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- (54) **Title:** AN APPARATUS AND METHOD FOR FACILITATING TREATMENT OF TISSUE

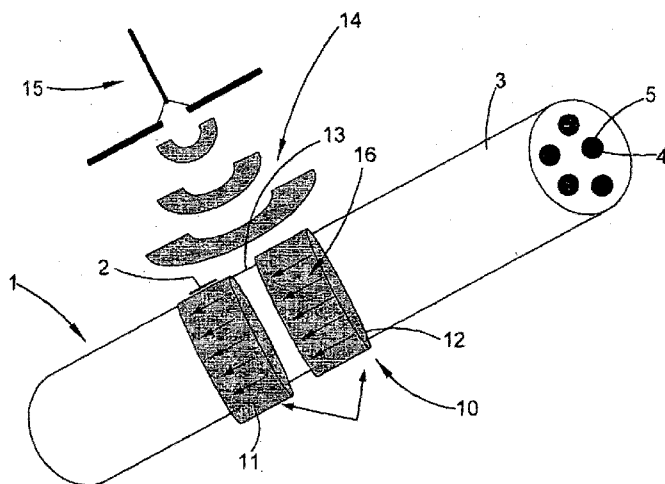


FIGURE 2

(57) **Abstract:** The present invention relates to an apparatus and method for facilitating treatment of nerve tissue. An apparatus body, in the form of a bio-compatible conduit, is placed about a nerve lesion. An antenna arrangement implanted in the patient is arranged to receive RF signals and induce a stimulating current in the bio-compatible conduit. The stimulating current electrically stimulates the nerve endings and promotes growth.



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AN APPARATUS AND METHOD FOR FACILITATING TREATMENT OF TISSUE

Field of the Invention

5

The present invention relates to an apparatus and method for facilitating treatment of tissue and, particularly, but not exclusively, to a method and apparatus, for facilitating repair of nerve tissue.

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Background of the Invention

Nervous injury, from trauma, disease or otherwise, is a major medical problem. Mature neurons do not undergo
15 cell division and therefore it is very difficult to achieve successful rehabilitation after nerve injuries. It is known, however, that where the injury causes gaps in axons, it is possible for the axons to regenerate over the gaps, such that a proximal and distal axon stump can
20 reconnect. This occurs slowly, however, and with difficulty. Where the gap is too large, or the injury too extensive in another manner, regeneration to bridge the gap may not occur at all.

It is known to surgically suture nerve endings.
25 Suturing success is limited, however, and depends much on the nature and extent of the injury and the skill of the surgeon. Where the gap between the proximal and distal ends of the nerve is too great, suturing will not be an option.

30 It is known to use grafting techniques to insert a segment of nerve to bridge a gap. Autograft and allograft

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techniques are used and both have their problems. Autografts are associated with limited availability of nervous tissue for grafting, and permanent de-nervation of the donor site. Allografts require immunosuppressant
5 drugs and have been reported to have a poor clinical success rate.

It is also known to use grafts of tissue to provide conduits across a gap between the distal and the proximal nerve stumps, to allow the nerve to regenerate along the
10 conduit. The conduit, which may be of biocompatible materials, such as collagen, or non-biocompatible materials such as silicon, is grafted to the proximal and distal ends of the nerve stumps. Grafting can be via laser welding, soldering or use of chitosan or other
15 bioadhesives.

The grafts can be non-resorbable or biodegradable. Non-resorbable grafts (such as silicon) include complications such as cytotoxicity and nerve constriction, particularly over the long term. Biodegradable grafts do
20 not suffer from such problems as they are re-absorbed in the short term.

Grafts forming conduits can also provide support for substances which can facilitate nerve regrowth. These include nerve growth factors, Schwann cells, stem cells
25 and other substances. These can be injected into the conduit or otherwise housed by the conduit e.g. adsorbed by the conduit walls.

Using graft conduits has met with some success in peripheral nerve repair, but there is a further need for
30 new approaches to facilitate nerve repair and repair of other tissues.

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Summary of the Invention

In accordance with a first aspect, the present invention provides an apparatus for facilitating treatment
5 of tissue, comprising:

an apparatus body arranged to be positioned proximate the tissue to be treated; and

an antenna arrangement which is arranged to receive a stimulation signal and, in response to the stimulation
10 signal, to induce a stimulating signal arranged to treat the tissue.

In an embodiment, the antenna arrangement and apparatus body are arranged to be implanted within a patient proximate the tissue to be treated. In one
15 embodiment, the apparatus body is grafted to the tissue to be treated, which may be nerve tissue. In an embodiment, the apparatus body comprises at least a portion which forms a conduit arranged to bridge a gap between proximal and distal ends of nervous tissue. The gap may have been
20 caused by injury. In this embodiment, the conduit may facilitate growth of the axons within the nervous tissue so that they meet and close the gap. Advantageously, nerve growth is further facilitated by the stimulating signal. In an embodiment, the stimulating signal is
25 arranged to electrically stimulate the tissue. Electrical stimulation of nervous tissue can facilitate regrowth.

In an embodiment, the stimulating signal may cause or amplify release of substances to treat the tissue. For example, nerve growth factors may be released. In an
30 embodiment, the apparatus body may be arranged to contain substances for treating the tissue, such as nerve growth factors, Schwann cells, stem cells, or other substances. The stimulating signal may cause or amplify release of the

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substances.

In an embodiment, the antenna arrangement is arranged to induce the stimulating signal in the apparatus body.

In an embodiment, the apparatus body is conductive and
5 arranged to electrically stimulate the tissue in response to the induced stimulation signal.

In an embodiment, the antenna arrangement is formed by part or all of the apparatus body. The antenna arrangement may comprise a dipole antenna. In one
10 embodiment, the apparatus body comprises a pair of dipoles (which may be cylindrical) separated by an insulating gap. In this embodiment, the apparatus is an antenna arrangement in the form of a graft for nervous or other types of tissue.

15 In embodiments, the antenna arrangement may comprise a monopole antenna, strip antenna or any other type of antenna.

In an embodiment, the apparatus body is formed from biocompatible material, which may comprise one or more of
20 titanium, polypyrrole, chitosan, collagen and PEDOT (Poly (3,4 ethylenedioxythiophene)).

In an embodiment, the stimulation signal may be transmitted from a remote device, such as a stimulator apparatus external to the patient's body. The stimulator
25 apparatus may comprise a generator for generating the stimulation signal and a transmitter for transmitting the signal. The stimulation signal may be a radio frequency signal, and may be a microwave frequency signal. Radio signals can therefore be used to stimulate an implanted
30 graft which comprises an antenna, to provide a stimulating signal to tissue to facilitate regrowth of that tissue or otherwise treat the tissue. The tissue may be nervous tissue or, in other embodiments, other types of tissue, such as muscle tissue, for example. The radio frequency

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signal affects the antenna and causes an electrical current to flow in the apparatus body. In embodiments, the apparatus body includes conductive material in contact with the tissue to be stimulated. Current flowing in the
5 conductive material thus causes electrical stimulation of the tissue being treated.

In accordance with a second aspect, the present invention provides a stimulator apparatus for providing a signal for facilitating treatment of tissue, comprising a
10 signal generator arranged to generate a stimulation signal to be received by an apparatus in accordance with the first aspect of the invention, and a transmitter for transmitting the stimulation signal.

In accordance with a third aspect, the present
15 invention provides a system for facilitating treatment of tissue, comprising an apparatus in accordance with the first aspect of the invention and a stimulator apparatus in accordance with the second aspect of the invention.

In accordance with a fourth aspect, the present
20 invention provides a computer program, comprising instructions for controlling a processor to implement control of a stimulator apparatus in accordance with the second aspect of the invention.

The stimulator apparatus may comprise a processor
25 which is programmed to provide the stimulation signal.

In accordance with a fifth aspect, the present invention provides a computer readable medium, providing a computer program in accordance with the fourth aspect of the invention.

30 In accordance with a sixth aspect, the present invention provides a data signal, comprising a computer program in accordance with the fourth aspect of the invention.

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In accordance with a seventh aspect, the present invention provides a method of facilitating treatment of tissue, comprising the steps of receiving a wireless stimulation signal proximate the tissue to be treated, and, in response to the stimulation signal, inducing a stimulating signal arranged to treat the tissue.

In accordance with an eighth aspect, the present invention provides a method for treating tissue, comprising the steps of implanting an apparatus in accordance with the first aspect of the invention, proximate the tissue to be treated, within the body of the patient.

In accordance with a ninth aspect, the present invention provides an apparatus for facilitating treatment of tissue, comprising an apparatus body arranged to be grafted to the tissue to be treated and comprising an antenna arrangement.

In accordance with a tenth aspect, the present invention provides an apparatus for facilitating treatment of nerve tissue, comprising a conduit arranged to receive the nervous tissue and comprising a conductive arrangement arranged to receive a stimulation signal and, in response, to induce a stimulating signal to stimulate the nervous tissue.

The conduit may receive the stimulation signal via radio frequency antenna, as in the above embodiments. Alternatively, however, the conduit may receive a stimulation signal by other means. It may receive it via conductors and a battery implant, for example.

