Endoscopic Sympathectomy Systems and Methods

CROSS-REFERENCE TO RELATED APPLICATION

[0001] The present application is a national stage application of International Application No. PCT/US2013/042847~~an international application~~ which claims benefit of and priority to U.S. Provisional Application Ser. No. 61/652,426 filed on May 29, 2012, entitled "Endoscopic Sympathectomy Systems and Methods", by Landy Toth et al., the entire contents of which are both incorporated by reference herein for all purposes.

BACKGROUND

Technical Field

[0002] The present disclosure relates to the field of minimally invasive sympathectomy. The disclosure relates to methods for locating, monitoring, and/or mapping nerve distributions before, during, and/or following a surgical process. The disclosure relates to systems and methods for monitoring the extent of a surgical process as it pertains to a surgical goal, such as denervation. The invention also relates to endoscopic systems specifically designed for use in nerve monitoring and ablation.

Background

[0003] Congestive heart failure, hypertension, diabetes, and chronic renal failure have many different initial causes; however, all may include some form of renal sympathetic nerve hyperactivity. Renal sympathetic nerves communicate signals with sympathetic centers located in the spinal cord and brain via afferent renal nerve activity, increasing systemic sympathetic tone; meanwhile, through efferent activity, renal nerves and arteries participate in sympathetic hyperactivity in response to signals from the brain, further increasing systemic sympathetic tone.

[0004] Sympathetic activation can initially be beneficial but eventually becomes maladaptive. In a state of sympathetic hyperactivity, a number of pathological events take place: abnormalities of hormonal secretion such as increased catecholamine, renine and angiotensin II levels, increased blood pressure due to peripheral vascular constriction and/or water and sodium retention, renal failure due to impaired glomerular filtration and

sympathetic nervous activity, an electromyographic signal [EMG], a mechanomyographic signal [MMG], a local field potential, an electroacoustic event, vasodialation, vessel wall stiffness, muscle sympathetic nerve activity [MSNA], central sympathetic drive, nerve traffic, combinations thereof, or the like.

[0010] In aspects, one or more sensing tips may include an electrode. In aspects, the electrode may include embossed, plated, and/or filament loaded structures thereupon.

[0011] In aspects, the microsurgical tool may include a microcircuit, electrically coupled with one or more of the sensing tips.

[0011A] In aspects, the sensing tip is electrically coupled with a microcircuit, the microcircuit configured to condition the signal. In aspects, the microcircuit is embedded into the microsurgical tool and at least a portion of the electrical coupling is provided via the elongate structure. In aspects, the microcircuit is embedded into the sensing tip or the elongate structure.

[0012] In aspects, one or more of the sensing tips may include one or more needle electrodes and/or one or more whiskers each of which having a characteristic length and a tip, the needle electrode and/or whiskers arranged so as to extend from the sensing tip into the tissues adjacent thereto. In aspects, one or more of the needle electrodes and/or the whiskers may include electrical insulation along the length thereof and may include an electrically exposed tip. In aspects, one or more sensing tips may include a mechanomyographic (MMG) sensing element configured to generate a mechanomyographic signal (MMG) from the activity, a compliance sensor, configured to generate a tissue tone signal, or the like. In aspects, one or more sensing tips may include a microelectrode configured to interface with the adjacent tissues, the microelectrode having an area of less than 5000 μm^2~~squm~~, less than 1000 μm^2~~squm~~, less than 250 μm^2~~squm~~, less than 100 μm^2~~squm~~, or the like.

[0013] In aspects, the microsurgical tool may include one or more stimulating electrodes, each electrically and mechanically coupled to the elongate structure, the stimulating electrodes configured to provide a stimulating and/or ablating current to the adjacent tissues during use. In aspects, the microsurgical tool may be configured to coordinate stimulating and/or ablating currents between two or more of the stimulating

electrodes via the adjacent tissues. One of more of the sensing tips may be configured so as to monitor the effect of the stimulating and/or ablating current(s) on the adjacent tissues and/or tissues related thereto. In aspects, the stimulating electrodes may have an area of greater than 0.1 mm^2, 0.5 mm^2, 1 mm^2, 2 mm^2, or 10 mm^2. It will be appreciated that, by the word "or", the ranges can be taken separately.

[0014] In aspects, a microsurgical tool in accordance with the present disclosure may include means for delivering a therapeutic substance to the adjacent tissues. In aspects,

one or more sensing tips in accordance with the present disclosure may be configured to monitor the effect of the therapeutic substance on the adjacent tissues or tissues related thereto. In aspects, the therapeutic substance may include a chemical, a drug substance, a neuromodulating substance, a neuroblocking substance, an acid, a base, a denervating agent, or a combination thereof. In aspects, the therapeutic substance may include a ~~neutotoxin~~neurotoxin, a botulinum toxin, a tetrodotoxin, a tetraethylammonium, a chlorotoxin, a curare, a conotoxin, a bungarotoxin, arsenic, ammonia, ethanol, hexane, nitric oxide, glutamate, resiniferatoxin, alchohol, phenol, capaicin, an anesthetic, lidocaine, tetanus toxin, quaternary ammonium salts, a pachycurare, a leptocurare, acetylcholine, aminosteroids, a combination thereof, or the like.

[0015] In aspects, the therapeutic substance may include a restraining matrix, which may or may not be at least partially biodegradable. In aspects, the restraining matrix may include a photopolymerizable polymer, and the microsurgical tool may include a light source, for performing in situ photopolymerization thereof.

[0015A] In aspects, the microsurgical tool may include a clamp, one or more sensing tips and/or stimulating electrodes comprised within the clamp, arranged so as to bias towards the tissues when the clamp is closed thereupon. In aspects, the clamp is configured to controllably close down onto the tissues with a predetermined clamping force. In aspects, wherein the clamp is configured so as to produce a pressure of greater than 20mmHg, 40mmHg, 60mmHg, 80mmHg when closing down onto the tissues. In aspects, one or more sensing tips is configured to monitor the effect of the closing on the adjacent tissues.

[0015B] In aspects, the microsurgical tool includes a self-wrapping tool comprising one or more sensing tips and/or stimulating electrodes, the sensing tips and/or stimulating electrodes arranged so as to bias towards the tissues when the self-wrapping tool is bent there around.

[0016] In aspects, the microsurgical tool may include a clamp, a self-wrapping tool, or the like each in accordance with the present disclosure. In aspects, the self-wrapping tool may include an electroactive material actuator electrically and mechanically coupled to the elongate structure, to provide movement thereof during use.

