and/or any one or more other claims herein, wherein the treatment assembly comprises a tissue capture port configured to capture a portion of tissue to be treated by the system.
40. The system according to claim 39 and/or any one or more other claims herein, wherein the tissue capture port comprises two or more tissue capture ports.
41. The system according to claim 39 and/or any one or more other claims herein, wherein the tissue capture port comprises vacuum ports.
42. The system according to claim 39 and/or any one or more other claims herein, wherein at least one of the one or more electrodes comprises a needle and the needle is configured to penetrate tissue that is positioned within the tissue capture port.
43. The system according to claim 39 and/or any one or more other claims herein, wherein the one or more electrodes are positioned within the tissue capture port.
44. The system according to claim 1 and/or any one or more other claims herein, wherein the treatment assembly comprises a set of one or more flexible sheets configured to transition between a back-swept geometry and a forward-swept geometry.
45. The system according to claim 44 and/or any one or more other claims herein, wherein the electrode array is positioned on the set of flexible sheets.

46. The system according to claim 1 and/or any one or more other claims herein, wherein the first elongate shaft is configured to transition between a linear geometry and an offset geometry, wherein an axis of the distal portion of the first elongate shaft is offset from an axis of a proximal portion of the first elongate shaft in the offset geometry.
47. The system according to claim 46 and/or any one or more other claims herein, wherein the treatment assembly comprises an expandable structure positioned on the distal portion of the first elongate shaft.
48. The system according to claim 47 and/or any one or more other claims herein, wherein the expandable structure comprises a furlable substrate, and wherein the electrode array is positioned on the furlable substrate.
49. The system according to claim 48 and/or any one or more other claims herein, wherein the furlable substrate is configured to align with the axis of the distal portion of the first elongate shaft in the offset geometry.

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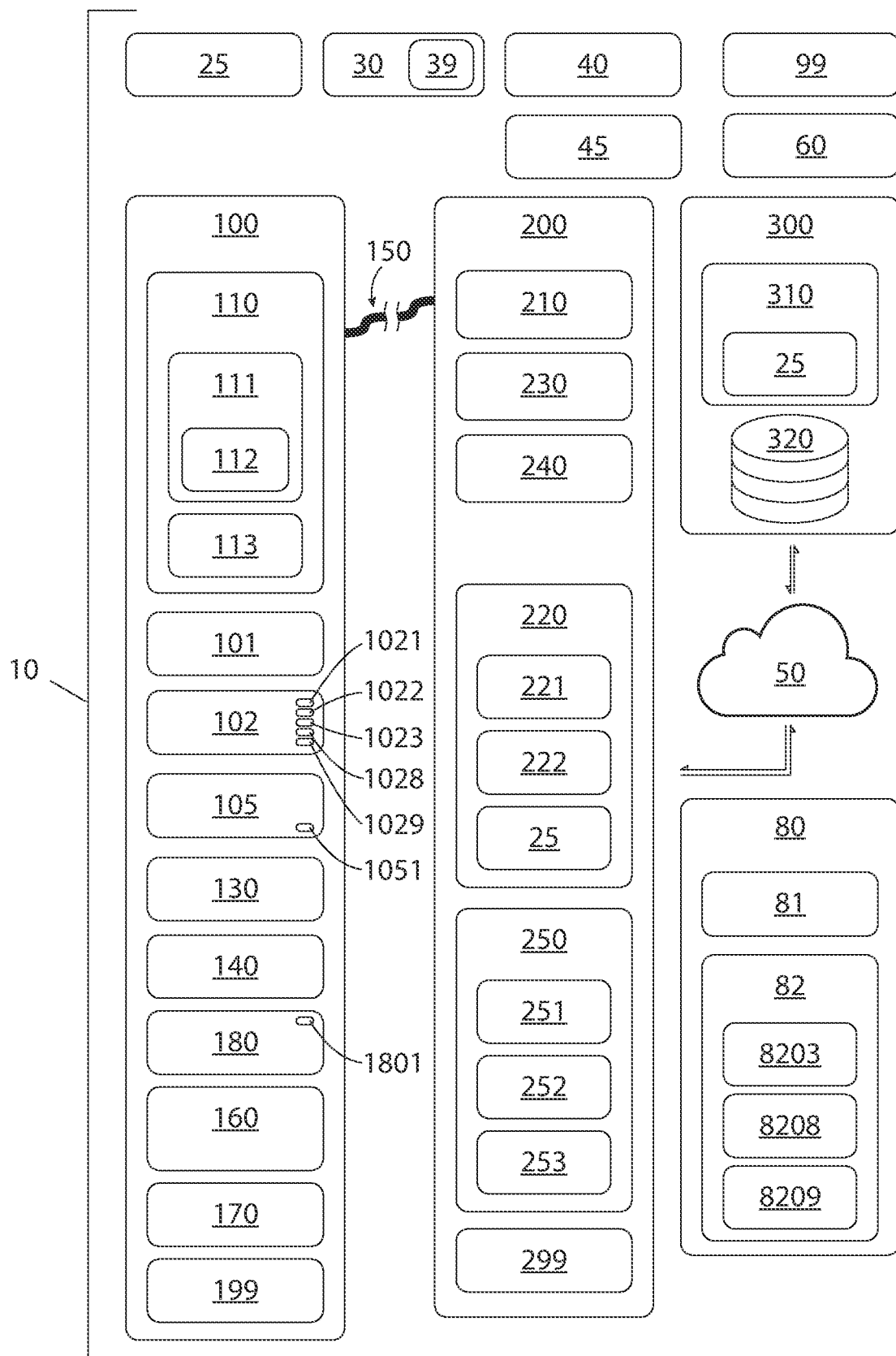