In accordance with an eleventh aspect, the present invention provides a method of facilitating treatment of nervous tissue, comprising the steps of inducing currents in a conductive conduit receiving nervous tissue, to stimulate nerve growth.

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Brief Description of the Drawings

Features and advantages of the present invention will become apparent from the following description of embodiments thereof, by way of example only, with
5 reference to the accompanying drawings, in which:

Figure 1 is a schematic diagram illustrating a nerve lesion and prior art graft;

Figure 2 is a schematic diagram illustrating a nerve lesion and apparatus in accordance with an embodiment of
10 the present invention;

Figure 3 is a schematic diagram illustrating a stimulator apparatus and apparatus facilitating treatment of nervous tissue, in accordance with an embodiment of the present invention;

15 Figure 4 is a schematic diagram of an apparatus in accordance with a further embodiment of the present invention, in the form of a patch antenna;

Figure 5 is a schematic diagram showing the apparatus of Figure 4 in place with respect to a nerve graft; and

20 Figure 6 is a schematic representation of an apparatus in accordance with yet a further embodiment of the invention shown in place with respect to a nerve graft;

Figure 7 is a block diagram of a further embodiment
25 of the present invention;

Figure 8 is a more detailed block diagram of part of the embodiment of Figure 7;

Figures 9A is a block diagram of the embodiment of Figures 7 and 8.

30 Figure 9B is a circuit diagram of part of the

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embodiment of Figures 7 and 8.

Figure 9C is a circuit diagram of part of the embodiment of Figures 7 and 8.

Figure 10 is a representation of components of the
5 embodiment of Figures 7, 8, 9A, 9B and 9C, to illustrate their relative size;

Figure 11 is an electro-micrograph (EMG) recording showing the effect of stimulation in accordance with an embodiment of the invention;

10 Figure 12 is a graph of Action Potential recorded in a median nerve following nerve-graft stimulation utilising an embodiment of the present invention;

Figures 13A and 13B are pictures illustrating development of neurites in response to in vitro
15 stimulation;

Figure 14A is an illustration of apparatus in accordance with an embodiment of the invention for in vitro stimulation of cells;

Figure 14B is a circuit diagram of part of the
20 embodiment of Figure 14A.

Figure 15 is a diagram of a circuit used to demonstrate that RF radiation can be used with an embodiment of the invention to facilitate drug release; and

25 Figure 16 is a plot illustrating results of the drug release experiment.

Detailed Description of Embodiments

Figure 1 is a diagram which schematically illustrates

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a nerve lesion and a graft arranged to facilitate repair of the nerve.

The nerve 1 may be any nerve, but in this example is a peripheral nerve. Peripheral nerve 1 has a break 2 because of injury by trauma, disease or other reason. The nerve is only shown schematically but will comprise an epineurium 3 and bundles of nerve fibres 4 within the epineurium and surrounded by tissues formed into fascicles 5. Each nerve fibre, as is well known, will consist of components including a myelin sheath and an axon running within the myelin sheath. This document is not concerned with a detailed description of the anatomy of nerves, as this will be understood by a skilled person, and no further description is given here.

Because of the lesion 2, nerve fibres 4 and the component axons have been disrupted. Nerve signal transmission cannot take place across the gap 6 formed by the lesion. In order to restore nervous function, the gap between proximal and distal ends of nerve fibres 4 must be bridged. As discussed above, this can be done in a number of ways, including by way of autografts or allografts of nervous material. These have problems, however, as discussed above.

Figure 1 illustrates the use of a graft 7 of material (shaded area) which forms a tube-like conduit system ("nerve conduit") bridging the lesion. Nerve conduit graft 7 may be of biocompatible material such as collagen or non-resorbable material such as silicon. Nerve conduit graft 7 operates to guide growing nerve fibres which sprout from the proximal nerve stump (the nerve stump closest to the cell body) towards the distal stump.

The hollow space within the graft 7 may be filled (by injection or otherwise) with substances which can facilitate nerve regrowth, such as nerve growth factor, a suspension of nerve supporting cells (eg Schwann cells) or

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other substances.

Resorbable grafts are biodegradable and avoid problems because they degrade. Silicon grafts and other grafts which do not degrade can cause long-term
5 complications, including cytotoxicity and nerve constriction. Biological tissues such as veins and arteries have also been used, but have the disadvantage that they require a donor site. Further, over the long term, these have been found to degrade the operation of
10 the nerve.

Figure 2 illustrates an apparatus in accordance with an embodiment of the present invention, for facilitating treatment of tissue. The apparatus is generally designated by reference numeral 10. In this embodiment,
15 the tissue being treated is nervous tissue in the form of a peripheral nerve 1 which has suffered an injury(not shown but the area of the lesion, which is covered by a graft described later, is indicated by reference numeral 2).

20 The apparatus 10 comprises an apparatus body, which in this example constitutes a pair of cylindrical components 11, 12 having an insulating space 13 between. In an alternative embodiment the insulating space 13 may be formed of insulating material so the two components 11
25 and 12 are separated by insulating material rather than a space.

The apparatus body, in this embodiment, forms an antenna arrangement, the components 11 and 12 forming two parts of a dipole antenna.

30 The antenna arrangement 11, 12 is arranged to receive a stimulation signal, schematically represented at 14, from a transmitter and antenna arrangement (schematically represented at 15). In response to the stimulation signal 14, the antenna 11, 12 is arranged to induce a stimulating

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signal arranged to treat the nervous tissue 1. In this example, the stimulating signal takes the form of induced currents 16 (represented by the arrows illustrated on the components 11, 12) in the apparatus body 11, 12. In this
5 example, the induced currents 16 electrically stimulate the nervous tissue. At least the conductive component 11 is arranged to directly contact the nervous tissue underneath the graft. The induced currents 16 in the graft 11 electrically stimulate the nervous tissue.

10 Electrical stimulation of the nervous tissue results in accelerated regrowth of the nerve fibres 4.

The transmitter and antenna 15 can be used outside a patient's body, so the treatment by the stimulation signal 14 is non-invasive.

15 The induced stimulating signal 16 may also cause release of substances such as Schwann cells, nerve growth factors, etc, which may be supported in the material of the apparatus body 11, 12.

 An embodiment of the invention will now be described
20 in more detail, with reference to Figure 3 as well as Figure 2. Figure 3 shows the same apparatus as Figure 2 and the same reference numerals have been used to indicate the same components as Figure 2. In Figure 3, the peripheral nerve 1 is represented as being within a
25 patient's body tissue 20.

 Represented positioned outside the body tissue 20, is a stimulator apparatus 21, which is operated to provide a stimulation signal to the apparatus 10.

 The apparatus 10 in this embodiment comprises hollow
30 cylinders 11, 12 made of titanium. Titanium is biocompatible and can sustain mechanical stress involved with a nerve graft. In this example the dimensions lengthwise of each of the cylinders 11, 12 are 2cm and

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they are 5mm approximately in diameter. Size of the cylinders may vary depending upon the application e.g. size of the graft and wavelength of stimulation radiation. One of the cylinders 11 bridges the lesion 2
5 the other of the cylinders 10 completes the apparatus body and the antenna arrangement forming a graft-antenna dipole 11, 12. In this embodiment, the dipole 11, 12 pair are separated by a gap of 1-2mm, for example. The dipole separation should not compromise its electro magnetic
10 receiving capability. Again, it will be appreciated that all dimensions (of the apparatus body 11, 12 and separation distance) may be varied depending upon application.

Other materials than titanium may be utilised.

15 Electrically conducting polymers, such as polypyrrole may be used. PEDOT may also be used, as may chitosan, or collagen. Other biocompatible and conductive materials may be used. In this embodiment, the apparatus body or at least a portion of the apparatus body is conductive to
20 enable currents 16 to be induced.

In embodiments, combinations of materials may form the apparatus body e.g. a combination of polypyrrole and chitosan. Other combinations may be used.

In this embodiment, the grafts 11, 12 are joined to
25 the nerve stumps by a suturing technique, fibrin glue or a minimal invasive laser technique. The latter exploits the adhesive properties of polymeric glues, which are activated by laser light delivered through an optical fibre. Laser welding with polymeric glues may be less
30 invasive than suturing and easier to execute. Where the graft is titanium, it is attached to the nerve by gluing the tube edges to tissue with fibrin glue. A solution of albumin (50% weight per volume) mixed with the dye indocyanine green (0.2% w/w) can be used as a laser
35 activated solder to fix the titanium graft to the nerve.

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In this case, the laser (wavelength 808nm) is selectively absorbed by the green die causing the fusion of albumin and collagen proteins, present in the nerve perineurium. This laser technique is minimally invasive and may cause
5 no or negligible nerve and tissue damage. Another alternative is to use albumin glues, which are stronger than fibrin glues.

Note that other materials may utilise other methods of fixation. For example a chitosan-polypyrrole, or
10 collagen-polypyrrole or PEDOT graft may be fixed on the nerve tissue by using either conventional suturing techniques or fibrin glue or laser activated albumin solder. In the case of chitosan-polypyrrole grafts, fixation can also be achieved without the aid of fibrin
15 glues or albumin solders as chitosan adhesion is greatly enhanced by laser irradiation. With a chitosan-polypyrrole graft, placed around the nerves, the laser energy will locally melt the tissue collagen at the graft edges, bonding firmly to the chitosan present in the graft.