[0017] In aspects, the self-wrapping tool may include one or more microchannels, the microchannels configured to support a vacuum to provide movement thereof during use, and/or facilitate attachment to the tissues. In aspects, the self-wrapping tool may include one or more tendons, each tendon arranged so as to run along the length of the elongate structure, the tendons arranged so as to provide the movement when pulled during use.

[0017A] In aspects, the microsurgical tool includes means to deliver a feature enhancing medium to the adjacent tissues. In aspects, the feature enhancing medium comprises a visual marking moiety to assist with visualization of a one or more tissue types in the adjacent tissue.

[0018] According to another aspect there is provided, use of a microsurgical tool in accordance with the present disclosure to monitor electrophysiological activity in the vicinity of a vessel, an artery, a vein, a tubule, a renal artery, an organ, a kidney, a spleen, a pancreas, a prostate, a combination thereof, or the like.

[0019] According to yet another aspect there is provided, use of a microsurgical tool in accordance with the present disclosure to perform a surgical procedure.

[0020] According to another aspect there is provided, use of a microsurgical tool in accordance with the present disclosure to perform a renal neuromodulation procedure.

[0021] According to yet another aspect there is provided, a system for neuromodulating an anatomical site in the vicinity of an organ or vessel, including a subsystem configured to perform a surgical procedure on the anatomical site; a microsurgical tool in accordance with the present disclosure configured to monitor electrophysiological activity in the vicinity of the site; and a control unit configured to accept signals from the microsurgical tool, and to adjust the surgical procedure dependent upon the signals, to display the signals, to evaluate the surgical procedure dependent upon the signals, to plan a surgical path dependent upon the signals, and/or to determine the extent of the procedure dependent upon the signals.

[0022] In aspects, the surgical procedure may be selected from an ablation, an excision, a cut, a burn, a radio frequency ablation, a cryoablation, a radiosurgical procedure, delivery of energy, an ultrasonic ablation, an abrasion, a biopsy, delivery of a substance, a combination thereof, or the like.

[0023] In aspects, the system may include a stimulation and/or ablation electrode configured so as to convey a pulsatile and/or radio frequency signal to the anatomical site from the control unit, the microsurgical tool configured to convey one or more feedback signals related to the pulsatile and/or radio frequency signals back to the control unit. In aspects, the feedback signals are related to an electrode impedance, a bioimpedance, a local electrical field, and/or an electrophysiological response to the pulsatile and/or radio frequency signal. In aspects, the stimulation and/or ablation electrode may be included within the microsurgical tool. In aspects, the stimulation and/or ablation electrode is comprised within the sensing tip. In aspects, the control unit is configured to sweep one or more of the sensing tips along the organ or vessel.

[0024] In aspects, the system may be configured to use one or more of the electrophysiological signals to locate the anatomical site.

[0025] In aspects, the control unit may be configured to use one or more of the electrophysiological signals to exclude the anatomical site from a surgical procedure.

[0026] According to yet another aspect there is provided a method for determining an afferent electrophysiological activity and an efferent physiological activity in the vicinity of an organ, including monitoring electrophysiological activity at a plurality of sites within the vicinity of the organ in regions proximal and distal to a target region as

-recording one or more electrophysiological signals from the activity in the vicinity of the electrode.

[0032] In aspects, the method may include recording one or more of an evoked potential, remote stimulation of nervous activity, an electromyographic signal [EMG], a mechanomyographic signal [MMG], a local field potential, an electroacoustic event, vasodialation, vessel wall stiffness, muscle sympathetic nerve activity [MSNA], central sympathetic drive, tissue tone, nerve traffic, combinations thereof, or the like in the vicinity of the electrode.

[0033] In aspects, the method may include electrically isolating the electrode from a cavity of the vessel, embedding the electrode into the wall of the vessel, sweeping the electrode along the wall of the vessel, generating a map of electrophysiological activity from the recordings obtained during the sweep, recording electrophysiological activity from a plurality of electrodes, cancelling one or more movement artifacts from the recordings, and/or biasing a mechanomyographic (MMG) sensing element against the wall of the vessel and recording a mechanomyographic signal (MMG) from the activity.

[0034] In aspects, one or more of the steps may be performed with a microsurgical tool in accordance with the present disclosure.

[0035] According to yet another aspect there is provided, a method for performing controlled neuromodulation in the vicinity of an organ or vessel, including: monitoring electrophysiological activity at one or more sites within the vicinity of the organ or vessel to obtain a first activity level; applying energy to a treatment site within the vicinity of the organ or vessel; monitoring electrophysiological activity at one or more sites within the vicinity of the organ or vessel to obtain a second activity level; and comparing the first activity level and the second activity level to determine if the energy application affected the electrophysiological activity, if sufficient energy was applied, or if further energy should be applied.

[0036] In aspects, the monitored electrophysiological activity comprises one or more of an evoked potential, remote stimulation of nervous activity, an electromyographic signal [EMG], a mechanomyographic signal [MMG], a local field potential, a

electroacoustic event, vasodialation, vessel wall stiffness, muscle sympathetic nerve activity [MSNA], central sympathetic drive, tissue tone, nerve traffic as measured in the vicinity of the organ or vessel.

[0036A] In aspects, the method may include determining if sufficient energy has been applied to the treatment site based on the comparison, evaluating the first activity level to determine a suitable treatment site in the vicinity of the organ or vessel, mapping electrophysiological activity in the vicinity of the organ or vessel using the first activity

level, applying a stimulus in the vicinity of the organ or vessel, recording electrophysiological activity before, during, and/or after the stimulus, recording electrophysiological activity in a proximal region and a distal region measured along the length of the organ or vessel as spaced with respect to the treatment site, to determine if the energy application affected the electrophysiological activity in the vicinity of the treatment site, and/or determining if the energy application was sufficient to form a neural block using the comparison.

[0037] In aspects, the method may include applying sufficient energy (i.e. RF energy, ultrasound energy, thermal energy, microwave energy, radiation, etc.) to the treatment site to form a temporary block and assessing if the change in electrophysiological activity is desirable, if so, applying sufficient energy to the treatment site so as to form a substantially irreversible block. In aspects, wherein the energy is in the form of a radio frequency current, an ultrasonic wave, or thermal energy.

[0038] In aspects, one or more of the steps may be performed using a microsurgical tool in accordance with the present disclosure.