FIG. 1

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METHOD 1000

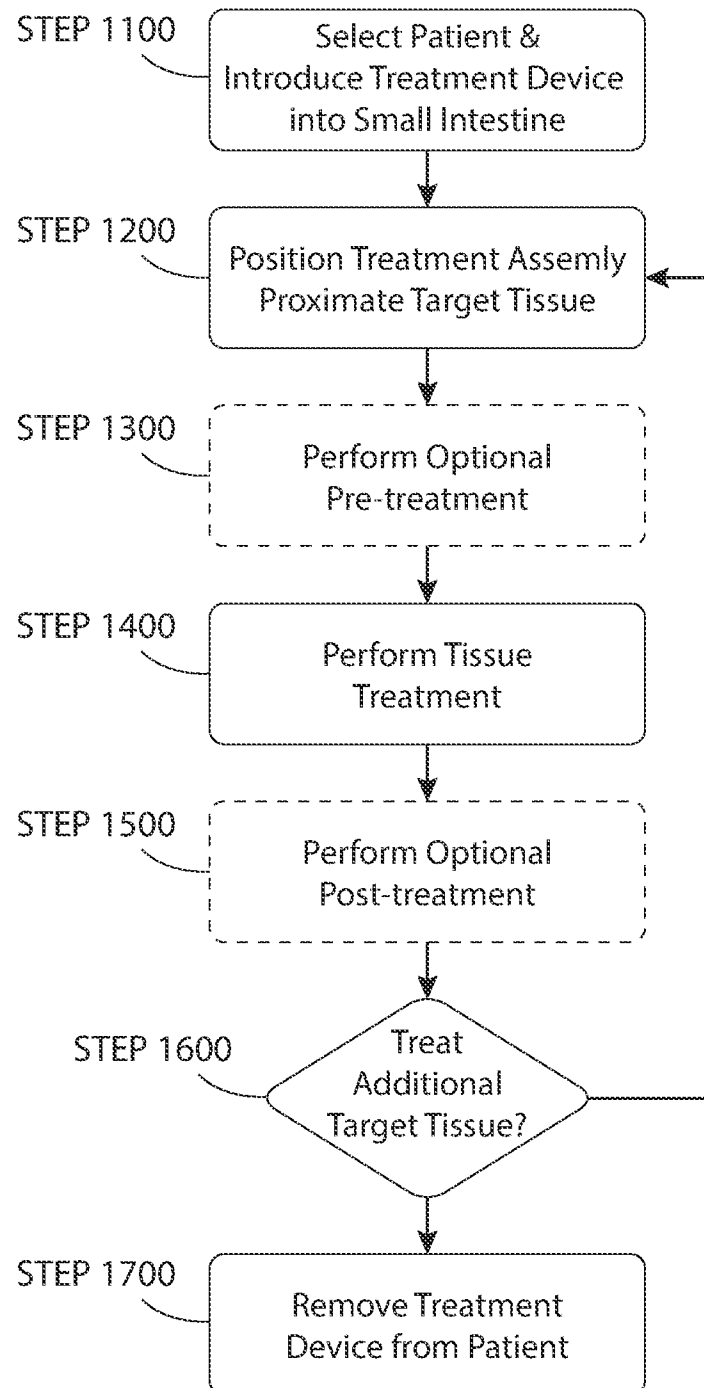


FIG. 1A

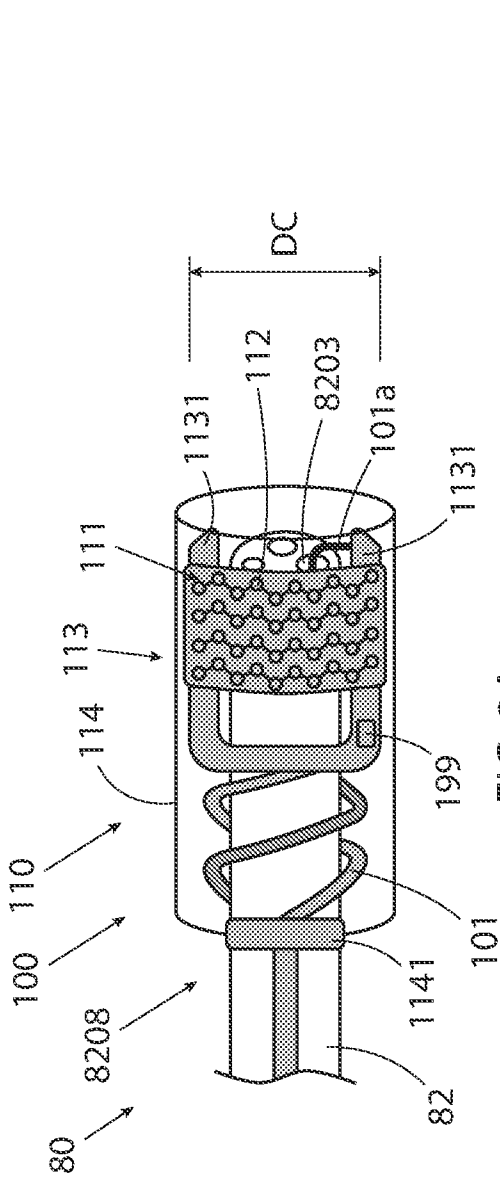


FIG. 3A

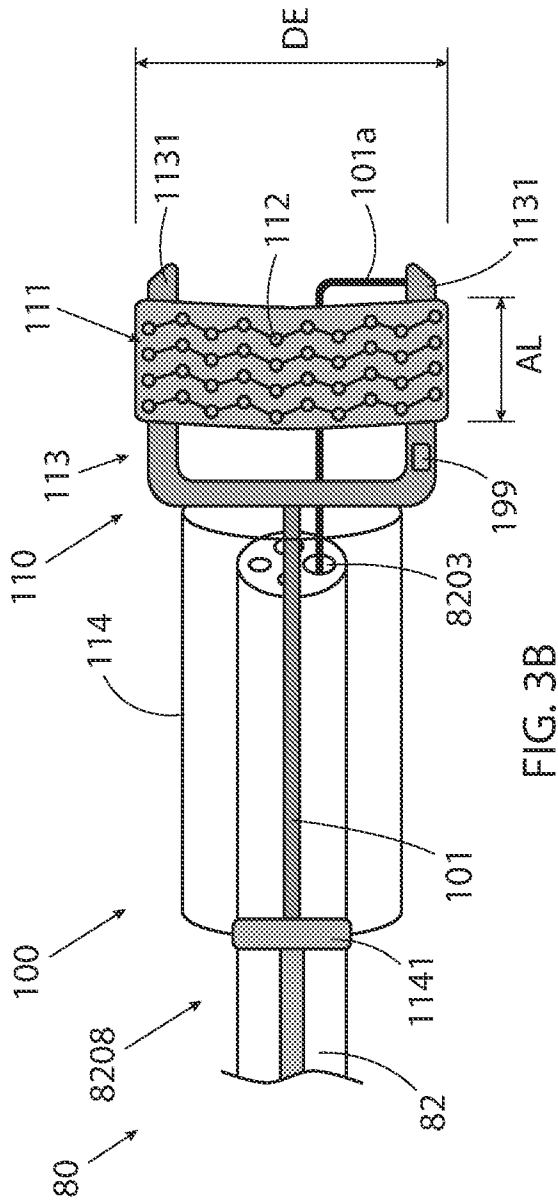


FIG. 3B

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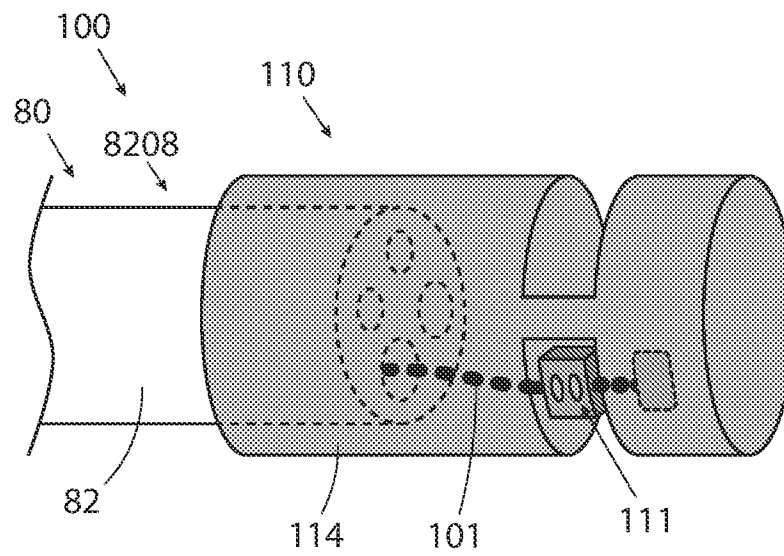