20 Other ways of attaching the components 11, 12 to the nerves may be utilised.

As discussed above, the antenna in this embodiment comprises the apparatus body 11, 12, formed as a dipole pair. The entire cylinders 11, 12 form the dipole pair.
25 The combined length of the dipole pair is chosen to receive the appropriate wavelength stimulation signal. In this embodiment, the stimulation signal frequency is a 3.8GHz microwave signal, half wavelength 4cm (approx). In operation, this induces a stimulation signal in the form
30 of a current of approximately 20 μ A in the apparatus body 11, 12 to electrically stimulate the nerve 1.

In other embodiments, other radio frequencies may be used to stimulate the tissue, obviously requiring changes in the size of the antenna as appropriate.

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In this embodiment, low energy doses of microwave radiation, which does not affect the surrounding tissue, can be used. Other ranges of frequencies can be used e.g. 1GHz to 5GHz, 0.01 milliamps to 2 milliamps. Power
5 levels in the range of mW e.g. 1 to 100 milliwatts can be utilised (or other power levels if appropriate). These power levels of the 1 to 5 GHz range are not harmful and can penetrate through tissue 20 to stimulate nerves remotely via the antenna.

10 The time of exposure to the radiation also varies and the number of treatments may be varied e.g. exposure times from 5 mins to several hours, and different frequencies of exposure to provide the appropriate treatment effect.

In the embodiment of Figures 2 and 3, the apparatus
15 body forms the antenna arrangement, in the form of a dipole antenna. The antenna arrangement could, alternatively, be formed by part only of the apparatus body. For example, the antenna arrangement could be a microstrip antenna supported by the apparatus body. It
20 could be a helical antenna wound around a supporting apparatus body. The antenna could be of any form. The dimensions of the antenna will be related to the wavelength of the radiation being used for treatment.

Figure 4 illustrates an embodiment of an apparatus in
25 accordance with the present invention which comprises a patch antenna 50. The patch antenna 50 comprises conductive pattern mounted with respect to an insulating substrate 51. The pattern of the patch antenna 50 may be any appropriate pattern for receiving the stimulation
30 signal and producing the stimulating signal to affect the underlying tissue.

Figure 5 illustrates the patch antenna 50 and substrate 51 in position about a nervous tissue graft. The nerve is represented by reference numeral 52. Note
35 that the apparatus 50, 51 may form the graft, if of

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appropriate material. Note that Figure 5 is a schematic diagram and the apparatus 50, 51 may in fact be a complete cylinder forming the graft joining broken nerve endings together (not shown) underneath the apparatus 50, 51.

5 The conductive material of the patch antenna 50, in this embodiment, extends through the substrate material 51 so as to contact the underlying nerve tissue. In this way, electrical currents may be transmitted within the underlying nervous tissue in order to treat the tissue.

10 Note that in other embodiments, it is possible that the conductive material within which the stimulating signal is induced may not directly connect the underlying tissue. The stimulating signal may then cause currents to occur in the underlying tissue by way of induction.

15 Figure 6 shows a further embodiment of an apparatus in accordance with the present invention, this time comprising a strip antenna 60 mounted in a substrate 61. The strip antenna 60 is of conductive material and the substrate 61 is of non-conductive material. The strip
20 antenna 60 conductive material contacts the underlying tissue.

 As discussed above, the antenna may be any form of antenna. It is not limited to being a dipole (as in the embodiments of Figures 2 and 3), but may be a monopole or
25 patch antenna (as in Figure 6) or any other type of antenna. In another embodiment, the graft may comprise a single cylindrical component which acts as a monopole antenna, and which also bridges the break in the nervous tissue.

30 In the above embodiments, the apparatus body is formed by the antenna, or the antenna is an integral part of the apparatus body.

 In other embodiments, the antenna arrangement may be

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separate, but connected to, the apparatus body. For example, a separate antenna may be implanted proximate the apparatus body and connected to it by a conductor.

Advantageously, embodiments of the present invention
5 allow a graft to be implanted, forming the antenna or being connected to an antenna, for subsequent treatment by irradiation, without further invasion of the body tissue, treatment radiation being transmitted from a remote location, outside the patient's body.

10 In an embodiment, the stimulating signal 16 may prompt release of substances which may facilitate nerve growth and/or repair. For example, positively charged substances (eg nerve treating drugs) can be placed in a skeleton of polypyrrole strips. Inducing a current in the
15 polypyrrole skeleton can cause the drug to release. The apparatus body 10 can form a skeleton for retaining substances to be released in response to the stimulating signal. The apparatus body may be structured to contain the substances or may have a molecular configuration which
20 allows the substances to be absorbed or adsorbed and subsequently released. Substances can include nerve growth factors, cells which can assist in nerve growth e.g. Schwann cells, stem cells, and any other substance.

In embodiments, the stimulation signal 16 may be used
25 to only release substances and not to electrically stimulate the nerves. In other embodiments, it will be used only to stimulate the nerves and in yet other embodiments it may be used to electrically stimulate the nerve and also release substances to assist in nerve
30 regrowth and/or nerve repair.

Referring to Figure 3, in order to facilitate treatment of the tissue via the apparatus 10, stimulator apparatus 21 may be utilised. The stimulator apparatus 21 is illustrated schematically within a housing 22 which may be
35 of any convenient shape. The housing 22 may mount the

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user interface e.g. control buttons (not shown), for controlling the stimulator apparatus to produce the stimulation signal.

The stimulation apparatus comprises a RF signal generator 23 (in this case arranged to generate microwave signals), a matching circuit 24 and dipole antenna 25. The transmitting dipole antenna 25 is arranged to transmit the stimulating signal generated by the signal generator 23 for reception by the antenna 11, 12 of the apparatus body.

In this embodiment, the stimulator apparatus 21 also comprises a processor 26. The processor may contain programming for controlling the signal generator to implement various treatment regimes, and for general control of the stimulator. The programming may be software or firmware or any other appropriate way of instructing the processor.

Processor 26 may be programmed with an appropriate treatment regime, so that a patient may utilise the stimulator themselves for treatment of the nervous tissue.

A programmer device (not shown) may be utilised by a clinician to program the processor with the treatment regime.

A similar stimulator apparatus and programmer device may be used for other embodiments, such as, for example, the embodiments of Figures 4, 5 and 6.

The antenna 11, 12 formed by the apparatus body may also be used for transmission of signals to be received externally. For example, nerve signals may be detected by the antenna and a signal transmitted in response to those nerve signals to an external receiver (not shown) arranged for diagnostic purposes. The antennas of other embodiments, including the embodiments of Figures 4, 5 and

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6 may also be used for transmission of signals to be received externally.

In an alternative embodiment, an apparatus body and antenna arrangement in accordance with embodiments of the present invention may be used to transmit signals responsive to the tissue being treated, without being used to receive a stimulation signal for stimulation of the tissue. The signals may be used for diagnostic purposes, for example, and may be received externally of the body.

10 A further embodiment of the present invention is illustrated in Figures 7 to 10.

In this embodiment, the receiving antenna is separated from the apparatus body. The arrangement comprises a primary implant 100 and a secondary implant 15 101 connected by electrical connection means 108 such as a bio-compatible coated wire. The primary implant 100, comprises an energy harvesting antenna 102, a voltage rectifier and regulator 103 and an energy storage device, in this example being a supercapacitor 104. The voltage 20 rectifier and regulator may be embedded in a single microchip.

The secondary implant 101 comprises circuitry for driving stimulation electrodes 105 mounted about the nerve stumps of a nerve lesion, in this embodiment within a 25 bio-compatible graft which forms an anastomosis about the nerve lesion (see Figure 8). The secondary implant also comprises circuitry to receive the energy from the primary implant and drive the stimulation electrodes 105. This circuitry includes transistors, and a nerve driver 107. 30 The circuitry may optionally include an oscillator arrangement 106.

The primary implant 100 is encapsulated in a bio-compatible resin enclosure and, in use, is implanted directly under the skin of the patient. Placing the

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antenna close to the skin potentially reduces any adverse effect of RF radiation, and may allow greater RF power to be used, for example, while still avoiding tissue damage and skin irritations. The power harvested is temporarily
5 stored by storage device 104. Supercapacitors are used for the storage device (although other components may be used). For low power circuits, they do not require maintenance and they are sealed to avoid fluid leakage inside the body. The primary implant 100 also includes
10 circuitry arranged to avoid unwanted activation (turn ON key) which starts stimulation only when the recognised RF stimulator (external stimulator) is placed in proximity to the primary implant 100 (the turn ON key circuitry is not shown).

15 Circuitry for the secondary implant 106 can be encased in a small bio-compatible enclosure, which may be made of titanium, for example, and implanted so that the stimulation electrodes 105 are placed about the nerve (Figure 8) and the other circuitry of the secondary
20 implant 101 adjacent the nerve graft (see Figure 8). Connection between the primary 100 and secondary 101 implants is via bio-compatible shielded wires 108, which may be similar to those used for cardiac pacemakers.

Figure 8 is a schematic diagram showing the
25 embodiment of Figure 7 in place inside a patient's body. Nerve 110 has a nerve lesion 111, due to injury. The graft conduit, which may be of any of the materials discussed previously, 112 encases the titanium electrodes 105 which connect to the rest of the circuitry of the
30 secondary implant 101.