[0039] According to another aspect there is provided, a method for determining a state of a neurological connection along a neurological pathway between one or more regions in a body, including: applying a pacing signal to the wall of a vessel from the outside of the vessel in the vicinity of the neurological pathway; monitoring one or more of water concentration, tone, blood oxygen saturation of local tissues, evoked potential, stimulation/sensing of nervous activity, electromyography, temperature, blood pressure, vasodialation, vessel wall stiffness, muscle sympathetic nerve activity [MSNA], central sympathetic, tissue tone, blood flow, a blood flow differential signal, blood perfusion, a blood analyte level, nerve traffic, or combinations thereof, at one or more sites within the body to generate one or more physiological signals; and evaluating the influence of the pacing signal on the physiological signals and determining the state of neurological connection therefrom.

[0040] In aspects, the method may include applying energy in the vicinity of the vessel so as to induce a neurological block along the neurological pathway, pacing and

monitoring before and after induction of the neurological block, comparing the physiological signals obtained before the neurological block to those obtained during the

vasodialation, vessel wall stiffness, muscle sympathetic nerve activity [MSNA], central sympathetic drive, nerve traffic, or combinations thereof.

[0046] In aspects, one or more of the sensing tips may include one or more needle electrodes and/or one or more whiskers each of which having a characteristic length and a tip, the needle electrode and/or whiskers arranged so as to extend from the sensing tip into the tissues adjacent thereto. In aspects, one or more of the needle electrodes and/or the whiskers may include electrical insulation along the length thereof and/or electrically exposed tips. In aspects, one or more sensing tips may include a microelectrode configured to interface with the adjacent tissues, the microelectrode having an area of less than 5000 μm^2~~squm~~, less than 1000 μm^2~~squm~~, less than 250 μm^2~~squm~~, or less than 100 μm^2~~squm~~.

[0047] In aspects, the implantable device may include one or more stimulating electrodes electrically and mechanically coupled to one or more of the microfingers, the stimulating electrodes configured to provide a stimulating and/or ablating current to the adjacent tissues. Optionally, the microcircuit may be configured to coordinate stimulating and/or ablating currents between two or more of the stimulating electrodes via the adjacent tissues, and/or one or more of the sensing tips may be configured so as to monitor the effect of the stimulating and/or ablating current(s) on the adjacent tissues and/or tissues related thereto.

[0048] In aspects, an implantable device in accordance with the present disclosure may include means for delivering a therapeutic substance in accordance with the present disclosure to the adjacent tissues. In aspects, one or more of the sensing tips may be configured to monitor the effect of the therapeutic substance on the adjacent tissues or tissues related thereto. In aspects, the therapeutic substance is selected from a chemical, a drug substance, a neuromodulating substance, a neuroblocking substance, an acid, a base, a denervating agent, or a combination thereof. In other aspects, the therapeutic substance is a selected from a neurotoxin, a botulinum toxin, a tetrodotoxin, a tetraethylammonium, a chlorotoxin, a curare, a conotoxin, a bungarotoxin, arsenic, ammonia, ethanol, hexane, nitric oxide, glutamate, resiniferatoxin, alchohol, phenol, capaicin, an anesthetic, lidocaine, tetanus toxin, quaternary ammonium salts, a

pachycurare, a leptocurare, acetylcholine, aminosteroids, or a combination thereof. In aspects, the therapeutic substance is comprised within a restraining matrix. In aspects, the restraining matrix is at least partially biodegradable.

BRIEF DESCRIPTION OF THE DRAWINGS

[0049] Several aspects of the disclosure can be better understood with reference to the following drawings. In the drawings, like reference numerals designate corresponding parts throughout the several views.

[0050] Figs. 1a-f show aspects of a surgical tool in accordance with the present disclosure.

present disclosure, which may be configured to perform tasks such as pre-amplification, signal conditioning, RF signal routing, analog to digital conversion, signal buffering, communication with externally located hardware, multiplexing/demultiplexing functions, signal isolation, etc. The circuit 170 may be interconnected 125 with one or more of the hinge ~~130~~120, the clamp 110a, 110b, sensing tips located there upon, etc. The circuit 170 may be interconnected 175 with one or more controllers, interconnects, etc. located at a proximal tip of the arm 130 (i.e. equivalently a delivery catheter, a guidewire, an endoscope, etc.).

[00245] In the example shown in Fig. 1d, the local control circuit 170 is shown attached to the control arm 130 of the surgical tool, but may be placed anywhere on the tool, on the clamp members 110a, 110b, clamp faces 135, etc.

[00246] Fig. 1e shows a aspects of a surgical tool in accordance with the present disclosure interfacing with a vessel 1 (e.g. an artery, a renal artery, etc.). Some aspects of the included electrodes A-E are highlighted so as to demonstrate an aspect of how the device may function during ablation of a target tissue 3 (e.g. here shown as a target nerve). The electrodes to consider in this regard are labeled as sensory electrodes A-D, and ablation electrode pair E (i.e. a biopolar electrode aspect). The configuration shown in Fig. 1e is just to highlight some of the functionality of the system in practice. Each of the electrodes A-E are provided in communication with an external controller, interconnect, a microcircuit, or the like provided by one or more interconnects 125 arranged within the surgical tool.

[00247] Fig. 1f shows a time graph of signals to demonstrate a non-limiting example of how the clamp shown in Fig. 1e may be used in practice. To the left of the graph, one can see electrograms taken from electrodes A-D with respect to a reference electrode (e.g. a macro-electrode, a reference on the clamp, etc.). Before the ablation signal is applied, one can see significant activity in the vicinity of electrodes A and B, indicating the presence of the target nerve nearby. The signals 185 and 190 monitored at electrodes A and B may be indicative of an overactive nerve (i.e. if nerve activity exceeds a known threshold value, etc.) and thus may be considered directly to determine if the

nerve is the right target for a surgical procedure. Additionally, alternatively, or in combination, the

relationship between signals A and B may be used to determine the direction of signal traffic along the target nerve, perhaps to determine if it is the right target for a surgical procedure.

[00248] After application of an ablation current, represented as signal 195, to the ablation electrode pair E, a change in the signals as monitored by electrode A and B can be seen. In the example shown, the nerve activity at electrode B has decreased significantly indicating that the denervation procedure affected the target nerve and has successfully completed the denervation of the nerve.