FIG. 4A

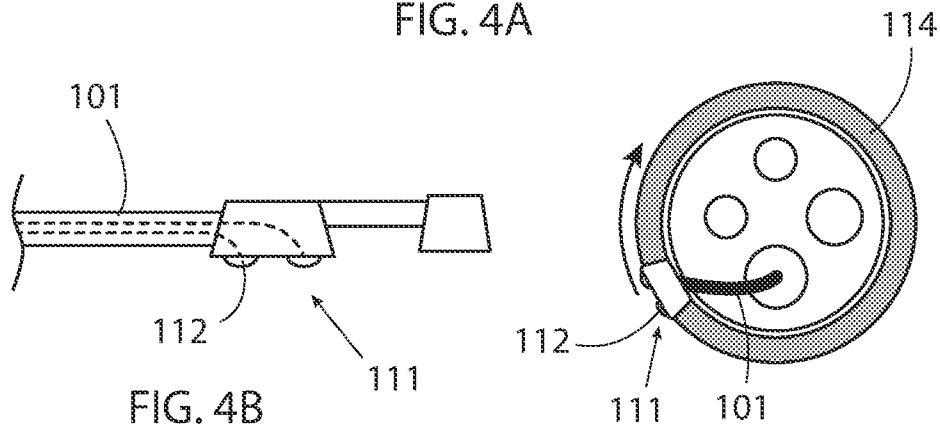


FIG. 4B

FIG. 4C

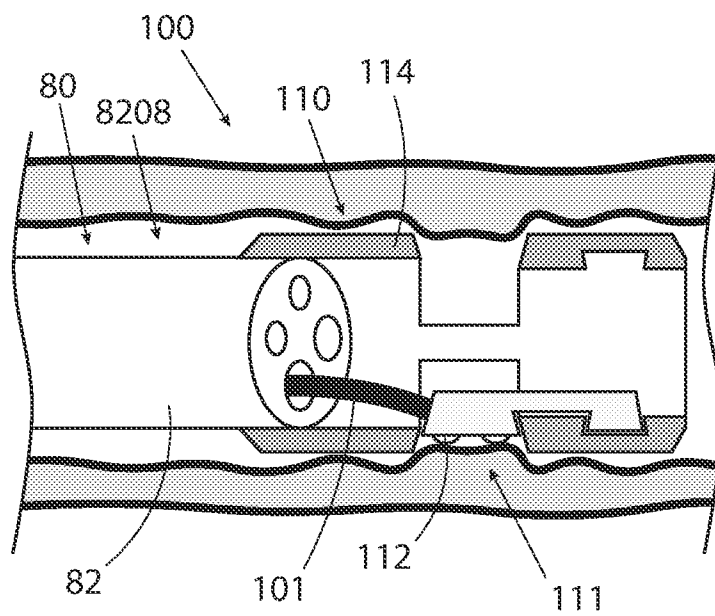


FIG. 4D

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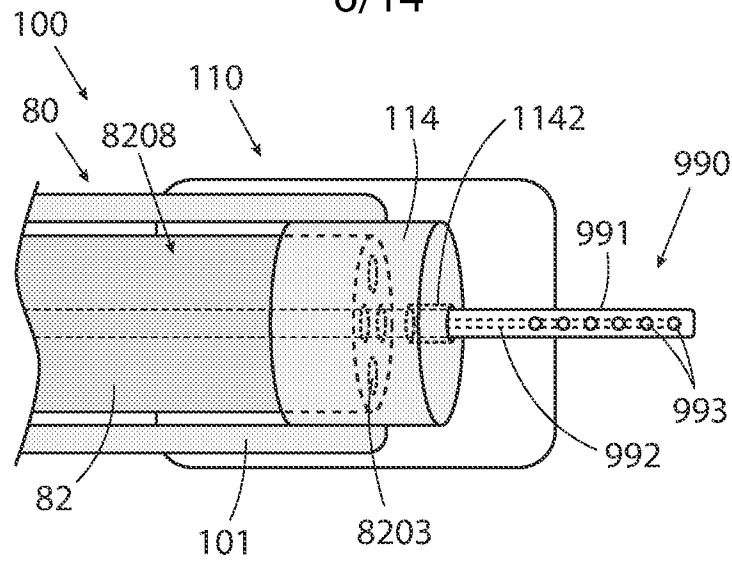