An external driver 113 provides radiofrequency signals to the primary implant 100. The external driver 113 may be similar in form to the stimulator apparatus 21 of preceding embodiments described above.

35 Figures 9A, 9B and 9C illustrate an example of

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electronic implementation of the embodiment of Figure 8. Figure 9A shows a schematic representation of the primary implant 100, which comprises an energy harvesting antenna 102, connected to the secondary implant 101, which
5 comprises an apparatus body module 101, by electrical connection means 108. The primary implant 100 comprises output electric terminals 173, 174 to transfer the harvested energy to the secondary implant 101. The secondary implant 101 comprises input electric terminals
10 175, 176 to receive energy.

Figure 9B illustrates one example of circuitry for the primary implant 100. Inductor 'L1' 180 permits the electromagnetic coupling between an external source of electromagnetic energy, such as the dipole antenna 15, and
15 an Energy Harvester EEPROM 181. The Energy Harvester EEPROM 181 comprises an output terminal 182 which is connected to a capacitor, in this example Super-Capacitor 'C1' 183. The Energy Harvester EEPROM 181 permits the storage of the energy received from an external source
20 into the Super-Capacitor 183. The output electric terminals 173, 174 of the primary implant 100 are connected across the Super-Capacitor 183.

Figure 9C illustrates one example of circuitry for the secondary implant 101. Input terminal 191 is connected
25 to Super-Capacitor 183 by connecting means 108 and to stimulation electrodes 105. Furthermore the input terminal 191 is connected to the base of a transistor 'Q1' 194 and a series of two diodes 'D1' and 'D2' 190 through the base resistor 'R1'. The diodes 190 fix the voltage on the base
30 of the transistor 194 and, as a consequence, on the emitter of the transistor 194. With this configuration, the current flowing through the electrodes connections 193 can be fixed selecting the value of the resistor 'R2' 195, which is connected to the emitter of the transistor 194.
35 In other embodiments, the resistor 'R2' 195 may be a trimmer or a digital trimmer (for precise calibration)

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controlled by the primary implant which may support digital communication.

In an embodiment, the circuit illustrated in Figure 9B may be implemented using an inductor 180 with an inductance of 47mH, a super-capacitor 104 with a capacitance of 100mF and an EEPROM 1781 M24LR64 from ST Microelectronics.

In an embodiment, the circuit illustrated in Figure 9C may be implemented using high conductance fast diodes 190 1N4148 and an NPN BJT transistor 194 BC847.

The primary implant, secondary implant architecture may have different circuitry than shown in the embodiments of Figures 7, 8, 9A, 9B and 9C, as long as the circuitry has the same function. The invention is not limited to the particular circuitry shown. For example, other rectifying arrangements may be used, other storage devices for the storage device 104, different circuitry may be used to drive stimulation electrodes 105, and other variations may be made.

Figure 10 illustrates the size of the components that may be utilised as primary implants. 1, 2 and 3 are all different forms of primary implant having circuitry implementing primary implant 100 shown next to a 10 cent piece to illustrate their size.

Stimulation can be implemented using constant current stimulation from the primary implant, pulsed current stimulation or other types of stimulation.

Examples

In Vivo Test

Stimulation up to 100µA was used for these tests. Wistar rats (n=4) were used for these experiments to confirm the device of Figures 7 through 10, can achieve nerve

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stimulation. The graft used in these experiments comprised two platinum cuffs 105. The primary implant 100 was implanted under the skin of the rat dorsum and connected to nerve graft 112 by platinum wires of 0.05mm gauge.

5 This implant was scheduled for later removal at the end of the stimulation. The nerve graft was fabricated using a chitosan-rose bengal biocompatible conduit and one pair of stimulation electrodes (cuffs) 105 made of pure platinum. These cuffs were carefully wrapped around the nerve at the
10 designated inter-electrodes distance. The primary implant 100 was designed to harvest energy from a 13.5 MHz field and convert the energy harvested in 25-35uA DC current (the circuit can work with a load up to 100k Ohms).

Tissue Fixation of the Nerve Graft

15 The chitosan nerve graft contained the biocompatible dye rose bengal and was fixed to the median nerve using a photochemical tissue bonding technique, as detailed in a previously published paper [Photochemical tissue bonding with chitosan adhesive films. Lauto A, Mawad D, Barton M, Gupta A, Piller SC, Hook J. Biomed Eng Online. 2010 Sep
20 8;9:47. doi: 10.1186/1475-925X-9-47; Fabrication and application of rose bengal-chitosan films in laser tissue repair. Lauto A, Stoodley M, Barton M, Morley JW, Mahns DA, Longo L, Mawad D. J Vis Exp. 2012 Oct 23;(68).
25 doi:p11: 4158. 10.3791/4158]. Briefly, the chitosan nerve graft was positioned around the bisected nerve with microforceps and was irradiated by a diode-pumped solid state green laser that was coupled to a multimode optical fibre (CNI Lasers, China). The fibre was inserted into a
30 hand-held probe to provide easy and accurate beam delivery. The laser emitted a power of 250 mW at 532 nm in a continuous wave, with a fibre core diameter of 200 µm and numerical aperture opening of 0.22. A Teflon "spacer" was mounted on the fibre probe to ensure the irradiation
35 of the adhesive was at the same distance with a beam spot size of ~ 0.6 cm. The rose adhesive was spot-irradiated ensuring each spot was irradiated for ~5 seconds before

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moving the beam to the adjacent spot. The laser beam scanned several times the whole surface area of the rose adhesive and it was strongly absorbed by the rose bengal inside the nerve graft. The combination of the laser and rose bengal produced photochemical reactions that crosslinked the chitsan graft to the nerve (epineurium) without significant heat production or thermal damage [Photochemical tissue bonding with chitosan adhesive films. Lauto A, Mawad D, Barton M, Gupta A, Piller SC, Hook J. Biomed Eng Online. 2010 Sep 8;9:47. doi: 10.1186/1475-925X-9-47; In vitro cell compatibility study of rose bengal-chitosan adhesives. Barton M, Piller SC, Mahns DA, Morley JW, Mawad D, Longo L, Lauto A. Lasers Surg Med. 2012 Nov;44(9):762-8. doi: 10.1002/lsm.22076. Epub 2012 Sep 21]. The bonding strength of the chitosan graft fixed on nerve was estimated to be ~17 KPa, in agreement with other reports.

Electrophysiology Test

The Long Evans rats were anaesthetized following the animal protocol procedure and the rectal temperature was monitored and maintained above 36°C using a feedback controlled heating pad. The median nerve was exposed and carefully dissected free from surrounding tissue above and below the region of the graft-antenna. A pair of silver/silver-chloride stimulating electrodes was positioned on the graft and a pair of recording electrodes proximal to the graft. Stimulating electrodes were separated by 2 mm, and their positions relative to the graft and the recording electrodes carefully measured. The stimulating electrodes stimulated the nerve in order to rule out any nerve damage before using the graft-antenna, which stimulated in turn nerve action potentials. These stimulating electrodes were not used otherwise as the graft-antenna provided the stimuli to induce an action potential.

A similar set up, as the one described above, was used to

- 24 -

evaluate and record the electrical activity produced by the distal arm muscles (flexor digitorum superficialis) following the nerve action potential produced by the graft-antenna. The flexor digitorum superficialis muscle
5 is indeed innervated by the median nerve. The recording electrode was in this case placed in the flexor muscle; this technique is also known as Electromyography or EMG.

The nerve was electrically stimulated using rectangular pulses (duration 0.1 to 0.3 ms, repetition rate 1 Hz) by
10 means of the cuffs in the graft, which was remotely powered by RF, or by the silver/silver-chloride stimulating electrodes (control stimulation). Stimulation and recording was carried out using a PowerLab (Model 26T, ADInstruments Pty Ltd, NSW, Australia).

15 The compound action potential (CAP) and electrical response of the distal arm muscles (EMG of the flexor flexor superficialis) was assessed using the following parameters: (i) the threshold to activation of the CAP, (ii) the amplitude of the CAP measured from the base line
20 to the maximum amplitude at supra-maximal stimulation. (iii) action potential duration at 90% of maximal amplitude measured following supra-maximal stimulation (iv) conduction velocity measured from the stimulus artifact to the onset of the CAP.

25 Results showed that wireless electrical stimulation (direct current at 5-30 μ A) applied on healthy median nerves with a 2 mm inter-electrodes distance can elicit Action Potentials (APs). These APs were also detectable as muscle activation (surface EMG) at the peripheral muscles
30 innervated of the median nerve. The activation was also clearly visible through the arm twitch of the rat when the stimulation was "ON" (Figures 11 and 12). Remarkably, APs could be elicited even when the graft-antenna delivered 6 μ A to the median nerve. These APs had amplitude values and
35 shape characteristics similar to APs of healthy nerves.

- 25 -

Figure 11 is an EMG recording showing clear muscle activity following activation (RF - ON) and deactivation (RF - OFF) of a nerve graft external field.

Figure 12 shows the Action Potential recorded in the wrap
5 median nerve following the nerve graft stimulation. The first peak is the stimulus artefact while the second peak is the triggered AP.