[00249] Figs. 2a-b show aspects of non-limiting examples of stimulation and monitored procedures of electrophysiological signals in accordance with the present disclosure. Fig 2a shows the signal B obtained at a monitoring location within the body during a procedure. The signal shows the stimulus pulse 201 followed by the evoked response 205 from the nerve in question. Evident from the figure is the latency, amplitude, and character of the evoked response 205. One or more of these aspects may be used to determine the effectiveness or state of completion of a surgical procedure applied to the nerve under study.

[00250] Fig. 2b shows aspects of a non-limiting example of monitoring an evoked nervous response at a monitoring location in response to a stimulus applied at a stimulating location within the body. The stimulus 220 is shown as a sequentially applied train of pulses and the monitored evoked response is shown before 210 and after a partial completion 215 of a surgical procedure (given the same stimulus pulse train). As shown, a change in the frequency characteristics can be seen in the signal response after the procedure has been at least partially completed. Demonstrated examples of changes include a shift in the frequency response 230 of the evoked potential spectrum, and changes over a region 225 of the spectrum indicative of changing functionality of the associated anatomical features (i.e. the nerves under study). Such changes may be used to determine if the surgical procedure is being applied to the proper target tissues, if the procedure is effectively completed or if further procedure is necessary.

[00251] Additionally, alternatively, or in combination, the stimulus may result from a sequence of input pulses, perhaps caused by an associated ablation procedure (e.g. as

decision if it is completed. The method includes making a decision as to if the overall surgery is completed. If it is not complete the method includes moving (i.e. so as to remove the tool from the anatomical site, move to another target location, etc.) the tool to another target surgical site, and/or selecting another set of electrodes to test for the presence of a target tissue. If the overall procedure is complete, the method includes detaching the tool from the surgical site. Further aspects of such methods are discussed throughout the present disclosure.

[00254] Figs. 4a-b show aspects of signals associated with a method for monitoring electrophysiological activity at one or more locations on a body in accordance with the present disclosure. Fig. 4a shows an exemplar pulse train 405, highlighting various aspects that may be adjusted during a surgical intervention so as to better elucidate the physiological signals from at a monitoring location. A non-limiting example of the pulse train characteristics that may be varied to highlight characteristics of the evoked response include the amplitude 420, pulse spacing 415, pulse width 410, the number of pulses, etc. Other aspects of suitable stimulation signals are discussed throughout the present disclosure.

[00255] Fig. 4b shows an electrophysiological response measured at a monitoring location in accordance with the present disclosure. The time characteristics of the evoked response demonstrates aspects of the sensed signal such as latency 425, amplitude 430, and character (frequency content, signal shape, etc.) that may change as surgical procedure is performed on the target tissues. Other aspects of the evoked signal responses are discussed throughout the present disclosure.

[00256] Figs. 5a-b show aspects of a multi-tool surgical system for performing a surgical procedure in accordance with the present disclosure. The system includes a plurality of self-wrapping tools 510a, 510b (in this case, two self-wrapping tools), arranged around the circumference of a target anatomical structure 1 (in this case, a renal artery), and a surgical tool for applying a surgical procedure ~~530~~ (in this case an ablation procedure) at one or more surgical locations along the vessel 1. Each self-wrapping tool 510a, 510b includes a plurality of electrodes a-d, A-D for interfacing with the adjacent tissue (here labeled electrodes a-d and electrodes A-D). A target nerve is shown on the

on the body (such as an entry port, etc.). The tether 1430 may include means for electrically communicating between an externally placed device and the interfacing potion of the tool 1420 and/or sensing tips include therein. The tether 1430 may include a lubricous coating to substantially limit bonding between the tether 1430 and adjacent tissues during the placement period. The interfacing portion of the tool 1420 may be equipped to monitor one or more physiological parameters of the adjacent anatomical structure for a prolonged period following placement. A plurality of sensing tips within the interfacing portion of the tool 1420 may be arranged so as to more precisely monitor activity of target anatomy 12, which may be arranged heterogeneously about the target anatomical site 11.

[00279] The second implantable surgical tool 1440 shown in Fig. 14 includes means for wirelessly communicating 1450 with an extracorporeal reader, so as to remotely monitor the surgical site 11 for prolonged periods of time without the need for physical access to the site during the monitoring period. Such an implantable tool 1440 may include a plurality of sensing tips, a microcircuit, etc. each in accordance with the present disclosure. The implantable tool 1440 may further include a power source, or means for harvesting energy from a provided signal (i.e. an RF signal), local kinetic motion, undulation of the underlying anatomical structure 11, or the like. Further aspects of implantable surgical tools 1420, 1440 are discussed elsewhere in the present disclosure.

[00280] Figs 15a-b show aspects of an implantable and at least partially biodegradable surgical tool in accordance with the present disclosure. Fig. 15a shows an implantable surgical tool in accordance with the present disclosure including a clip 1510a, 1510b, 1520 arranged with one or more sensing tips 1535. The implantable surgical tool also includes a biodegradable material (i.e. in this case shown the regions of the clip 1510a, 1510b), configured so as to degrade over a period of time after placement thereof within the body. An optional tether 1540 is attached to the clip 1510a, 1510b, 1520 via a substrate 1530, 1520, the substrate configured to interconnect 1525 one or more of the sensing tips 1535 with a controller, microcircuit, etc. The tether 1540 may be configured to access an extracorporeal reader, an extracorporeal port, a body port, etc. The tether 1540 may be configured for easy removal 1560 of the implantable tool after the monitoring

present disclosure. In aspects, the tissue interfacing tool 2030 may be electrically interconnected 2025 with a controller, a microcircuit, an operator, an interconnect, etc.

[00297] Fig. 20b shows aspects of a non-limiting example of a tissue interfacing tool 2010 in accordance with the present disclosure. The tool 2010 includes a row of electrode elements 2030 arranged so as to cover at least a portion of an adjacent vessel during use (optionally in a circumferential direction, a longitudinal direction, etc.). Other aspects of such tools are discussed elsewhere in the present disclosure.

[00298] Fig. 20c show aspects of a non-limiting example of a tissue interfacing tool 2050 in accordance with the present disclosure. The tool 2050 includes multiple rows of electrode elements 2055, 2060 arranged so as to cover at least a portion of an adjacent vessel during use (optionally in a circumferential direction, a longitudinal direction, etc.). Other aspects of such tools are discussed elsewhere in the present disclosure.