FIG. 5A

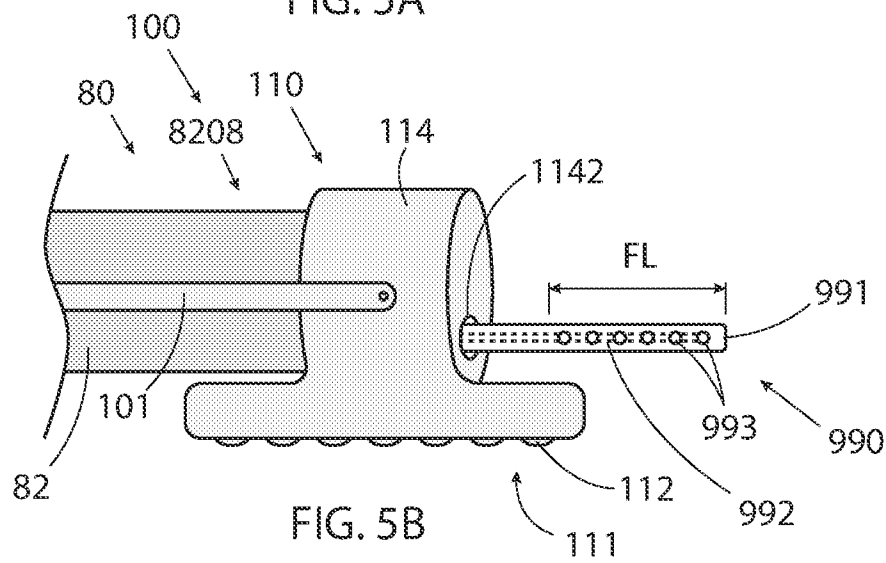


FIG. 5B

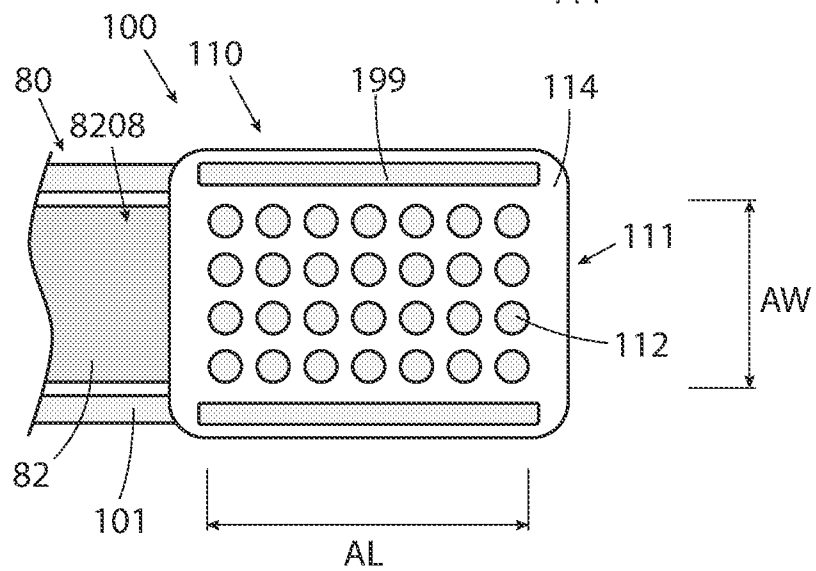


FIG. 5C

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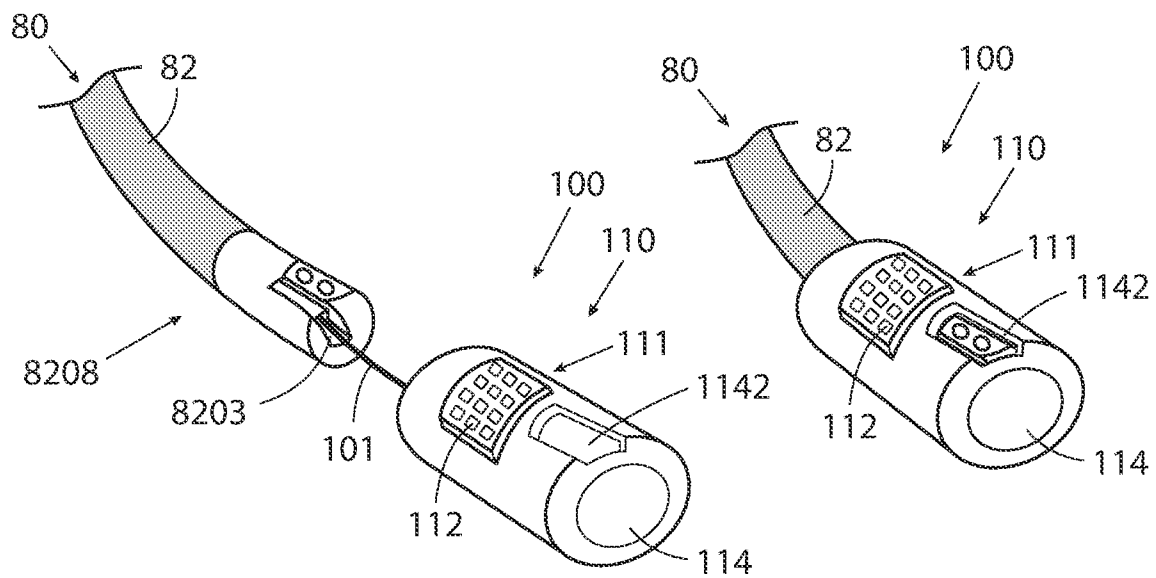


