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(54) **SYSTEMS AND METHODS FOR APPLYING A SELECTED TREATMENT AGENT INTO CONTACT WITH TISSUE**

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(57) **ABSTRACT**

Systems and methods that treat disorders of the gastrointestinal tract by applying one or more treatment agents to tissue at or near the region where abnormal neurological symptoms or abnormal tissue conditions exist. The treatment agent is selected to either disrupt the abnormal nerve pathways and/or to alleviate the abnormal tissue conditions. The treatment agent can include at least one cytokine and/or at least one vanilloid compound to evoke a desired tissue response. The systems and methods can be used a primary treatment modality, or as a neoadjuvent or adjuvant treatment modality.

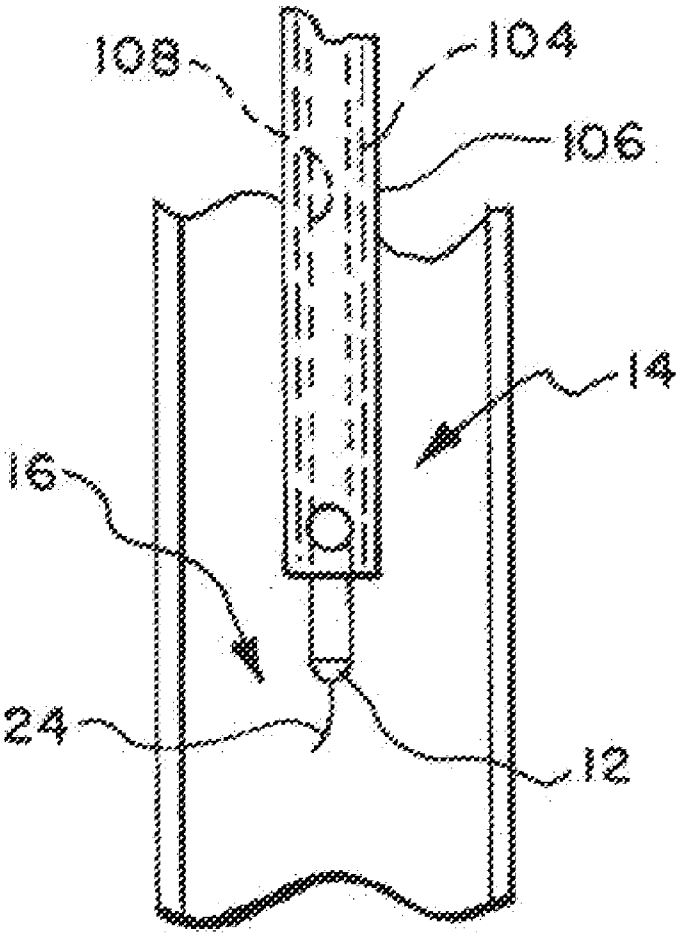


FIG. 1A

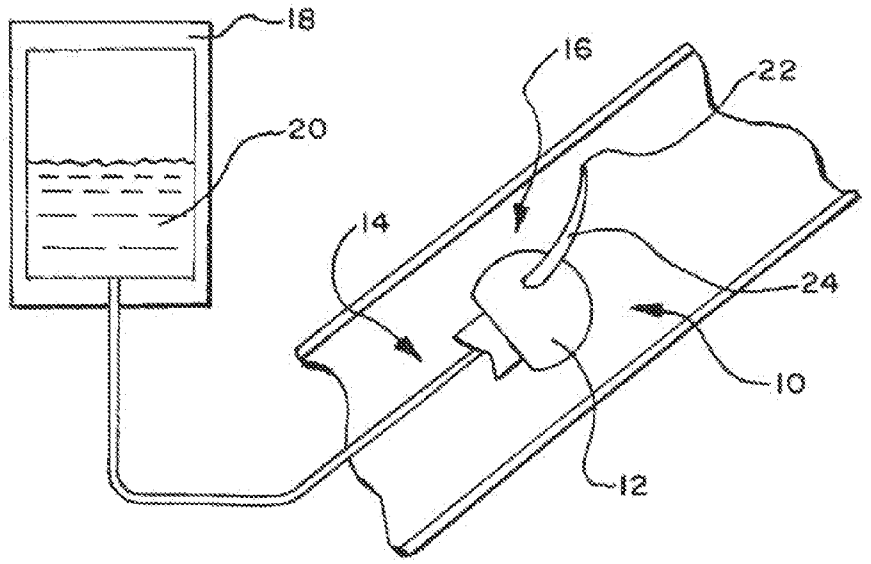


FIG. 1B

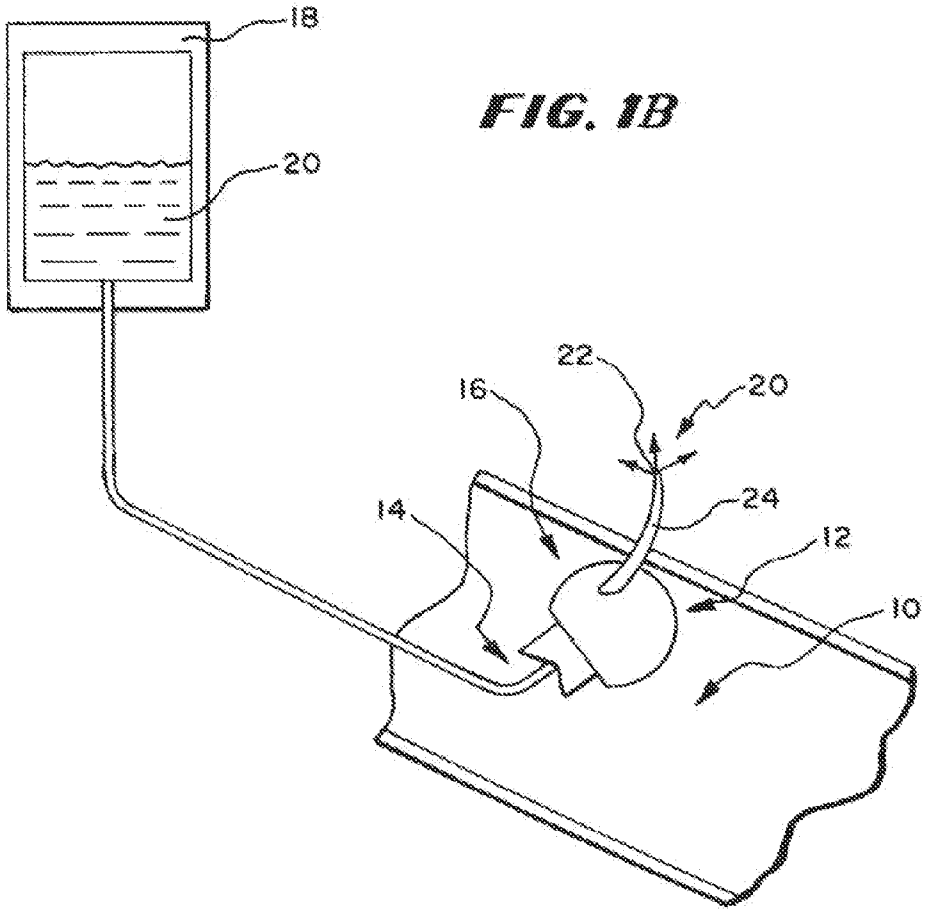
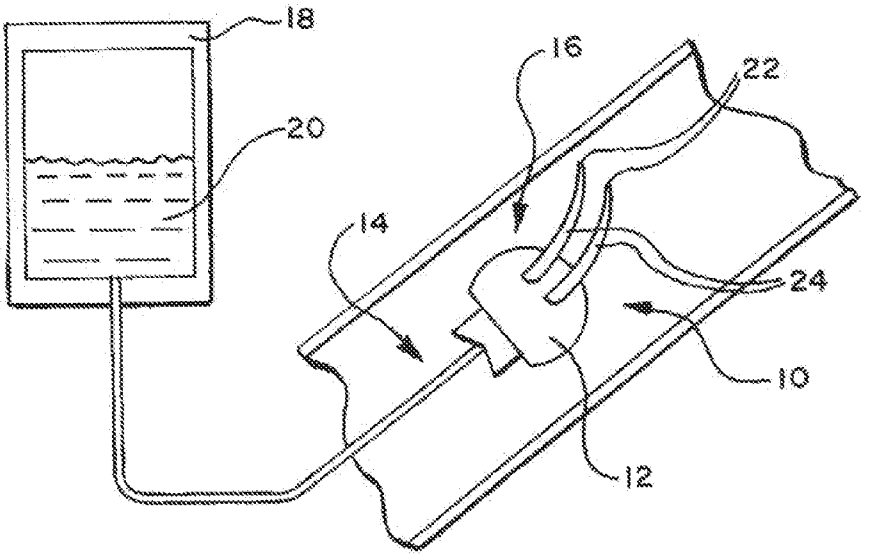