[00299] The interfacing tool 2050 includes a local control circuit 2070 in accordance with the present disclosure. In this non-limiting example, the local control circuit 2070 is configured to multiplex, pre-amplify, and/or digitize signals obtained 2065 from one or more electrodes 2055, 2060 on the tissue interfacing tool 2050 and to communicate 2075 with an external controller, interconnect, operator, etc. during use.

[00300] Figs. 21a-b show aspects of an implantable device for sustained release of a neuromodulating substance in accordance with the present disclosure. Fig. 21a shows an implantable device 2105 placed in the vicinity of a renal artery 20 as part of a procedure in accordance with the present disclosure (i.e. as part of a denervation procedure). In aspects, such an implantable device 2105 may be placed by a surgical tool in accordance with the present disclosure. In aspects, the implantable device 2105 may include a neuromodulating substance 2109, perhaps confined in a retaining medium (i.e. a hydrogel matrix, etc.) and may leach into the surrounding tissues over time, after placement during a surgical procedure. In aspects, the neuromodulating substance may be a potent denervating agent (i.e. a ~~neutotoxin~~neurotoxin, a botulinum toxin, a tetrodotoxin, a tetraethylammonium, a chlorotoxin, a curare, a conotoxin, a bungarotoxin, arsenic, ammonia, ethanol, hexane, nitric oxide, glutamate, resiniferatoxin, alchohol, phenol,

etc.), a neuroblocking agent (capaicin, an anesthetic, lidocaine, tetanus toxin, quaternary ammonium salts, a pachycurare, a leptocurare, acetylcholine, aminosteroids, etc.).

[00301] In aspects, the implantable device 2105 may be injected into the body and cross-linked in place in order to form the final structure. The retaining medium may be configured so as to crosslink via a radial polymerization procedure (i.e. photopolymerization), a click polymerization procedure (i.e. an oxime click chemistry based hydrogel), or the like. Such form-in-place hydrogels known in the art of bioscaffold formation and bioadhesives may be adapted for use in this application.

[00302] In aspects, the retaining medium may be configured with one or more biodegradable aspects, such that over time (i.e. in a controlled fashion), the retaining medium may breakdown and further neuromodulating substance may be released into the surrounding tissues.

[00303] Fig. 21b shows an implantable device 21242 including a neuromodulating substance 21224 in accordance with the present disclosure placed within the renal pelvis of a kidney 24. In aspects, the implantable device 21242 may have been placed 2126, injected, or formed in place via access through the ureter 23, through the wall of the kidney 24, etc. In aspects, the implantable device 21242 may be formed with a shape (i.e. a cage, a horned shape, etc.) so as to improve retention of the implanted device within the renal pelvis of the kidney 24. The implantable device 21242 may include a retaining medium in accordance with the present disclosure for providing a controlled release of the neuromodulating substance into the renal pelvis of the kidney 24.

[00304] In aspects, the implantable devices discussed in Figs. 21a,b may be combined with the implantable devices discussed in Figs. 14, 15a,b, 22, etc. in order to provide a means for monitoring the effect of the neuromodulating substance over time, for following up on a surgical procedure, etc.

[00305] Fig. 22 shows aspects of an implantable device for monitoring and/or modulating neural activity in accordance with the present disclosure. The implantable device includes one or more microfingers 2210 each in accordance with the present disclosure. Each microfinger includes one or more sensing tips 2215a-d configured so as to monitor one or physical or physiological parameters in the vicinity thereof during a

5. The microsurgical tool in accordance with any preceding claim, wherein the sensing tip is electrically coupled with a microcircuit, the microcircuit configured to condition the signal.

6. The microsurgical tool in accordance with claim 5, wherein the microcircuit is embedded into the microsurgical tool and at least a portion of the electrical coupling is provided via the elongate structure.

7. The microsurgical tool in accordance with claim 6, wherein the microcircuit is embedded into the sensing tip or the elongate structure.

8. The microsurgical tool in accordance with any preceding claim, wherein: one or more sensing tips comprises one or more needle electrodes and/or one or more whiskers each of which having a characteristic length and a tip, the needle electrode and/or whiskers arranged so as to extend from the sensing tip into the tissues adjacent thereto.

9. The microsurgical tool in accordance with claim 8, wherein one or more of the needle electrodes and/or the whiskers comprise electrical insulation along the length thereof and electrically exposed tips.

~~10. The microsurgical tool in accordance with any preceding claim, wherein one or more sensing tips comprise a mechanomyographic (MMG) sensing element configured to generate a mechanomyographic signal (MMG) from the activity.~~

~~11. The microsurgical tool in accordance with any preceding claim, wherein one or more sensing tips comprise a compliance sensor, configured to generate a tissue tone signal.~~

~~12.~~10. The microsurgical tool in accordance with any preceding claim, wherein one or more sensing tips comprise a microelectrode configured to interface with the adjacent tissues, the microelectrode having an area of less than 5000squm, less than 1000squm, less than 250squm, or less than 100squm.

~~13.~~11. The microsurgical tool in accordance with any preceding claim, comprising one or more stimulating electrodes electrically and mechanically coupled to the elongate structure, the stimulating electrodes configured to provide a stimulating and/or ablating current to the adjacent tissues.

~~14.~~12. The microsurgical tool in accordance with claim ~~13~~11, comprising a plurality of stimulating electrodes, the microsurgical tool configured to coordinate stimulating and/or ablating currents between two or more of the stimulating electrodes via the adjacent tissues.

~~15.~~13. The microsurgical tool in accordance with claim ~~13~~-11 or ~~14~~12, the sensing tip configured so as to monitor the effect of the stimulating and/or ablating current(s) on the adjacent tissues and/or tissues related thereto.

~~16.~~14. The microsurgical tool in accordance with any one of claims ~~13~~-11 – ~~15~~13, wherein the stimulating electrodes have an area of greater than 0.1sqmm~~, 0.5sqmm, 1sqmm, 2sqmm, or 10sqmm~~.

~~17.~~15. The microsurgical tool in accordance with any preceding claim comprising means for delivering a therapeutic substance to the adjacent tissues.

~~18.~~16. The microsurgical tool in accordance with claim ~~17~~-15 wherein the sensing tip is configured to monitor the effect of the therapeutic substance on the adjacent tissues or tissues related thereto.