In Vitro Cell Stimulation

10 We have also conducted a parallel study using a graft-antenna prototype for cell stimulation. In this instance, two separate harvesting-current rectifier systems were used:

1. The RF and current rectifier system was similar to
15 the system used in the rat median nerve stimulation. Continuous RF radiation was captured with a microstrip antenna and made to produce a usable dc current on a mylar-gold ribbon where neuroblastomas were cultured (n=4).
2. Continuous microwave radiation (RF) was captured with
20 a dipole microstrip antenna, in the near field in air, and made to produce a usable dc current. The capture unit was fabricated on glass and located near the receiving antenna tuned to 3 GHz (figure 14A and
25 14B). The collected RF energy was full wave rectified and voltage multiplied to produce adequate EMF (up to 3 V and ~1 mA current). The magnitude of the current could be controlled remotely by adjusting the radiated and received power. Continuous RF radiation
30 was captured with a microstrip antenna and made to produce a usable dc current on a mylar-gold ribbon where neuroblastomas were cultured (n=4). Figure 14A is a representation of the device used for this approach. Reference numeral 120 illustrates the gold

- 26 -

on mylar ribbon which was fitted to a 10cm round dish 121 containing the neuroblastomers. The other components illustrated in Figure 14A include the RF harvester 122 and the stimulation circuitry 123.

5 The electrical circuit corresponding to the RF harvester and stimulation circuitry is illustrated in Figure 14B. In this example circuit, radio frequency energy is received via the antenna 102 and rectified by diodes D1 and D2 (voltage rectifier 103). The

10 rectified energy is stored by capacitors C1 and C4. This circuitry includes transistors and an oscillator arrangement.

Cell Culture and Stimulation

Gold on mylar ribbons were fitted to 10cm round dishes in the laminar flow cabinet. The ribbon was 5mm wide and

15 100mm long showing some 50 Ω resistance, dry. At each end of the ribbon 20mm was bent vertically to protrude through slots in the upper lid to provide electrical connection to the harvested dc current. The remaining 60mm of ribbon

20 (gold side up) was available to be plated with cells introduced into the culture dish. Cultured cells were plated at densities expect to reach confluence in two to three days. In the incubator, up to four dishes were connected in series (more if run in a series/ parallel

25 configuration to allow split current sharing). As is usual, cultures were incubated in 95% O₂ and 5% CO₂ and at 37°C in sterile conditions. Care was taken to ensure the ribbon remained flat and was not disturbed during the cell settling and attachment period of some 4 to 6 hours after

30 plating. Whereupon dc currents of 30 μ A were applied for one hour to the gold monolayer on the mylar ribbon that supported growing cells submerged in culture medium. Current levels were monitored throughout and controlled with the transmitted power (~ 10 mW at 3 GHz). The RF

35 power was conducted into the incubator to the transmitting antenna through a "phase stable" cable. Control dishes were treated similarly but without electrification.

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At 24 hours following the electrification of the ribbon (30 μ A for 60 minutes) using both systems (1 and 2), more and longer neurites 123 (Figure 13B) developed in several cells on the electrified ribbon when compared to control
5 cells (Figure 13A). It appeared that neurite growth was promoted by a single exposure to current, which was set at the same level of the current generated by the graft-antenna (30 μ A). These results indicate that axons in peripheral nerves may also be stimulated to grow following
10 the electrical stimulation of the graft-antenna described before in the *in vivo* test.

Similar rewrite outgrowth was outlined with the energy harvester-rectifier system 2.

Drug Release Test

15 The basic construction of the dipole system, which was used in this experiment, is shown in Figure 15. The system consists of a signal generator 150 connected to a transmitting dipole antenna 151 via a matching circuit 152, a receiving Au-Mytilar dipole antenna coated with
20 Polypyrrole (doped with phenol red), connected to a power meter 154 via a matching circuit 155. In this setup it is possible to control the power received by the receiving antenna and hence the induced current. Our results have shown that this setup can be used to emit radiation ($P=$
25 10-20 mW) and induce currents in the range of 0.5 mA to 2 mA at 1.5 GHz on 9-cm polypyrrole dipole. We have also tested that a copper dipole emitting a microwave power of ~10 mW can induce ~20 μ Amps currents at a frequency of 3.8 GHz in an identical receiving 4-cm dipole (tube length = 2
30 cm, diameter = 5mm). This current intensity is in the range of normal physiological currents in peripheral human nerves. Further, these power levels at 1.5 and 3.8 GHz are not harmful and can penetrate through tissue to stimulate peripheral nerves remotely [Carr, KL. Microwave
35 radiometry: its importance to the detection of cancer. Microwave Theory and Techniques, IEEE Transaction; 37,

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12:1862-69, 1989].

Tests were also carried out to see if RF radiation could be used to stimulate drug release.

Drug Delivery from Conducting Polymer Dipoles

5 When electrodes induce the passage of current in polypyrrole strips, these can release the positively charged drug that is placed inside them (the dopant for the conducting polymer) [Wanga C, Whittena PG, Tooja CO and Wallace G. A galvanic cell driven controlled release
10 system based on conducting polymers. Sensors and Actuators B: Chemical;129: 2, 605-611, 2008; Thompson BC, Moulton SE, Wallace GG, Clark GM. Optimising the incorporation and release of a neurotrophic factor using conducting polypyrrole. J Control Release; 116(3):285-94,2006]. In
15 our experiment we aim to extend the release capability of polypyrrole strips to current induced by microwaves, without the aid of electrodes. We obtained encouraging results that indicate the possibility of drug release from polypyrrole dipoles if irradiated by microwaves.
20 Polypyrrole strips (dipole) were coated on Au-Mylar and tested for drug release using microwave irradiation as a source of current. The dopant used in the polypyrrole strips was phenol red. 300ml of PBS (Ph~7.4) were placed on the polypyrrole strips and irradiated for 1 hour; the
25 PBS+Phenol red was then collected to measure the optical density (OD) of these samples with a visible spectrophotometer. A control dipole was also prepared in the same way as described above, but no radiation was shined on it. The length of the dipole was 9 cm (half
30 wavelength); the irradiating copper dipole was also 9 cm long. The transmitting power was ~19 mW and the received power was 0.28 mW.

The irradiated strips released more phenol red (OD= 0.4±0.1, n=8) than the non-irradiated strips (OD= 0.3±0.1, n=8, p=0.04). Data were analysed using the Student's t-

35

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test (two tails and unpaired). Although the strip fabrication, by which phenol red is incorporated, should be improved and optimized we can affirm that the measured OD at 411 nm is only due to the release of phenol red and
5 the thus our preliminary experiment showed that microwaves may induce more dye release than non irradiated samples (Figure 15).

Embodiments of the present invention may facilitate repair and regeneration of injured peripheral nerves.
10 They may also be used for repair of nerves in the CNS (Central Nervous System). Use of an implanted antenna arrangement which can be stimulated remotely, reduces the need for invasive secondary surgery. Existing transmission technology, e.g. existing microwave
15 technology, may be utilised.

Embodiments of the present invention may have applications to spinal cord injuries. For example, they may be used to graft spinal cord injuries to repair nerves within the spinal cord.

20 Treatment may result in improvements to functional recovery after conduit grafting and the ability to repair longer nerve gaps.

Embodiments of the present invention may be used with autologous nerve grafts or nerve allografts, as well as on
25 engineered nerve cells, engineered neuron cells or neuron networks.

In embodiments of the present invention, multiple antennas may be used with a single apparatus body, or multiple antennas with multiple apparatus bodies, to treat
30 large groupings or bundles of nerve fibres.

In embodiments, the invention may be used with central nervous system injuries, such as spinal cord injuries. Embodiments of the apparatus may be applied in

- 30 -

the dorsel route ganglia, and their central axons that project into the spinal cord. Other applications may be in the corticospinal or pyramidal tract where a collection of axons travels between the cerebral cortex of the brain
5 and the spinal cord.

In the above embodiments, when the apparatus comprises a graft, the graft is an entirely closed cylinder. In embodiments it need not be a closed cylinder, but could be of other form. For example, it
10 could be a "patch" grafted onto a break.

Embodiments of the present invention are not limited to treatment of nerve tissue. Embodiments may be used for treatment of other tissue. For example, repair of muscle tissue. The form of the apparatus may vary depending upon
15 the treatment required. For example, if muscle tissue is torn, the apparatus body may form a patch grafted over the muscle tissue, with the antenna arrangement providing stimulation to the muscle tissue. Any form of apparatus body that is convenient for treatment may be utilised.

20 As discussed above, any appropriate conductor materials may be used to form the apparatus body/antenna of the present invention. Materials may include the following:

Conductive Materials (apart from metals)

25 a. Conductive polymers

- Poly(pyrrole)s
- Poly(acetylene)s
- Polyanilines
- Poly(thiophene)s (PEDOT is part of this
30 polymer group)

b. Materials that are conductive and can

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incorporate nano-carbon tubes, metal nanoparticles or nanoroads. Examples of conductive nanostructures: carbon nanotubes, gold and silver nanoparticles/nanorods.

5 c. Materials that are conductive and can incorporate semiconductive nanoparticles. Examples of semiconductive nanostructures: quantum dots.

d. Conductive materials that are neither metals nor conducting polymers and are biocompatible.
10 Example: Indium Tin Oxide (ITO).