FIG. 2A



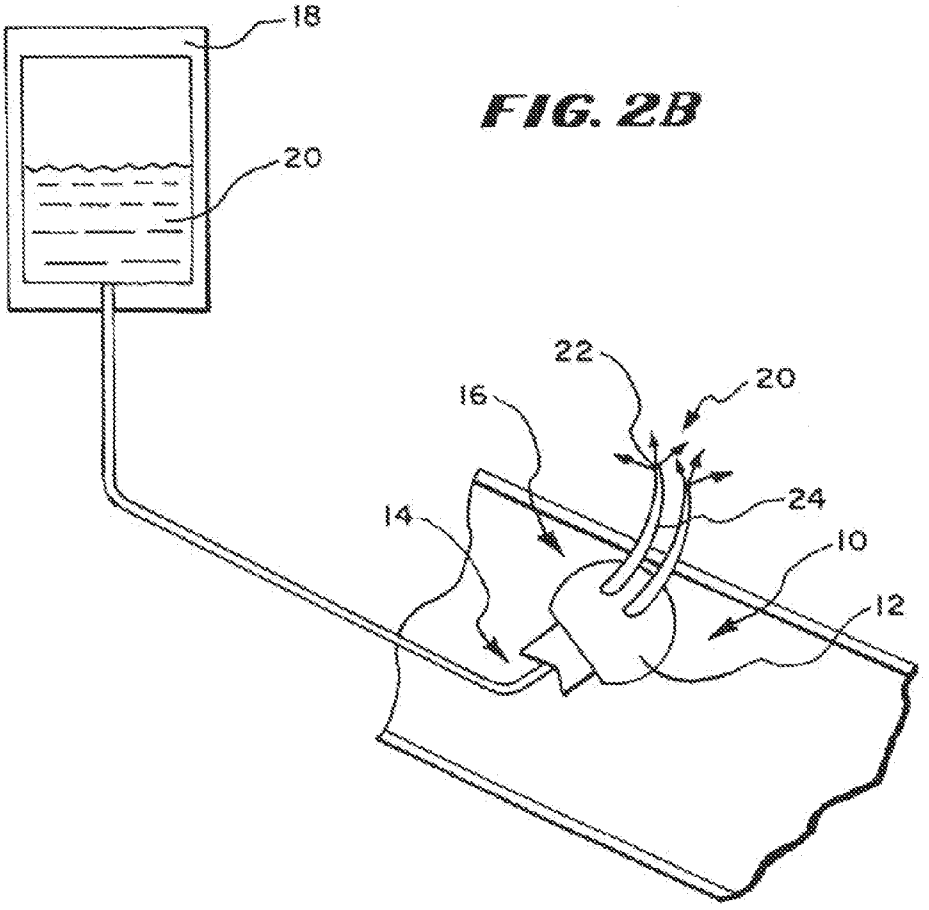


FIG. 2B

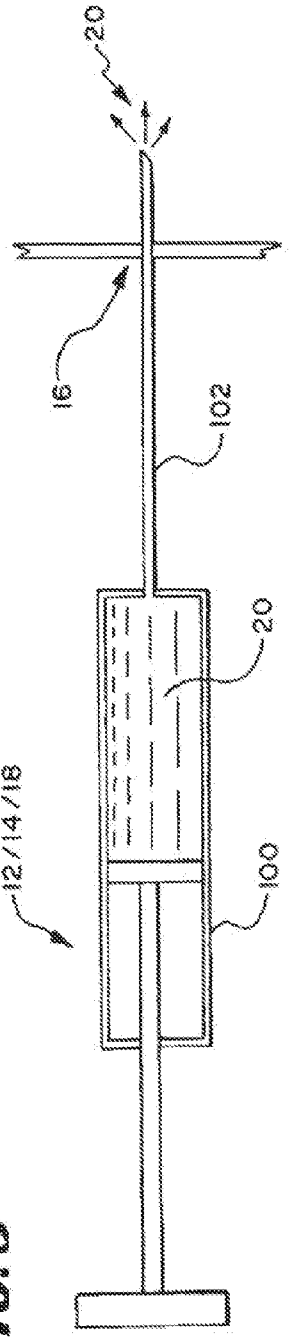


FIG. 3

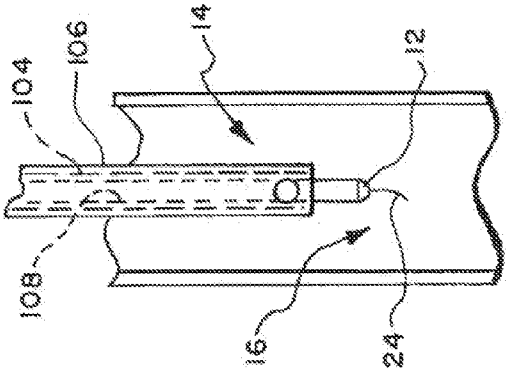


FIG. 4

SYSTEMS AND METHODS FOR APPLYING A SELECTED TREATMENT AGENT INTO CONTACT WITH TISSUE

RELATED APPLICATIONS

[0001] This application is a continuation of co-pending U.S. patent application Ser. No. 11/906,457, filed Oct. 2, 2007, which is a divisional of U.S. patent application Ser. No. 10/912,268, filed Aug. 5, 2004 (now U.S. Pat. No. 7,293,563), which is divisional of U.S. patent application Ser. No. 09/994,375, filed Nov. 26, 2001 (now U.S. Pat. 6,790,207), which is a continuation-in-part of U.S. patent application Ser. No. 09/304,737, filed May 4, 1999 (now U.S. Pat. No. 6,464,697), and a continuation-in-part of U.S. patent application Ser. No. 09/090,794, filed Jun. 4, 1998 (now abandoned).

FIELD OF THE INVENTION

[0002] In a general sense, the invention is directed to systems and methods for treating interior tissue regions of the body. More specifically, the invention is directed to systems and methods for treating dysfunctions of organs and tissue in the gastrointestinal tract.

BACKGROUND OF THE INVENTION

[0003] Disorders of organs or tissue of the gastrointestinal tract can be caused by as neurological factors (such as abnormal nerve impulses) or by physical factors (such as excess tissue volume).

[0004] For example, intestinal motility (i.e., the contraction of intestinal muscles and the propulsion and movement of the lumenal contents) is controlled by nerves and hormones, as well as by electrical activity in the muscular wall of the intestine. There are several disorders that involve abnormal motility and result in abnormal and uncomfortable visceral sensations. These disorders can cause significant discomfort and distress in the absence of gross physical abnormality of the intestine.