~~19.~~17. The microsurgical tool in accordance with claim ~~17~~15 or ~~18~~16, wherein the therapeutic substance is selected from a chemical, a drug substance, a neuromodulating substance, a neuroblocking substance, an acid, a base, a denervating agent, or a combination thereof.

~~20.~~18. The microsurgical tool in accordance with any one of claims ~~17~~15 – ~~19~~17, wherein the therapeutic substance is a selected from a ~~neutotoxin~~neurotoxin, a botulinum toxin, a tetrodotoxin, a tetraethylammonium, a chlorotoxin, a curare, a conotoxin, a bungarotoxin, arsenic, ammonia, ethanol, hexane, nitric oxide, glutamate, resiniferatoxin, alchohol, phenol, capaicin, an anesthetic, lidocaine, tetanus toxin, quaternary ammonium salts, a pachycurare, a leptocurare, acetylcholine, aminosteroids, or a combination thereof.

~~21.~~19. The microsurgical tool in accordance with any one of claims ~~17~~15 – ~~20~~18, wherein the therapeutic substance is comprised within a restraining matrix.

~~22.~~20. The microsurgical tool in accordance with claim ~~21~~19, wherein the restraining matrix is at least partially biodegradable.

~~23. The microsurgical tool in accordance with claim 21 or 22, wherein the restraining matrix comprises a photopolymerizable polymer and the microsurgical tool comprises a light source electrically and mechanically coupled to the elongate structure, for performing in situ photopolymerization thereof.~~

~~24. The microsurgical tool in accordance with any preceding claim, comprising a clamp, one or more sensing tips and/or stimulating electrodes (when in accordance with any one of claims 13 – 16) comprised within the clamp, arranged so as to bias towards the tissues when the clamp is closed thereupon.~~

~~25. The microsurgical tool in accordance with claim 24, wherein the clamp is configured to controllably close down onto the tissues with a predetermine clamping force.~~

~~26. The microsurgical tool in accordance with claim 24 or 25, wherein the clamp is configured so as to produce a pressure of greater than 20mmHg, 40mmHg, 60mmHg, 80mmHg when closing down onto the tissues.~~

~~27. The microsurgical tool in accordance with any one of claims 24—26, wherein one or more sensing tips is configured to monitor the effect of the closing on the adjacent tissues.~~

~~28. The microsurgical tool in accordance with any preceding claim, comprising a self-wrapping tool comprising one or more sensing tips and/or stimulating electrodes, the sensing tips and/or stimulating electrodes arranged so as to bias towards the tissues when the self-wrapping tool is bent there around.~~

~~29. The microsurgical tool in accordance with claim 28, wherein the self-wrapping tool comprises an electroactive material actuator electrically and mechanically coupled to the elongate structure, to provide movement thereof during use.~~

~~30. The microsurgical tool in accordance with claim 28, wherein the self-wrapping tool includes one or more microchannels, the microchannels configured to support a vacuum to provide movement thereof during use, and/or facilitate attachment to the tissues.~~

~~31. The microsurgical tool in accordance with claim 28, wherein the self-wrapping tool includes one or more tendons, each tendon arranged so as to run along the~~

~~length of the elongate structure, the tendons arranged so as to provide the movement when pulled during use.~~

~~32. The microsurgical tool in accordance with any preceding claim, comprising means to deliver a feature enhancing medium to the adjacent tissues.~~

~~33. The microsurgical tool in accordance with claim 32, wherein the feature enhancing medium comprises a visual marking moiety to assist with visualization of a one or more tissue types in the adjacent tissue.~~

~~34. Use of a microsurgical tool in accordance with any one of claims 1—33, to monitor electrophysiological activity in the vicinity of a vessel, an artery, a vein, a tubule, a renal artery, an organ, a kidney, a spleen, a pancreas, a prostate, or a combination thereof.~~

~~35. Use of a microsurgical tool in accordance with any one of claims 1—33, to perform a surgical procedure.~~

~~36. Use of a microsurgical tool in accordance with any one of claims 1—33, to perform a renal neuromodulation procedure.~~

~~37. A system for neuromodulating an anatomical site in the vicinity of an organ or vessel, comprising:~~

- ~~a subsystem configured to perform a surgical procedure on the anatomical site;~~
- ~~a microsurgical tool in accordance with any one of claims 1—33, configured to monitor electrophysiological activity in the vicinity of the site; and~~

~~a control unit configured to accept signals from the microsurgical tool, and to adjust the surgical procedure dependent upon the signals, to display the signals, to evaluate the surgical procedure dependent upon the signals, to plan a surgical path dependent upon the signals, and/or to determine the extent of the procedure dependent upon the signals.~~

~~38. The system in accordance with claim 37, wherein the surgical procedure is selected from an ablation, an excision, a cut, a burn, a radio frequency ablation, a cryoablation, a radiosurgical procedure, delivery of energy, an ultrasonic ablation, an abrasion, a biopsy, delivery of a substance, or a combination thereof.~~

~~39. The system in accordance with claim 37 or 38, comprising a stimulation and/or ablation electrode configured so as to convey a pulsatile and/or radio frequency signal to the anatomical site from the control unit, the microsurgical tool configured to convey one or more feedback signals related to the pulsatile and/or radio frequency signals back to the control unit.~~

~~40. The system in accordance with claim 39, wherein the feedback signals are related to an electrode impedance, a bioimpedance, a local electrical field, and/or an electrophysiological response to the pulsatile and/or radio frequency signal.~~

~~41. The system in accordance with any one of claims 37-40, wherein the stimulation and/or ablation electrode is comprised within the microsurgical tool.~~

~~42. The system in accordance with claim 41, wherein the stimulation and/or ablation electrode is comprised within the sensing tip.~~

~~43. The system in accordance with any one of claims 37-42, wherein the control unit is configured to sweep one or more of the sensing tips along the organ or vessel.~~

~~44. The system in accordance with any one of claims 37-43, wherein the control unit is configured to use one or more of the electrophysiological signals to locate the anatomical site.~~

~~45. The system in accordance with any one of claims 37-44, wherein the control unit is configured to use one or more of the electrophysiological signals to exclude the anatomical site from a surgical procedure.~~

~~46.~~21. A method for determining an afferent electrophysiological activity and an efferent physiological activity in the vicinity of an organ, comprising:

- monitoring electrophysiological activity at a plurality of sites within the vicinity of the organ in regions proximal and distal to a target region as measured along a length of the organ or the location of the organ in relation to a connected neurological structure;
- applying energy to a site within the target region to form a neurological block thereby; and
- extracting an afferent signal from activity in the distal region and an efferent signal from activity in the proximal region.