The invention is not limited to these materials, and other appropriate materials may also be used.

Where methods and apparatus relating to embodiments of the present invention may be implemented by software
15 applications, or partly implemented by software, then they may take the form of program codes stored or available from computer readable media, such as CD-ROMs or any other machine readable media, the program code comprising instructions which, when loaded onto a machine such as a
20 computer, the machine then becomes an apparatus for carrying out the invention. The computer readable medium may include transmission media, such as cabling, fibre optics or any other form of transmission media. The software may include a data signal.

25 In the claims which follow and in the preceding description of the invention, except where the context requires otherwise due to express language or necessary implication, the word "comprise" or variations such as "comprises" or "comprising" is used in an inclusive sense,
30 i.e. to specify the presence of the stated features but not to preclude the presence or addition of further features in various embodiments of the invention.

It will be understood to persons skilled in the art

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of the invention that many modifications may be made without departing from the spirit and scope of the invention.

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THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. An apparatus for facilitating treatment of tissue,
comprising:

5 an apparatus body arranged to be positioned proximate
the tissue to be treated; and

an antenna arrangement which is arranged to receive a
stimulation signal and, in response to the stimulation
signal, to induce a stimulating signal arranged to treat
10 the tissue.

2. An apparatus in accordance with Claim 1, the antenna
arrangement being arranged to induce the stimulating
signal in the apparatus body.

15

3. An apparatus in accordance with Claim 2, wherein the
apparatus body is conductive, and arranged to electrically
stimulate the tissue in response to the induced
stimulation signal.

20

4. An apparatus in accordance with Claim 1, 2 or 3,
wherein the induced stimulating signal is arranged to
cause release of a substance for treating the tissue.

25 5. An apparatus in accordance with Claim 4, wherein the
apparatus body is arranged to contain the substance for
treating the tissue, prior to release in response to the
stimulating signal.

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6. An apparatus in accordance with any one of the preceding claims, wherein the antenna arrangement is arranged to receive the stimulation signal in the form of a radio frequency signal.

5

7. An apparatus in accordance with Claim 6, wherein the antenna arrangement is arranged to receive the stimulation signal in the form of a microwave frequency signal.

10 8. An apparatus in accordance with any one of the preceding claims, wherein the antenna arrangement forms a dipole antenna.

9. An apparatus in accordance with any one of the
15 preceding claims, wherein the antenna arrangement is formed by part or all of the apparatus body.

10. An apparatus in accordance with any one of the preceding claims, the apparatus body being arranged to be
20 connected to the tissue to be treated.

11. An apparatus in accordance with Claim 10, the apparatus body comprising a graft arranged to be grafted to the tissue to be treated.

25

12. An apparatus in accordance with Claim 11, the apparatus body comprising a first and second substantially cylindrical portion, the first and second portions being arranged to be grafted to the tissue, leaving an

- 35 -

insulating gap there between, and forming a dipole antenna arrangement.

13. An apparatus in accordance with Claim 12, wherein the
5 first and second cylindrical portions are formed of
conductive material, whereby to form the dipole antenna
arrangement.

14. An apparatus in accordance with Claim 12 or Claim 13,
10 wherein the apparatus body is arranged to form a conduit
to provide a channel for the tissue to be stimulated.

15. An apparatus in accordance with any one of Claims 1
to 11, wherein the antenna arrangement comprises a patch
15 antenna.

16. An apparatus in accordance with any one of Claims 1
to 11, wherein the antenna arrangement comprises a strip
antenna.

20

17. An apparatus in accordance with Claim 15 or Claim 16,
wherein the apparatus body is arranged to form a conduit
to provide a channel for the tissue to be stimulated.

25 18. An apparatus in accordance with any one of Claims 1
to 8, where the antenna arrangement is separate from the
apparatus body.

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19. An apparatus in accordance with Claim 18, where the antenna arrangement is connected to electrodes in or on the apparatus body arranged to be proximate to the tissue to be treated.

5

20. An apparatus in accordance with Claim 18 or Claim 19, wherein the antenna, in use, is arranged to be placed under the skin of a patient.

10 21. An apparatus in accordance with any one of the preceding claims, wherein the apparatus body comprises one of or a combination of one or more of the following materials: Titanium; Polypyrrole; Chitosan; Collagen; PEDOT (Poly (3,4 ethylenedioxythiophene)).

15

22. An apparatus in accordance with any one of the preceding claims, arranged for treatment of nerve tissue.

20 23. An apparatus in accordance with any one of the preceding claims, arranged for treatment of muscle tissue.

24. An apparatus in accordance with any one of the preceding claims, wherein the antenna arrangement is arranged to transmit a signal from the apparatus to a
25 remote location, whereby tissue diagnostic signals may be remotely monitored.

25. An apparatus in accordance with any one of the preceding claims, the apparatus body and antenna

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arrangement arranged to be implanted within a patient's body proximate the tissue to be treated.

26. An apparatus in accordance with Claim 25, when
5 implanted in a patient's body.

27. A stimulator apparatus for providing a signal for facilitating treatment of tissue, comprising a signal generator arranged to generate a stimulation signal to be
10 received by an apparatus in accordance with any one of Claims 1 to 23, and a transmitter for transmitting the stimulation signal.

28. A stimulator apparatus in accordance with Claim 27,
15 wherein the signal generator is arranged to generate a radio frequency signal as the stimulation signal.

29. A stimulator apparatus in accordance with Claim 28,
wherein the signal generator is arranged to generate a
20 microwave frequency signal as the stimulation signal.

30. A system for facilitating treatment of tissue, comprising an apparatus in accordance with any one of Claims 1 to 26, and a stimulator apparatus in accordance
25 with any one of Claims 27 to 29.

31. A computer program, comprising instructions for controlling a processor to implement a stimulator apparatus in accordance with any one of Claims 27 to 29.

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32. A computer readable medium, providing a computer program in accordance with Claim 31.

5 33. A data signal, comprising a computer program in accordance with Claim 31.

34. A method of facilitating treatment of tissue, comprising the steps of receiving a wireless stimulation
10 signal to be treated, and, in response to the stimulation signal, inducing a stimulating signal arranged to treat the tissue.

35. A method in accordance with Claim 34, wherein the
15 step of receiving the wireless stimulation signal, comprises receiving the wireless stimulation signal internally of a patient.

36. A method in accordance with Claim 34 or Claim 35,
20 comprising the step of the induced stimulating signal electrically stimulating the tissue.

37. A method in accordance with Claim 34, 35 or 36, comprising the step of the induced stimulating signal
25 causing release of a substance for treating the tissue.

38. A method in accordance with any one of Claims 34 to 37, wherein the step of inducing the stimulating signal comprises the step of inducing the stimulating signal in

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an apparatus body implanted within a patient.

39. A method in accordance with Claim 38, wherein the apparatus body is connected to the tissue to be treated.

5

40. A method in accordance with Claim 39, wherein the apparatus body comprises a graft grafted to the tissue to be treated.

10 41. A method in accordance with any one of Claims 34 to 40, wherein the stimulation signal is a radio frequency signal.

15 42. A method in accordance with Claim 41, wherein the stimulation signal is a microwave frequency signal.

43. A method in accordance with any one of Claims 34 to 42, wherein the tissue to be treated is nerve tissue.

20 44. A method in accordance with any one of Claims 34 to 43, wherein the tissue to be treated is muscle tissue.

45. A method for treating tissue, comprising the steps of implanting an apparatus in accordance with any one of
25 Claims 1 to 26, proximate the tissue to be treated, within the body of a patient.

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46. A method in accordance with Claim 45, comprising the step of securing the apparatus body to the tissue.
47. A method in accordance with Claim 46, wherein the
5 step of securing the apparatus body to the tissue, comprises the step of grafting the apparatus body to the tissue.
48. An apparatus for facilitating treatment of tissue,
10 comprising an apparatus body arranged to be grafted to the tissue to be treated and comprising an antenna arrangement.
49. An apparatus in accordance with Claim 48, wherein the
15 antenna arrangement is arranged to receive a stimulation signal and, in response to the stimulation signal, to induce the stimulating signal arranged to treat the tissue.
- 20 50. An apparatus in accordance with Claim 48 or Claim 49, wherein the antenna arrangement is arrangement to transmit a signal in response to activity of the tissue being treated.
- 25 51. An apparatus for facilitating treatment of nerve tissue, comprising a conduit arranged to receive the nervous tissue and comprising a conductive arrangement arranged to receive a stimulation signal and, in response, to induce a stimulating signal to stimulate the nervous
30 tissue.

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52. A method of facilitating treatment of nervous tissue,
comprising the steps of inducing currents in a conductive
conduit receiving nervous tissue, to stimulate nerve
5 growth.