[0005] For example, irritable bowel syndrome (IBS) is a common disorder of the intestines. IBS can lead to crampy pain, gassiness, bloating, and changes in bowel habits. Some people with IBS have constipation (difficult or infrequent bowel movements) others have diarrhea (frequent loose stools, often with an urgent need to move the bowels); and some people experience both symptoms intermittently. Sometimes the person with IBS has a crampy urge to move the bowels, but cannot do so. The cause of IBS is not known, and as yet there is no cure. IBS can be characterized as a functional disorder because there is no sign of disease when the intestine is examined, often IBS is just a mild annoyance, but for some people it can be disabling.

[0006] Dyspepsia is another example. Dyspepsia is literally translated as 'bad digestion" and is commonly known as indigestion. Motility-like dyspepsia causes persistent or recurring abdominal pain that is centered in the upper abdomen. People with motility associated dyspepsia also may experience bloating, nausea, burping and a feeling of fullness that occurs soon after eating. It is an extremely common symptom complex, affecting as much as one-fourth of the United States adult population.

[0007] There are other disorders affecting the gastrointestinal tract that are characterized by abnormal tissue conditions not associated with neural abnormalities.

SUMMARY OF THE INVENTION

[0008] One aspect of the invention provides a method of treating tissue within a body. The method comprises selecting at least one treatment agent comprising at least one of a vanilloid compound and a cytokine compound. The method provides a source of the treatment agent. The method includes deploying through the interior lumen of the endoscope a catheter carrying on its distal end a tissue-piercing element adjacent to the targeted tissue region. The method includes coupling the catheter to the source of the treatment agent, and applying through the tissue-piercing element the treatment agent into contact with the targeted tissue region.

[0009] In one embodiment, the method injects the treatment agent into subsurface tissue in the targeted tissue region.

[0010] In one embodiment, the method includes providing a guide wire to facilitate deployment of the catheter.