~~47.~~22. The method in accordance with claim ~~46~~21, comprising comparing activity measured in the proximal region and the distal region to determine if the energy application affected the electrophysiological activity in the vicinity of the target region.

~~48.~~23. The method in accordance with claim ~~47~~22, comprising evaluating the coherence between activities measured in the proximal region and the distal region.

~~49.~~24. The method in accordance with claim ~~48~~23, comprising using the coherence to evaluate the extent of the neural block.

~~50. The method in accordance with any one of claims 46 – 49, wherein the application of energy is sufficient to form a temporary neural block.~~

~~51.~~25. The method in accordance with claim ~~50~~24, comprising comparing activities from the proximal region and the distal region during the temporary neural block ~~and diagnosing a neurological condition, evaluating a neurological state, or determining if a permanent surgical procedure is required~~to determine at least one of a bioimpedance, an evoked potential, neural activity, an electromyographic signal, an electrocardiographic signal, a mechanomyographic signal, a local field potential, nervous activity, blood perfusion, tissue oxygenation, tissue carbon dioxide levels, local temperatures, tissue tonal changes and muscular sympathetic nerve activity.

~~52. A method for evaluating sympathetic tone of a subject, comprising:~~

~~– inserting a microsurgical tool in accordance with any one of claims 1 – 33 into the subject within the vicinity of a target organ or vessel;~~

~~– recording the electrophysiological signals conveyed by the microsurgical tool;~~

~~– removing the microsurgical tool from the subject; and~~

~~– generating a metric relating to sympathetic tone from the recorded signals.~~

~~53. The method in accordance with claim 52, comprising monitoring another physiological parameter remotely from the target organ or vessel to generate a corrective~~

~~signal and using the corrective signal to remove movement artifacts from the electrophysiological signals.~~

~~54. The method in accordance with one of claims 52 or 53, comprising stimulating one or more anatomical sites in the subject during the recording.~~

~~55. The method in accordance with any one of claims 52 – 54, comprising diagnosing a medical condition based at least in part upon the metric.~~

~~56.~~26. A method for monitoring and/or evaluating electrophysiological activity in the vicinity of a vessel, comprising:

- biasing an electrode against a wall of the vessel from the outside of the vessel; and
- recording one or more electrophysiological signals from the activity in the vicinity of the electrode.

~~57.~~27. The method in accordance with claim ~~56~~26, comprising recording one or more of an evoked potential, remote stimulation of nervous activity, an electromyographic signal [EMG], a mechanomyographic signal [MMG], a local field potential, an electroacoustic event, vasodialation, vessel wall stiffness, muscle sympathetic nerve activity [MSNA], central sympathetic drive, tissue tone, nerve traffic, or combinations thereof in the vicinity of the electrode.

~~58. The method in accordance with claim 56 or 57, comprising electrically isolating the electrode from a cavity of the vessel.~~

~~59. The method in accordance with any one of claims 56 – 58, comprising embedding the electrode into the wall of the vessel.~~

~~60. The method in accordance with any one of claims 56-59, comprising sweeping the electrode along the wall of the vessel.~~

~~61. The method in accordance with claim 60 comprising generating a map of electrophysiological activity from the recordings obtained during the sweep.~~

~~62.~~28. The method in accordance with ~~any one of claims 56—61~~ claim 26 or 27 comprising recording electrophysiological activity from a plurality of electrodes.

~~63.~~29. The method in accordance with any one of claims ~~56~~ 26 – ~~62~~ 28 comprising cancelling one or more movement artifacts from the recordings.

~~64. The method in accordance with any one of claims 56—63 comprising biasing a mechanomyographic (MMG) sensing element against the wall of the vessel and recording a mechanomyographic signal (MMG) from the activity.~~

~~65. The method in accordance with any one of claims 56—64 wherein one or more of the steps are performed using a microsurgical tool in accordance with any one of claims 1—33.~~

~~66. A method for performing controlled neuromodulation in the vicinity of an organ or vessel, comprising:~~

~~— monitoring electrophysiological activity at one or more sites within the vicinity of the organ or vessel to obtain a first activity level;~~

~~— applying energy to a treatment site within the vicinity of the organ or vessel;~~

~~— monitoring electrophysiological activity at one or more sites within the vicinity of the organ or vessel to obtain a second activity level; and~~

~~comparing the first activity level and the second activity level to determine if the energy application affected the electrophysiological activity, if sufficient energy was applied, or if further energy should be applied.~~

~~67. The method in accordance with claim 66 wherein the monitored electrophysiological activity comprises one or more of an evoked potential, remote stimulation of nervous activity, an electromyographic signal [EMG], a mechanomyographic signal [MMG], a local field potential, an electroacoustic event, vasodialation, vessel wall stiffness, muscle sympathetic nerve activity [MSNA], central sympathetic drive, tissue tone, nerve traffic as measured in the vicinity of the organ or vessel.~~

~~68. The method in accordance with claim 66 or 67, comprising determining if sufficient energy has been applied to the treatment site based on the comparison.~~

~~69. The method in accordance with any one of claims 65-66 comprising evaluating the first activity level to determine a suitable treatment site in the vicinity of the organ or vessel.~~

~~70. The method in accordance with any one of claims 65-69 comprising mapping electrophysiological activity in the vicinity of the organ or vessel using the first activity level.~~

~~71. The method in accordance with any one of claims 65-69 comprising applying a stimulus in the vicinity of the organ or vessel.~~

~~72. The method in accordance with claim 71 comprising recording electrophysiological activity before, during, and/or after the stimulus.~~

~~73. The method in accordance with any one of claims 65—72 comprising recording electrophysiological activity in a proximal region and a distal region measured along the length of the organ or vessel as spaced with respect to the treatment site, to determine if the energy application affected the electrophysiological activity in the vicinity of the treatment site.~~

~~74. The method in accordance with any one of claims 65—73 comprising determining if the energy application was sufficient to form a neural block using the comparison.~~

~~75. The method in accordance with claim 74 comprising applying sufficient energy to the treatment site to form a temporary block and assessing if the change in electrophysiological activity is desirable, if so, applying sufficient energy to the treatment site so as to form a substantially irreversible block.~~

~~76. The method in accordance with any one of claims 65—75 wherein the energy is in the form of a radio frequency current, an ultrasonic wave, or thermal energy.~~