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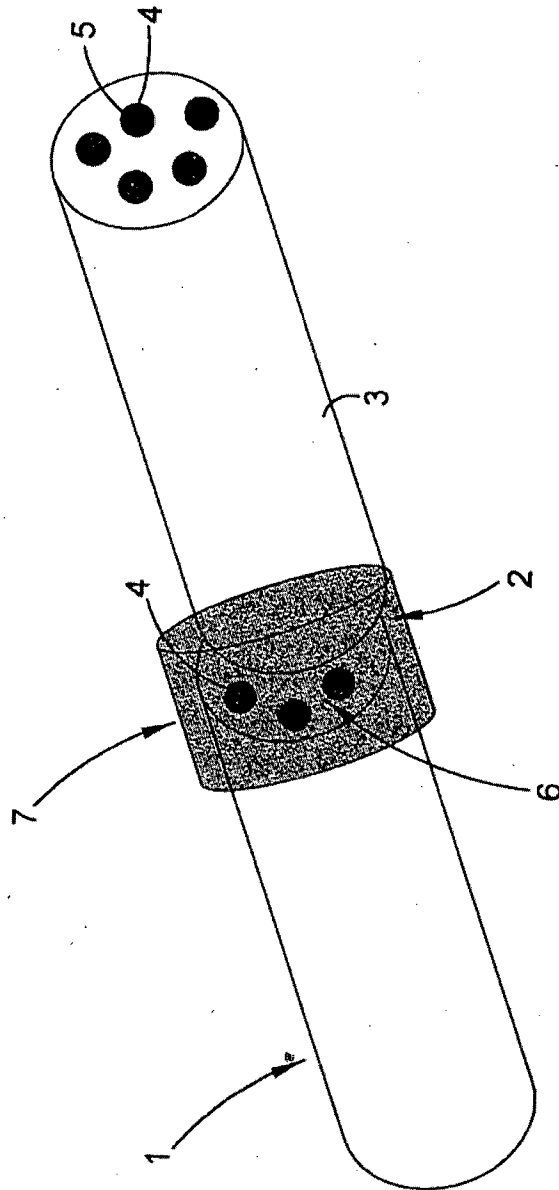


FIGURE 1 (PRIOR ART)

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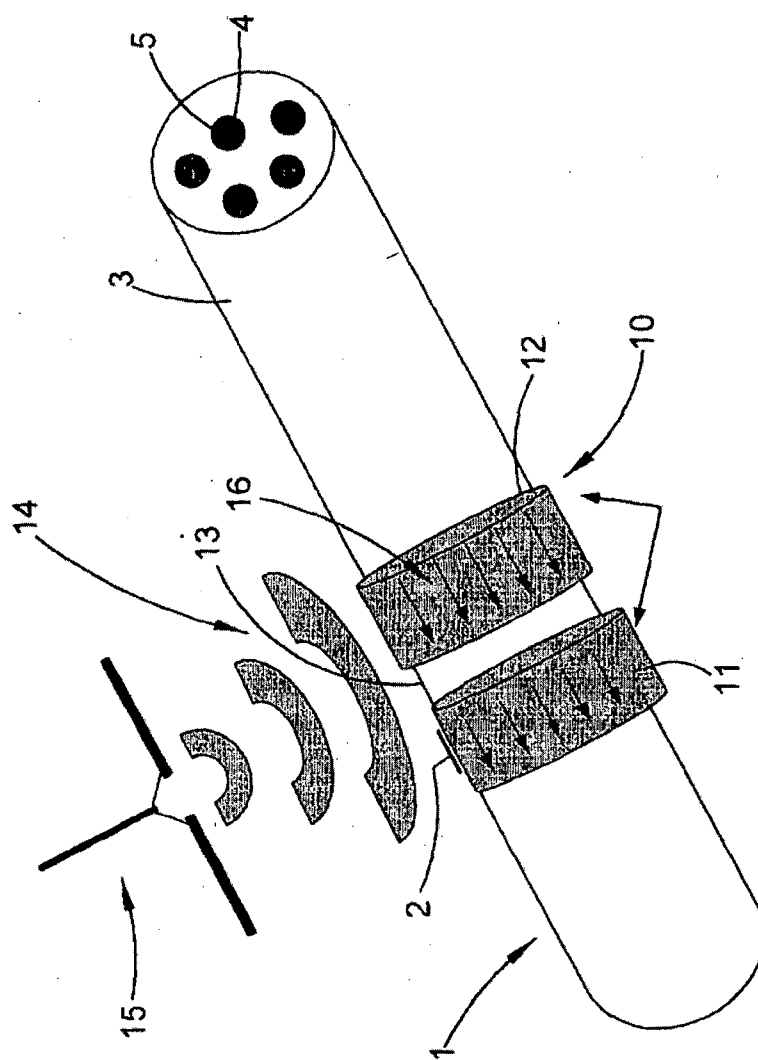


FIGURE 2

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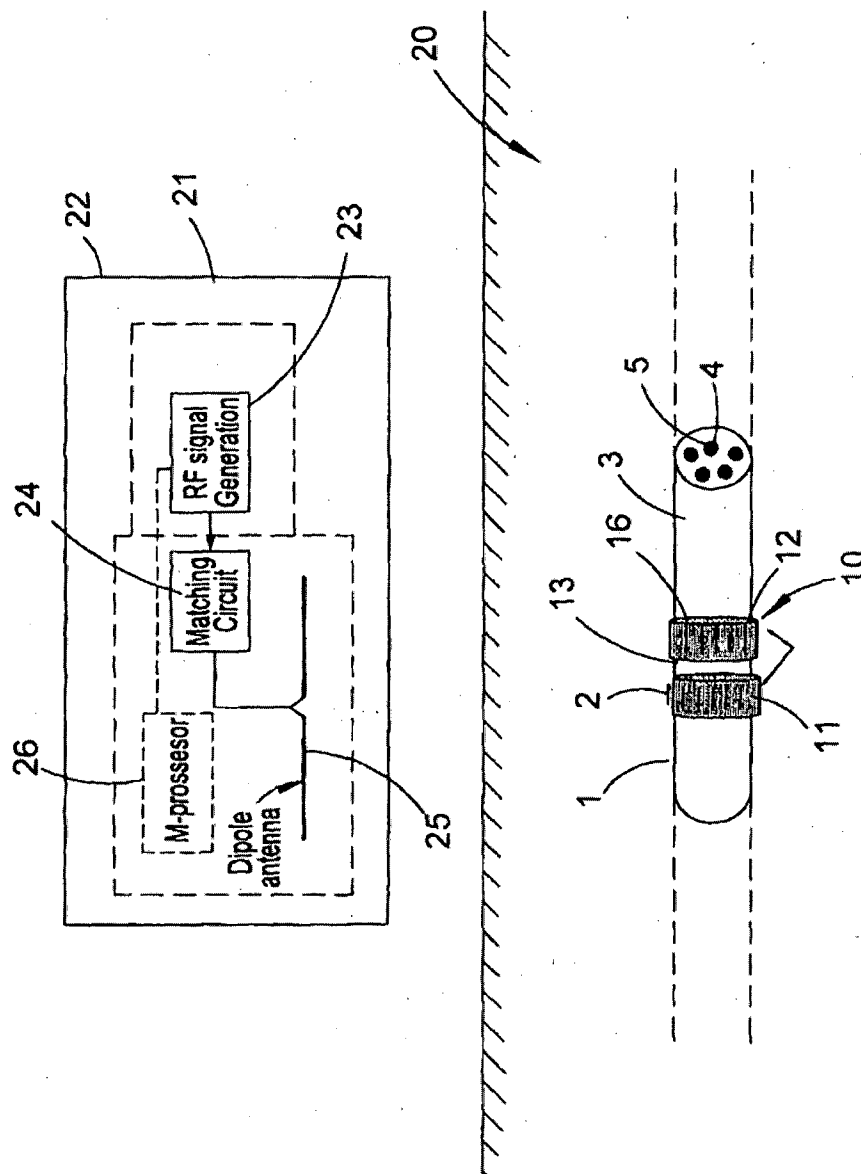