[0011] Features and advantages of the inventions are set forth in the following Description and Drawings, as well as in the appended Claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] FIGS. **1**A and **1**B are schematic views of a system for treating tissue that includes a treatment device with a tissue piercing member that embodies features of the invention, FIG. **1**A showing the treatment device deployed in a tissue region and FIG. **1**B showing the treatment device piercing the tissue region to inject a treatment agent;

[0013] FIGS. **2**A and **2**B are schematic views of a system for treating tissue that includes a treatment device with multiple tissue piercing members that embodies features of the invention, FIG. **2**A showing the treatment device deployed in a tissue region and FIG. **2**B showing the treatment device piercing the tissue region to inject a treatment agent;

[0014] FIG. **3** is an embodiment of a tissue treatment device that takes the form of a syringe and a needle for injecting a treatment agent into a tissue region that can be visualized from outside the body; and

[0015] FIG. **4** is an embodiment of a tissue treatment device for injecting a treatment agent into a tissue region that cannot be visualized from outside the body.

[0016] The invention may be embodied in several forms without departing from its spirit or essential characteristics. The scope of the invention is defined in the appended claims, rather than in the specific description preceding them. All embodiments that fall within the meaning and range of equivalency of the claims are therefore intended to be embraced by the claims.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0017] This Specification discloses various systems and methods for treating dysfunctions of organs or tissue in the gastrointestinal tract. Still, it should be appreciated that the disclosed systems and methods are applicable for use in treating other dysfunctions elsewhere in the body, e.g., for treating sphincter barrier dysfunctions in the lower gastrointestinal tract or in the upper gastrointestinal tract. The systems and methods that embody features of the invention are adaptable

for use with catheter-based systems and surgical techniques, as well as systems and surgical Techniques that are not necessarily catheter-based.

I. System Overview

[0018] A tissue treatment system **10** that embodies features of the invention is shown in FIGS. **1**A and **1**B. The tissue treatment system **10** includes a tissue treatment device **12** and an apparatus **14** to deliver the tissue treatment device **12** to a tissue region **16** targeted for treatment.

[0019] The treatment system **10** also includes a source **18** of a treatment agent **20**.

A. The Tissue Treatment Device

[0020] The tissue treatment device **12** serves to apply the treatment agent **20** to the targeted tissue region **16** to obtain a desired therapeutic effect. The therapeutic effect can comprise either alteration of nerve impulse pathways in the region **16** or a physical alteration of tissue characteristics in the region **16**.

[0021] The tissue treatment device **12** includes one or more agent delivery ports **22**. The one or more delivery ports **22** can apply the treatment agent **20** to surface tissue in the region **16**. Desirably (as FIG. **1**A shows), the port **20** is located at the end of a tissue piercing member **24**. In this arrangement, the treatment agent **20** may be injected into subsurface tissue.

[0022] The tissue treatment device **12** can include single or multiple ports **22** located single or multiple tissue piercing members **24** to inject the treatment agent **20**. As FIGS. **1**A and **1**B show, a single tissue piercing member **24** (with a single port **22**) may be used. Alternatively, as FIGS. **2**A and **2**B show, the treatment device **24** can carry multiple tissue piercing members **24**, each with a port **22**. Desirably, the multiple tissue piercing members **24** are arranged in a spaced-apart array, to apply the treatment agent **20** in a prescribed pattern at the targeted site.

[0023] Alternatively, the tissue treatment device **12** may employ air powered, needle-less injection technology.

B. The Delivery Device

[0024] The configuration of the delivery apparatus **14** for the device **12** can also vary, depending upon the accessibility of the treatment site and the particular treatment objectives desired. If the treatment site can be directly visualized the delivery apparatus **14**, the source **18**, and the treatment device **12** can comprise a syringe **100** and a needle **102**, as FIG. **3** shows.

[0025] If the treatment site can not be directly visualized or is otherwise not as readily accessible, the delivery apparatus **14** can comprise an endoscope **106** having an interior lumen **104** passed down the esophagus through the mouth, as FIG. **4** shows. In this arrangement, the treatment device **12** is desirably carried on the distal end of a catheter tube **108** for passage through the endoscope lumen **104** to the targeted site. A guidewire may be used, if desired, to further facilitate deployment of the endoscope and treatment device to the targeted site.

C. The Tissue Treatment Agent

[0026] The treatment agent **20** is selected from a group of candidate agents based upon the physiologic effect or effects that are desired. One or more candidate agents may be applied, either as a primary treatment modality, a neoadjuvent treatment modality, or an adjuvent treatment modality.