~~77. The method in accordance with any one of claims 65—76 wherein one or more of the steps are performed using a microsurgical tool in accordance with any one of claims 1—33.~~

~~78. A method for determining a state of a neurological connection along a neurological pathway between one or more regions in a body, comprising:~~

~~applying a pacing signal to the wall of a vessel from the outside of the vessel in the vicinity of the neurological pathway;~~

~~monitoring one or more of water concentration, tone, blood oxygen saturation of local tissues, evoked potential, stimulation/sensing of~~

~~nervous activity, electromyography, temperature, blood pressure, vasodialation, vessel wall stiffness, muscle sympathetic nerve activity [MSNA], central sympathetic, tissue tone, blood flow, a blood flow differential signal, blood perfusion, a blood analyte level, nerve traffic, or combinations thereof, at one or more sites within the body to generate one or more physiological signals; and~~

~~evaluating the influence of the pacing signal on the physiological signals and determining the state of neurological connection therefrom.~~

~~79. The method in accordance with claim 78, comprising applying energy in the vicinity of the vessel so as to induce a neurological block along the neurological pathway.~~

~~80. The method in accordance with claim 79, comprising pacing and monitoring before and after induction of the neurological block.~~

~~81. The method in accordance with claim 80, comprising comparing the physiological signals obtained before the neurological block to those obtained during the neurological block to determine the influence of the neurological block there upon.~~

~~82. The method in accordance with any one of claims 79—81, comprising determining if the neurological block is favorable in terms of treating an underlying disease state in the body.~~

~~83. The method in accordance with any one of claims 78—82, comprising applying energy in the vicinity of the vessel so as to induce a substantially permanent neurological block along the neurological pathway.~~

~~84. The method in accordance with any one of claims 78—83, comprising monitoring electrophysiological activity at a plurality of sites in the vicinity of the vessel in regions proximal and distal to the pacing site and/or to the site of a suspected or known neurological block.~~

~~85. The method in accordance with claim 84, comprising extracting an afferent signal from activity in the distal region and an efferent signal from activity in the proximal region.~~

~~86. The method in accordance with claim 85, comprising comparing activity measured in the proximal region and the distal region to determine if the energy application affected the electrophysiological activity in the vicinity of the target region.~~

~~87. The method in accordance with any one of claims 78—86 wherein one or more of the steps are performed using a microsurgical tool in accordance with any one of claims 1—33.~~

~~88. Use of a method in accordance with any one of claims 78—87 for evaluation of the effectiveness of a neuromodulation procedure within a body.~~

~~89. An implatable device for monitoring electrophysiological activity within the vicinity of an organ within a body, the implantable device comprising:~~

- ~~a housing comprising a microcircuit configured acquire and communicate signals, and a power supply or energy harvesting element;~~
- ~~one or more microfingers attached to the housing, configured so as to extend from housing to the vicinity of the organ; and~~
- ~~one or more sensing tips electrically and mechanically coupled to one or more of the microfingers, configured to interface with tissues in the~~

~~vicinity of the organ, the sensing tips configured to convey one or more electrophysiological signals associated with the activity to the microcircuit.~~

~~90. The implantable device in accordance with claim 89, wherein the electrophysiological signals are related to one or more of water concentration, tissue tone, evoked potential, remotely stimulated nervous activity, sympathetic nervous activity, an electromyographic signal [EMG], a mechanomyographic signal [MMG], a local field potential, an electroacoustic event, vasodialation, vessel wall stiffness, muscle sympathetic nerve activity [MSNA], central sympathetic drive, nerve traffic, or combinations thereof.~~

~~91. The implantable device in accordance with claim 89 or 90, wherein one or more of the sensing tips comprises one or more needle electrodes and/or one or more whiskers each of which having a characteristic length and a tip, the needle electrode and/or whiskers arranged so as to extend from the sensing tip into the tissues adjacent thereto.~~

~~92. The implantable device in accordance with claim 91, wherein one or more of the needle electrodes and/or the whiskers comprise electrical insulation along the length thereof and electrically exposed tips.~~

~~93. The implantable device in accordance with any one of claims 89—92, wherein one or more sensing tips comprise a microelectrode configured to interface with the adjacent tissues, the microelectrode having an area of less than 5000squm, less than 1000squm, less than 250squm, or less than 100squm.~~

~~94. The implantable device in accordance with any one of claims 89 – 93, comprising one or more stimulating electrodes electrically and mechanically coupled to one or more of the microfingers, the stimulating electrodes configured to provide a stimulating and/or ablating current to the adjacent tissues.~~

~~95. The implantable device in accordance with any one of claims 89 – 94, comprising a plurality of stimulating electrodes, the microcircuit configured to coordinate stimulating and/or ablating currents between two or more of the stimulating electrodes via the adjacent tissues.~~

~~96. The implantable device in accordance with any one of claims 89 – 95, one or more of the sensing tips configured so as to monitor the effect of the stimulating and/or ablating current(s) on the adjacent tissues and/or tissues related thereto.~~

~~97. The implantable device in accordance with any one of claims 89 – 96, comprising means for delivering a therapeutic substance to the adjacent tissues.~~

~~98. The implantable device in accordance with any one of claims 89 – 97, wherein one or more of the sensing tips is configured to monitor the effect of the therapeutic substance on the adjacent tissues or tissues related thereto.~~

~~99. The implantable device in accordance with any one of claims 89 – 98, wherein the therapeutic substance is selected from a chemical, a drug substance, a neuromodulating substance, a neuroblocking substance, an acid, a base, a denervating agent, or a combination thereof.~~

~~100. The implantable device in accordance with any one of claims 89 – 99, wherein the therapeutic substance is a selected from a neutotoxin, a botulinum toxin, a tetrodotoxin, a tetraethylammonium, a chlorotoxin, a curare, a conotoxin, a~~

~~bungarotoxin, arsenic, ammonia, ethanol, hexane, nitric oxide, glutamate, resiniferatoxin, alchohol, phenol, capaicin, an anesthetic, lidocaine, tetanus toxin, quaternary ammonium salts, a pachycurare, a leptocurare, acetylcholine, aminosteroids, or a combination thereof.~~

~~101. The implantable device in accordance with any one of claims 89–100, wherein the therapeutic substance is comprised within a restraining matrix.~~

~~102. The implantable device in accordance with any one of claims 89–101, wherein the restraining matrix is at least partially biodegradable.~~