FIG. 6A

FIG. 6B

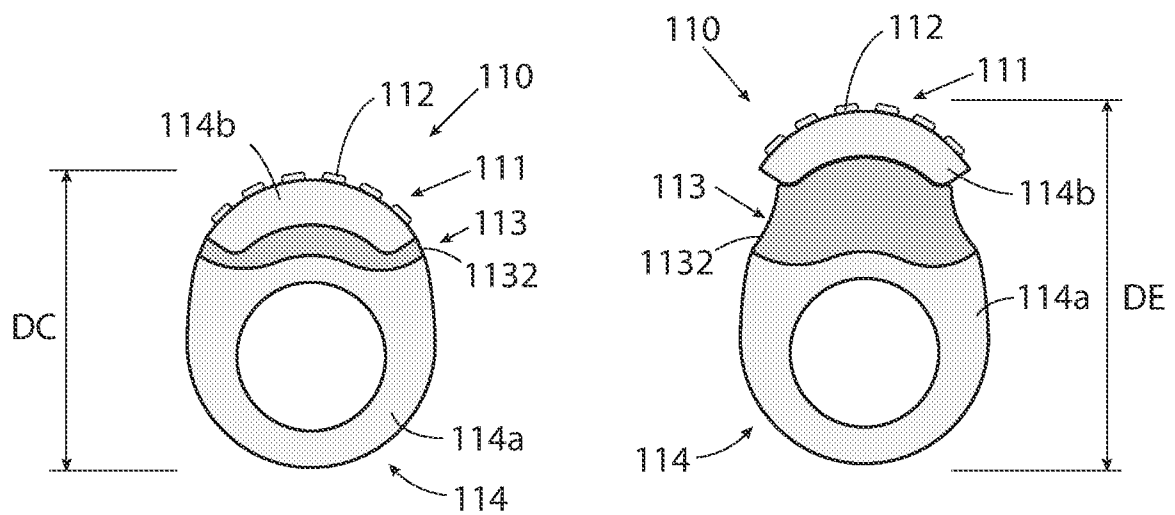


FIG. 6C

FIG. 6D

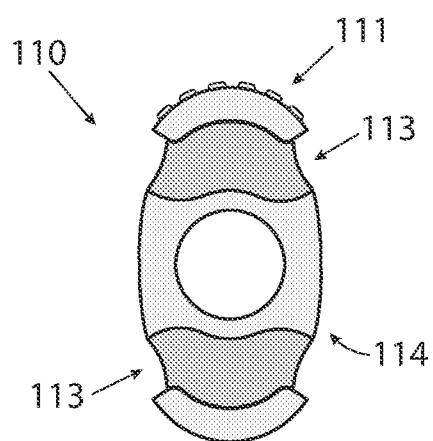


FIG. 6E

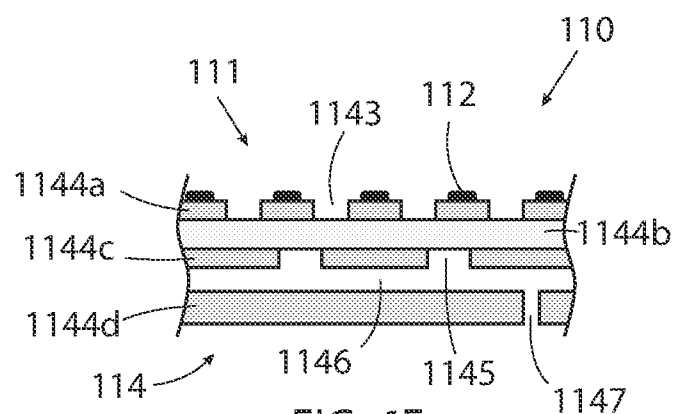


FIG. 6F

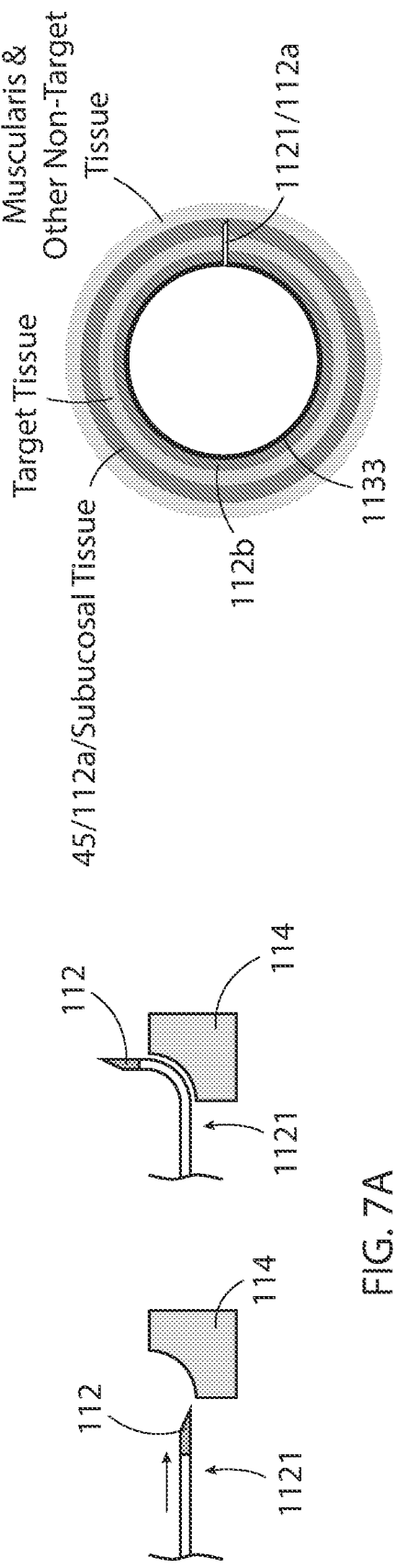


FIG. 7C

FIG. 7A

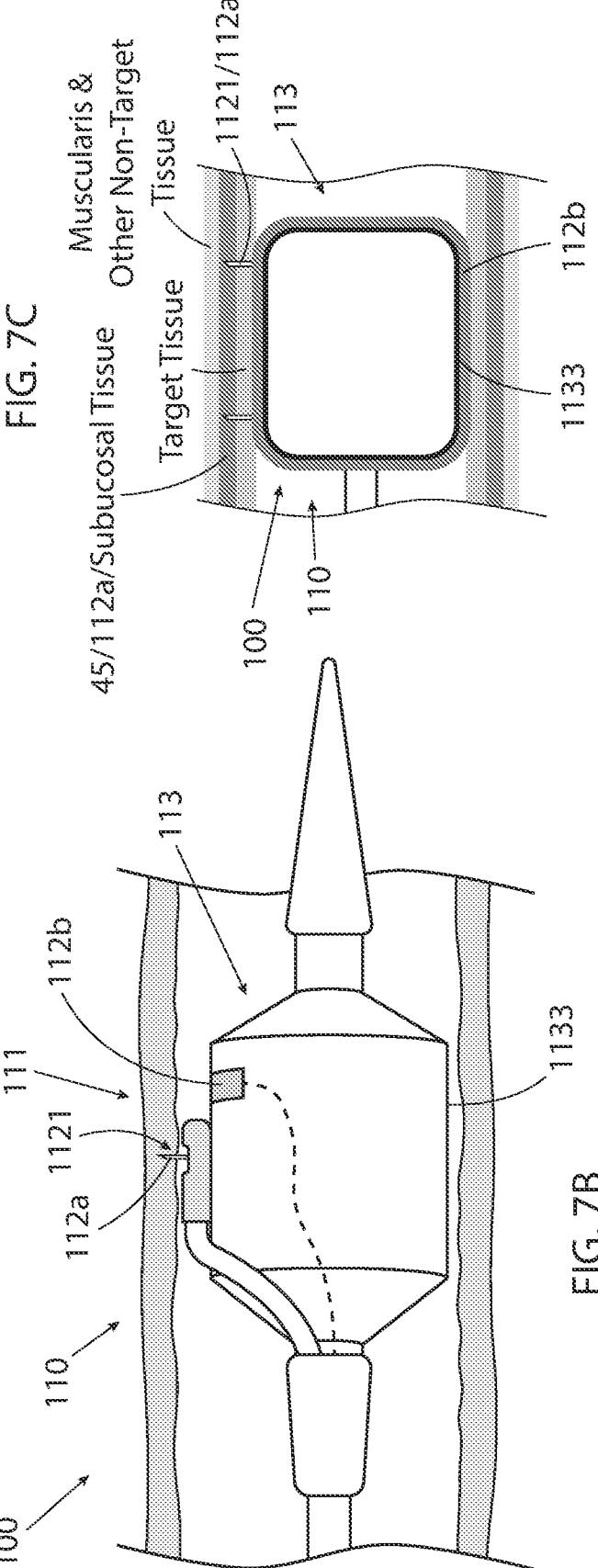


FIG. 7D

FIG. 7B

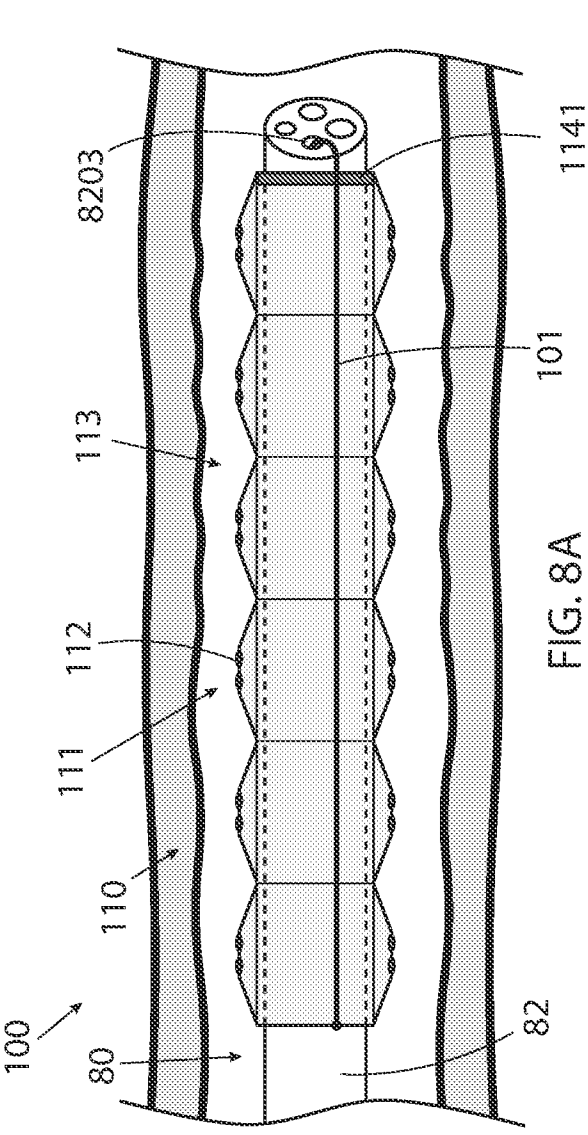