[0027] In the illustrated embodiment, the group consists essentially of two candidate agents: (1) Vanilloid Compounds, and (2) Cytokine Sub-Types.

1. Vanilloid Compounds

[0028] The treatment agent **20** can comprise a vanilloid compound. Vanilloid compounds have a unique capacity to bind to a membrane receptor in sensory neurons. Capsaicin is one of many vanilloid compounds. Capsaicin is a powerful basic compound which is derived from chili peppers.

[0029] The specific neuron for capsaicin is deemed "VR**1**". This receptor is expressed only on small unmyelinated C-fibers (nerves typically involved in special visceral sensation and pain).

[0030] Exposure to vanilloid compounds variably reduces the responsiveness of the neuron to stimuli. In many cases, the neuron may actually degenerate either temporarily or permanently, thus impairing transmission of pain signals or other special sensory signals.

[0031] The term "vanilloid compound" as used herein means a compound or a mixture of compounds having a biologically active vanillyl group. vanilloid compounds include both naturally occurring vanilloids, synthetic vanilloids, pharmaceutically acceptable salts of the vanilloid compound (whether natural or synthetic) as well as pharmaceutically acceptable derivatives and/or analogues thereof (whether natural or synthetic). Examples of natural vanilloid compounds include both the crude extracts and the purified extracts of active vanilloid compounds from: capsicum, cayenne pepper, black pepper, paprika, cinnamon, clove, mace, mustard, ginger, turmeric, papaya seed and the cactus-like plant *Euphorbia resinifera*.

[0032] Synthetic vanilloid compounds such as synthetic capsaicin are disclosed in WO 96/40079, which is incorporated herein by reference. The vanilloid compound family includes: Capsaicin; Dihydrocapsaicin: Nordihydrocapsaicin; Homocapsaicin: Homodihydrocapsaicin. Alternatively, resiniferotoxin (RTX) is derived from the euphorbia cactus and is considered a capsaicin-like compound. This substance also activates the VR**1** receptor and attenuates or eliminates afferent nerve function, although it may not illicit the rapid heat sensation that other vanilloids produce.

[0033] Other examples of vanilloid compounds include capsaicin ((E)-(N)-[(4-hydroxy-3-methoxyphenyl)-methyl]-8-methyl-6-nonenamide); eugenol (2-methoxy-4-(2-propenyl)phenol);zingerone (4-(4-hydroxy-3-methoxyphenyl)-2-butanone); curcumin (1,7-bis (4-hydroxy-3-methoxyphenyl)-1, 6-heptadiene-3, 5-dione); piperine (1-[5-(1,3-benzodioxol-5-yl)-1-oxo-2,4-pentadienyl] piperidine); resiniferatoxin(6, 7-deepoxy-6, 7-didehydro-5-deoxy-21-dephenyl-21-(phenylmethyl)-20-(4-hydroxy-3-thoxybenzeneacetate)) or pharmaceutically effective salts, analogues, derivatives or equivalents thereof.

[0034] The treatment agent **20** can include capsaicin, another vanilloid compound, RTX, or combination thereof, alone or in combination with other substances (which will be generically called a vanilloid-containing treatment agent **20**).

[0035] The vanilloid-containing treatment agent can be applied through the port **22** or ports **22** to the mucosal lining or extrinsically to the outside of an organ. The vanilloid-containing treatment agent can also be injected into the targeted tissue region or organ wall.

[0036] The treatment agent **20** can be a solution, a gel, a powder, a pellet, or other form. The treatment agent may be released immediately, or, be a sustained release product such as a slow released implant, slow release gel, coated pellet, microsphere, or other form.

[0037] The vanilloid-containing treatment agent **20** may be applied or injected as primary therapy, or, as a neoadjuvant or adjuvant procedure. For example, RF energy may be used to incite a wound, followed by application of the vanilloid-containing treatment agent to facilitate exuberant wound healing.

[0038] In dyspepsia and irritable bowel syndrome, the use of a vanilloid-containing treatment agent can serve to diminish the pain impulses or could attenuate the dysmotility and alleviate the disease state.

[0039] An example of vanilloid materials that can be used is produced by Afferon and is called RTX, which has been instilled into the lumen of the urinary bladder for the treatment of urge incontinence. There are also several topical, over-the-counter capsaicin products for topical analgesic applications.

2. Cytokine Sub-Types

[0040] The treatment agent **20** can include one or more subtypes of cytokines. A cytokine, in the natural state within the body, is a protein produced and released by a biological cell that has an effect on the local environment surrounding the cell. Cytokines are involved in many cellular processes, such as wound healing. The mechanism of action would depend on the specific cytokine utilized.

[0041] The term "cytokine subtype" as used herein means any polypeptide that affects the functions of other cells, and is a molecule which modulates interactions between cells in the immune or inflammatory response. A cytokine subtype includes, but is not limited to monokines and lymphokines regardless of which cells produce them. For instance, a monokine is generally referred to as being produced and secreted by a mononuclear cell, such as a macrophage and/or monocyte but many other cells produce monokines, such as natural killer cells, fibroblasts, basophils, neutrophils, endothelial cells, brain astrocytes, bone marrow stromal cells, epideral keratinocytes, and B- lymphocytes. Lymphokines are generally referred to as being produced by lymphocyte cells. Examples of cytokine subtypes include, but are not limited to, interleukin-1. (IL-1), tumor necrosis factor-alpha (TNF alpha) and tumor necrosis factor beta (TNF beta).

[0042] Other cytokine subtypes include TGF-β (transforming growth factor β); PDGF (platelet derived growth factor) b-FGF (basic fibroblast growth factor): IGF-1 (insulin-like growth factor 1); EGF (epidermal growth factor); and VEGF. Some of these cytokines are available commercially, could be produced commercially, or can be extracted from a persons harvested platelets (platelet releasates). The effects of a given cytokine upon tissue physiology can include one or more of the following: smooth muscle and fibroblast mitogenic effects (induces division and growth of cells); stimulation of the release of cytokines from other cells; chemoattractant (bringing new healing cells into local region); decrease of collagen enzyme activity allowing collagen to build up; inflammation; and angiogenesis (development of new blood vessels).

[0043] The treatment agent **20** can include a cytokine subtype or combination of cytokine sub-types, alone or in combination with other substances. The cytokine-containing treatment agent can be applied by the port or ports **22** to the tissue or organ wall, or injected into the tissue or organ wall.

[0044] The cytokine-containing treatment agent **20** can be a solution, a gel, a powder, a pellet, or other form. The treatment agent may be released immediately, or, be a sustained release product such as a slow released implant, slow release gel, coated pellet, microsphere, or other form.

[0045] The cytokine-containing agent **20** may be applied or injected as primary therapy, or, as a neoadjuvant or adjuvant procedure. For example, radio frequency (RF) energy may be used to induce the wound healing process, followed by cytokine application to facilitate more exuberant wound healing.

[0046] The application of a single cytokine or mixture thereof, as primary, neoadjuvant, or adjuvant therapy for abnormal tissue conditions (e.g., excess tissue volume) could have the various mechanical and therapeutic effects. With or without an inciting wound event (such as RF), cytokines can serve to initiate the process of healing within the local region. This process includes, but is not limited to, influx of white blood cells and macrophages, stimulation of fibroblast and smooth muscle division and collagen secretion, new blood vessel growth, wound contraction and tightening, maturation of the new or existing collagen framework, and reduced tissue compliance. These tissue effects could improve the compliance and reduce the tissue volume.

[0047] Examples of cytokine materials that can be used include commercially available Regranex, which is recombinant human PDGF-BB. This material has been applied as a gel for promoting the healing of diabetic foot ulcers. Platelet granules contain many of the cytokines listed above, and the cytokines can be extracted with a fairly simple technique (platelet releasates). Platelets (harvested as a pooled platelet product or from autologous donation) provide a source of cytokines for extraction. TGF-β and PDGF are considered to be the most important substances for the purpose of initiating the wound healing process.

[0048] Various features of the invention are set forth in the following claims.

We claim:

1. A method of treating tissue within a body comprising
selecting at least one treatment agent comprising at least one of a vanilloid compound and a cytokine compound,
providing a source of the treatment agent,
deploying through the interior lumen of the endoscope a catheter carrying on its distal end a tissue-piercing element adjacent to a targeted tissue region,
coupling the catheter to the source of the treatment agent, and
applying through the tissue-piercing element the treatment agent into contact with the targeted tissue region.

2. A method according to claim **1**
wherein the applying includes injecting the treatment agent into subsurface tissue in the targeted tissue region.

3. A method according to claim **1**
further including providing a guide wire to facilitate deployment of the catheter.

* * * * *