FIG. 8A

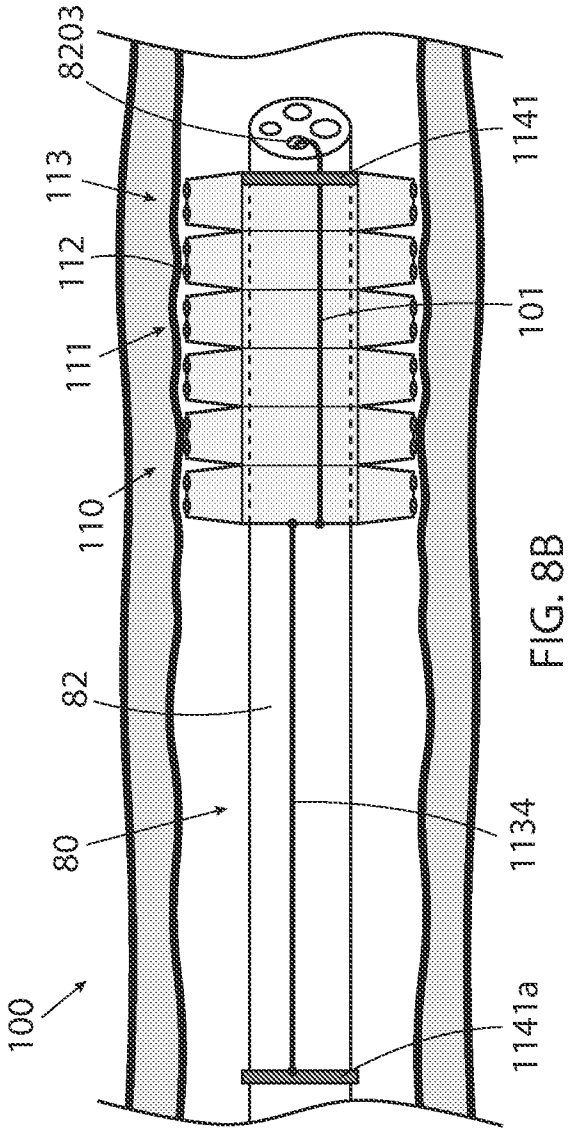


FIG. 8B

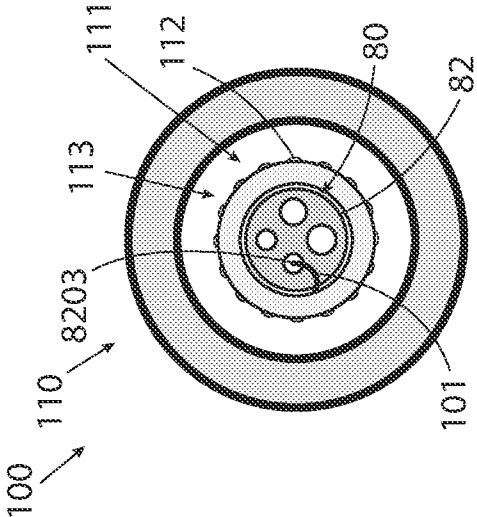


FIG. 8C

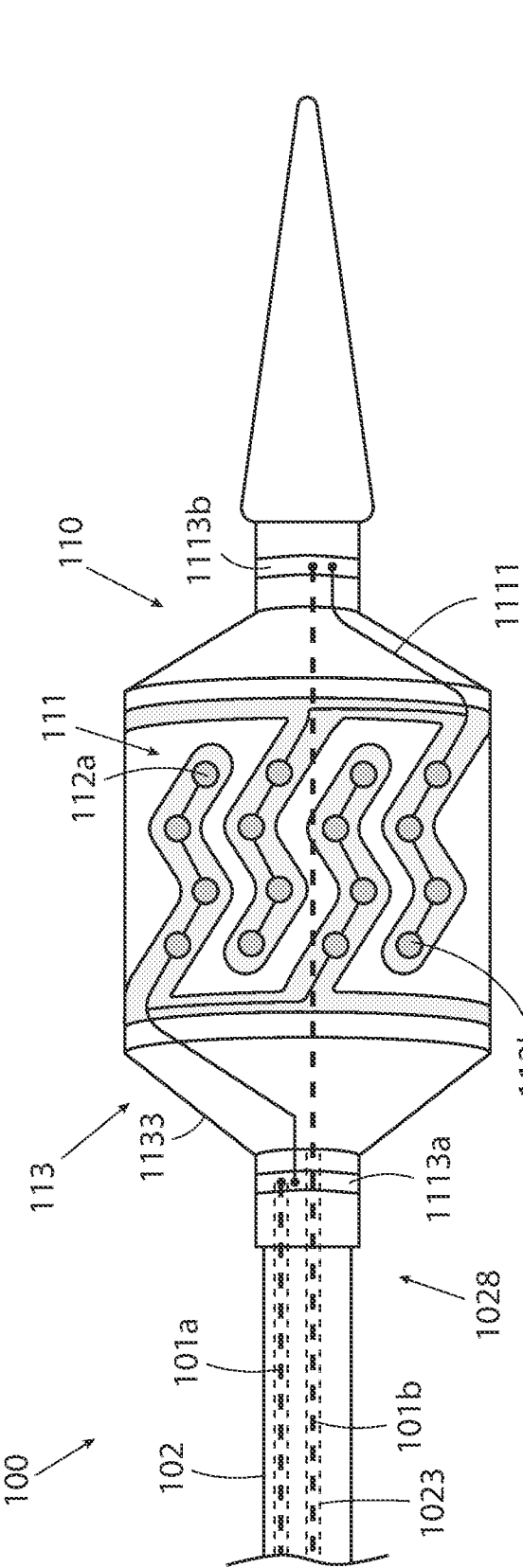


FIG. 9A

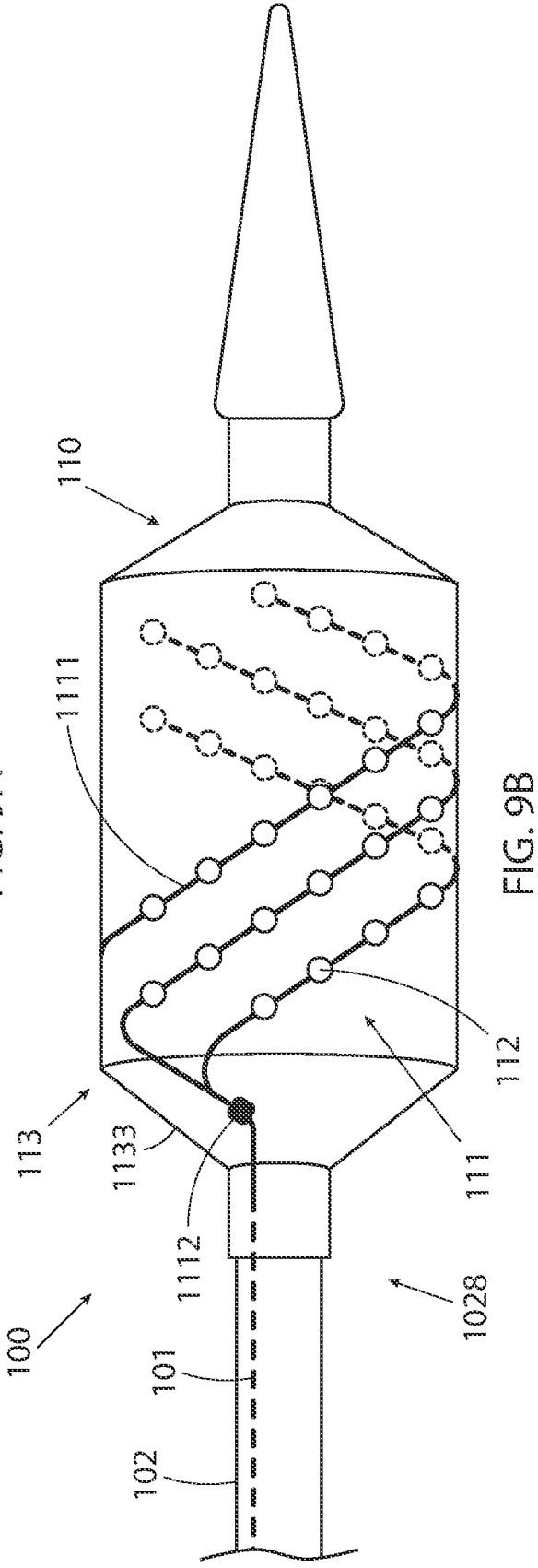


FIG. 9B

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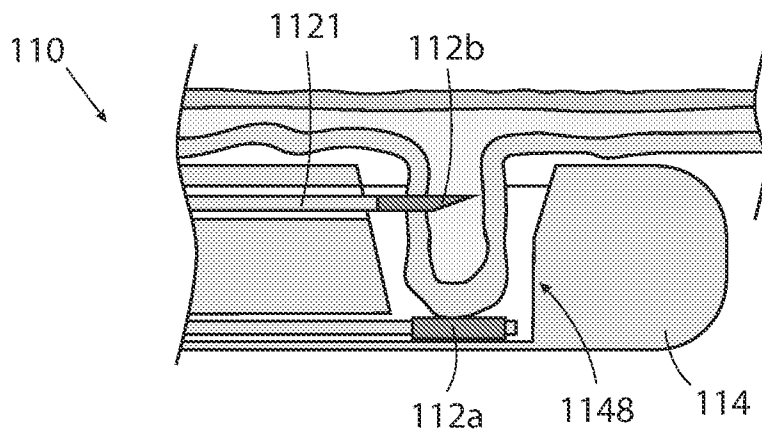


FIG. 10A

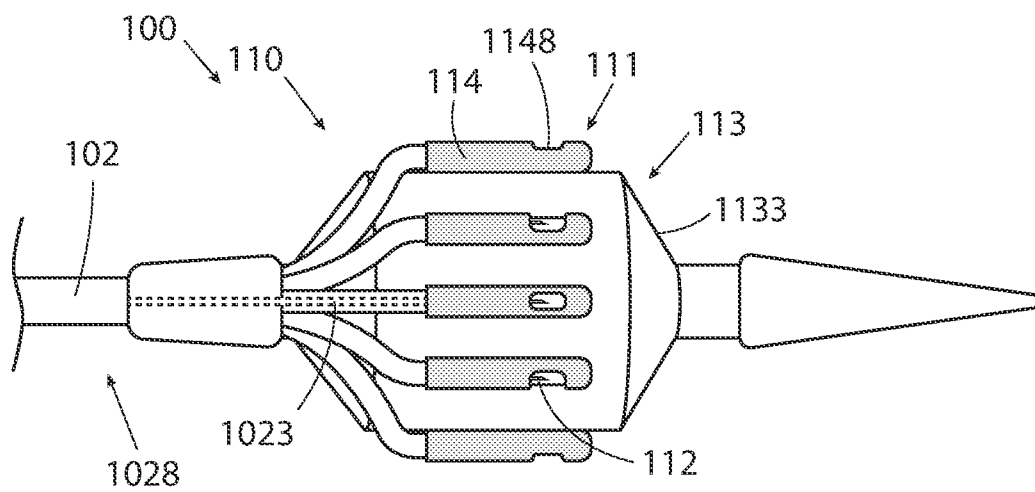


FIG. 10B

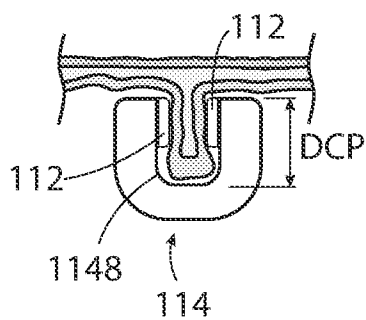


FIG. 10C

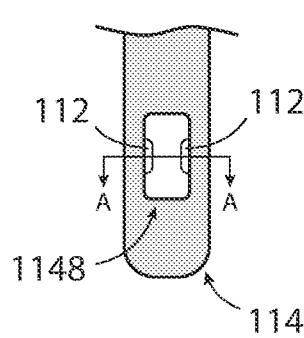


FIG. 10D

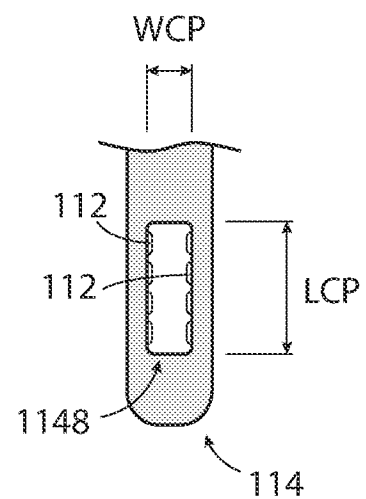


FIG. 10E

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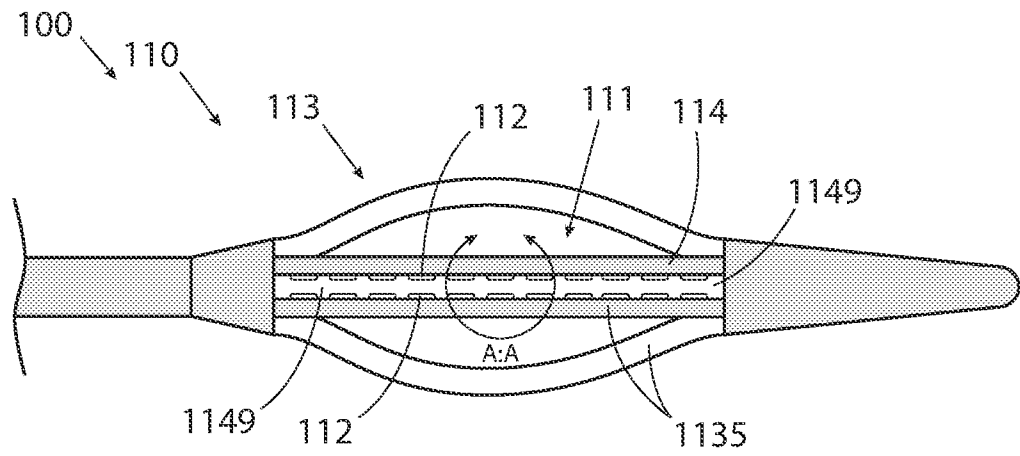


FIG. 11A

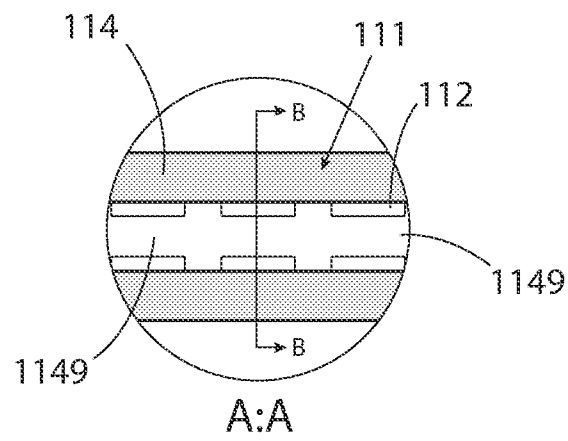


FIG. 11B

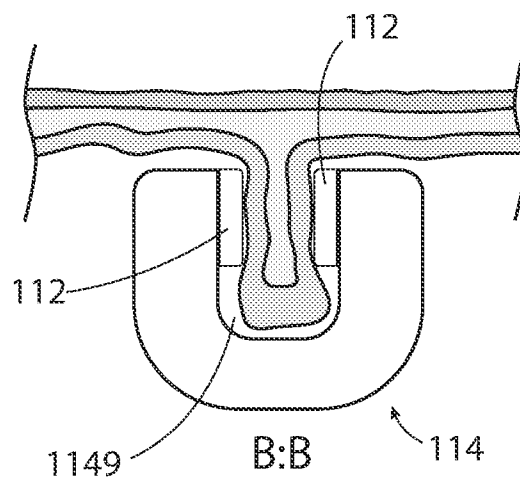


FIG. 11C

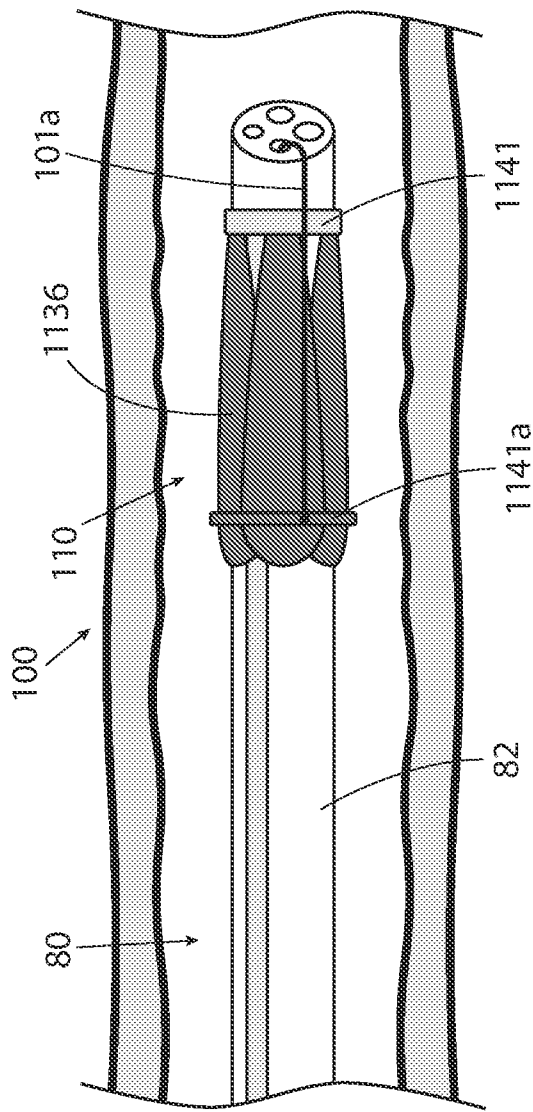


FIG. 12A

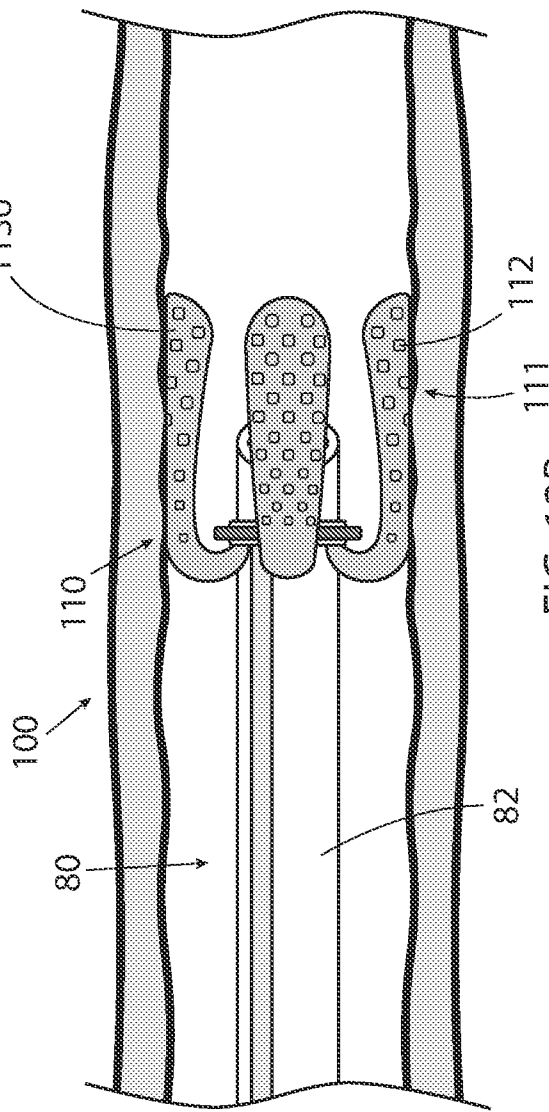
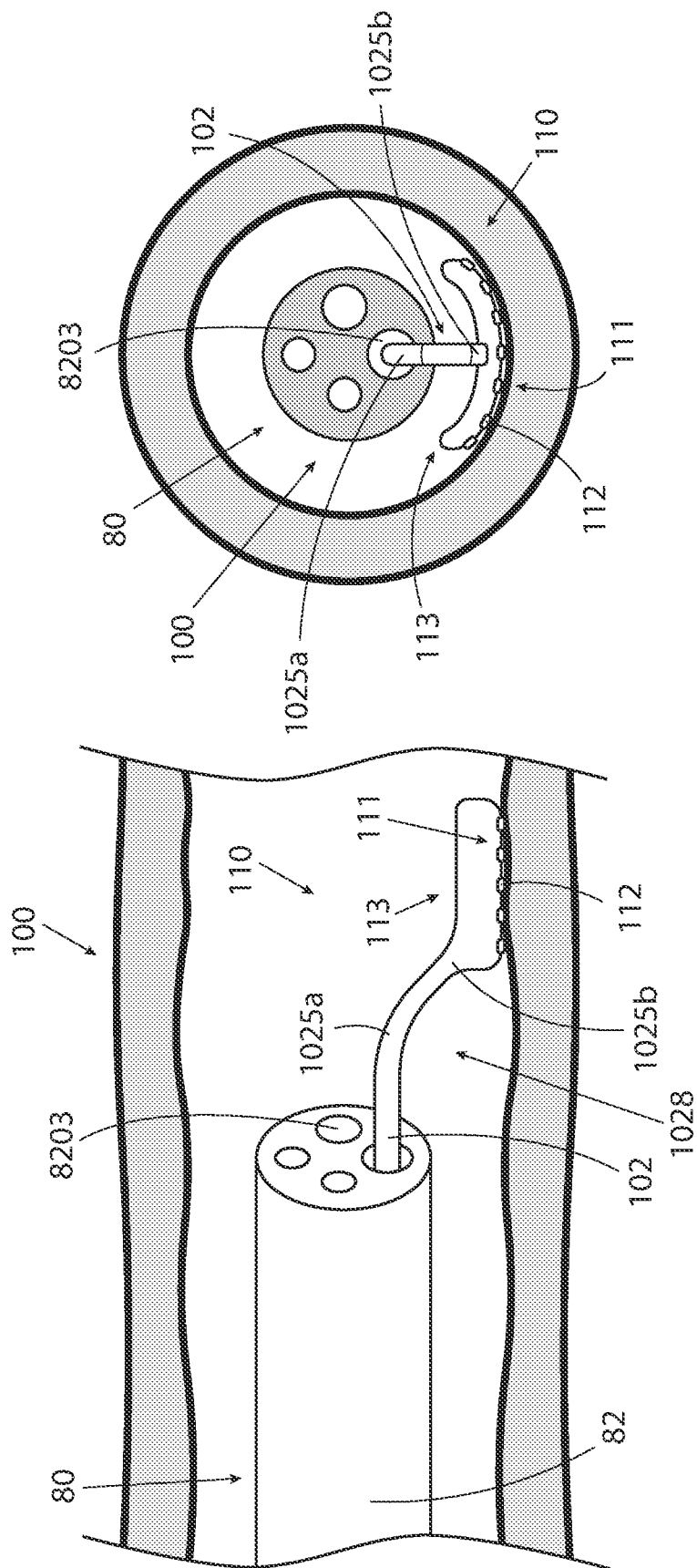


FIG. 12B



LE G. 13A

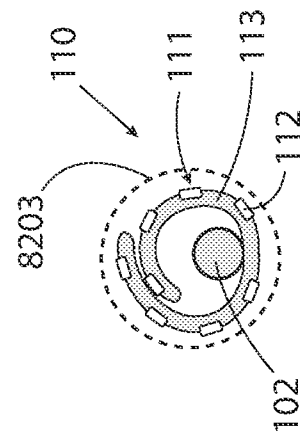


Fig. 13C