FIGURE 3

4/12

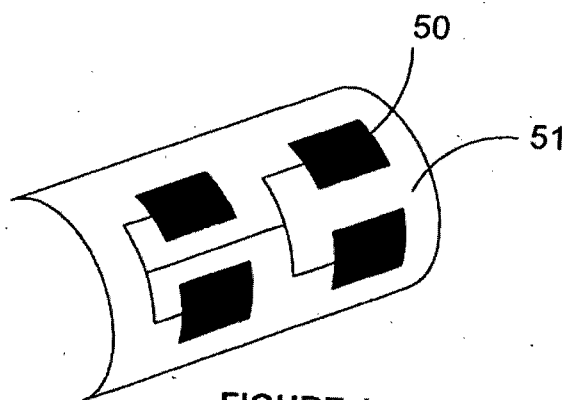


FIGURE 4

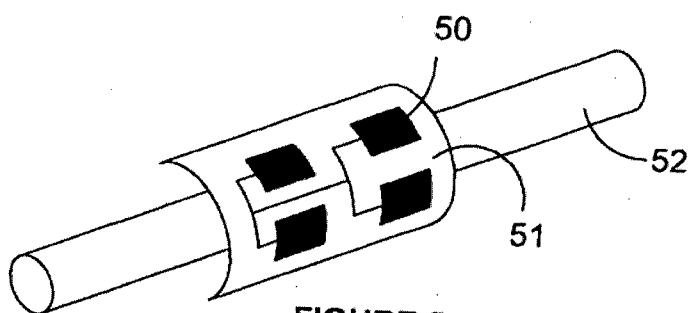


FIGURE 5

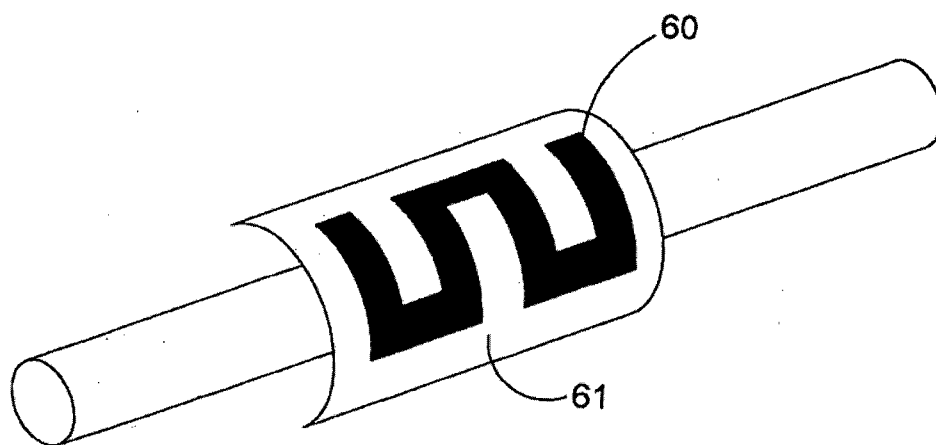
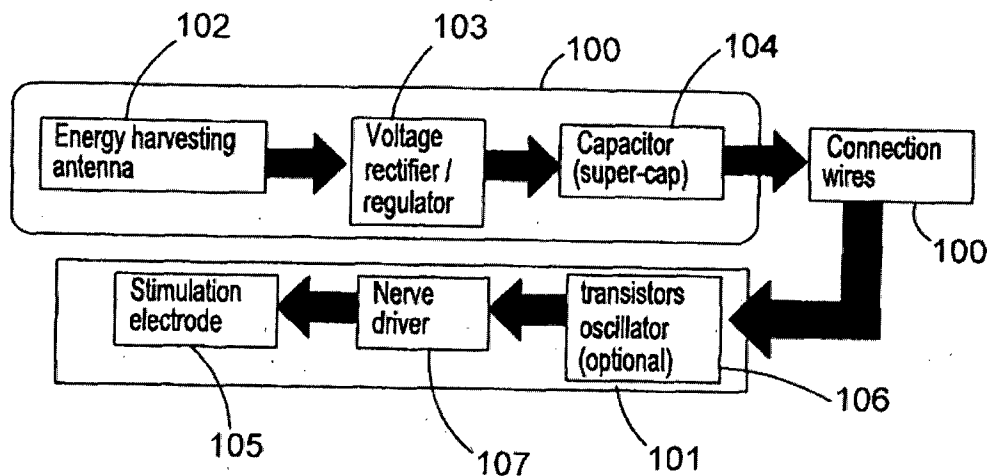
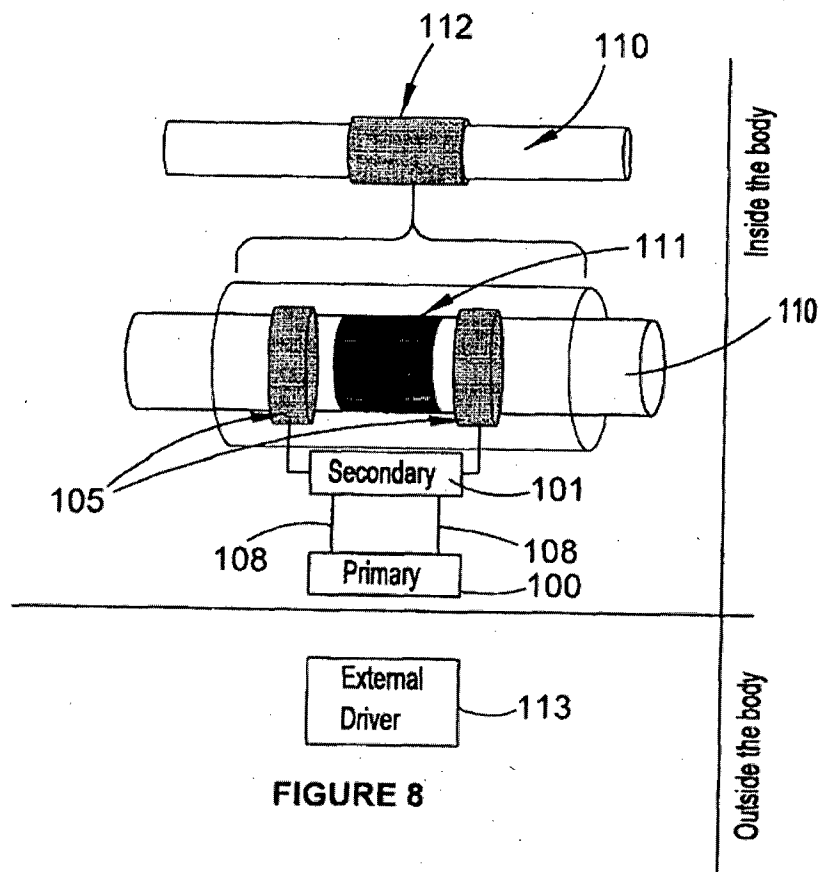


FIGURE 6

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**FIGURE 7****FIGURE 8**

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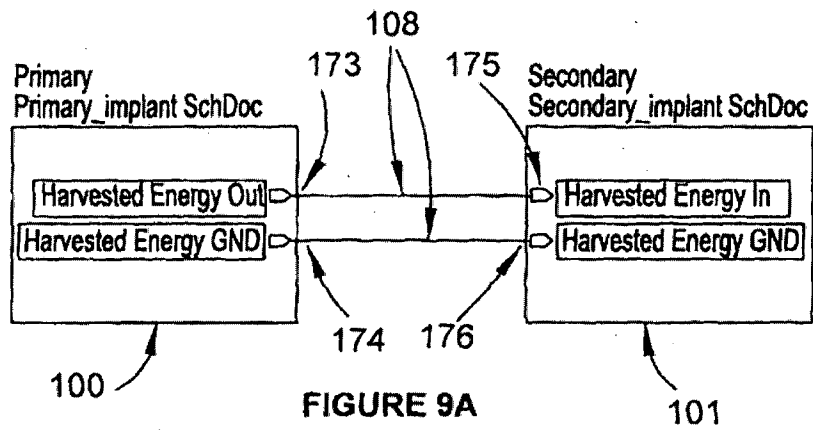


FIGURE 9A

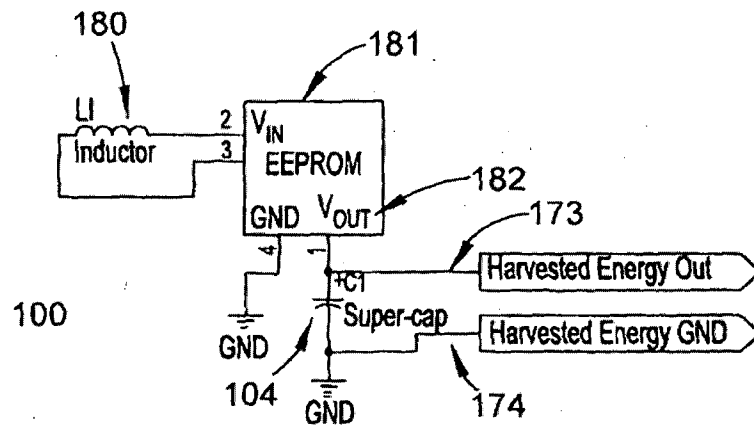


FIGURE 9B

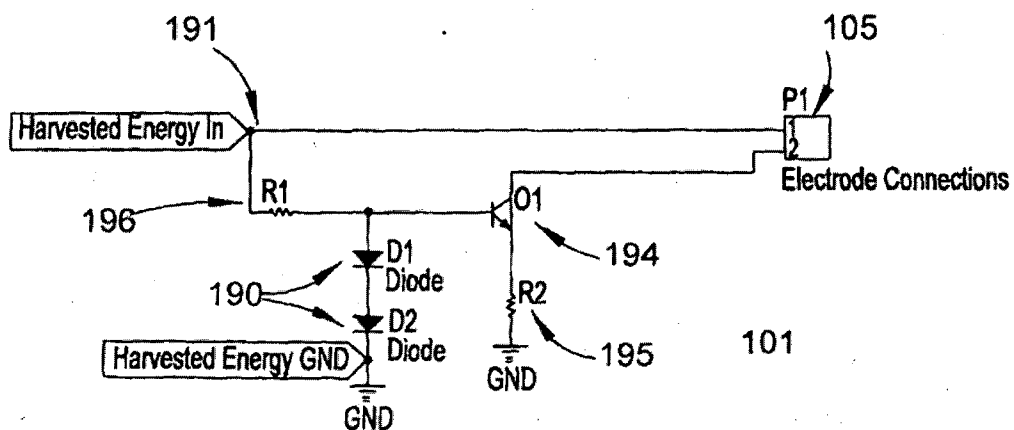


FIGURE 9C

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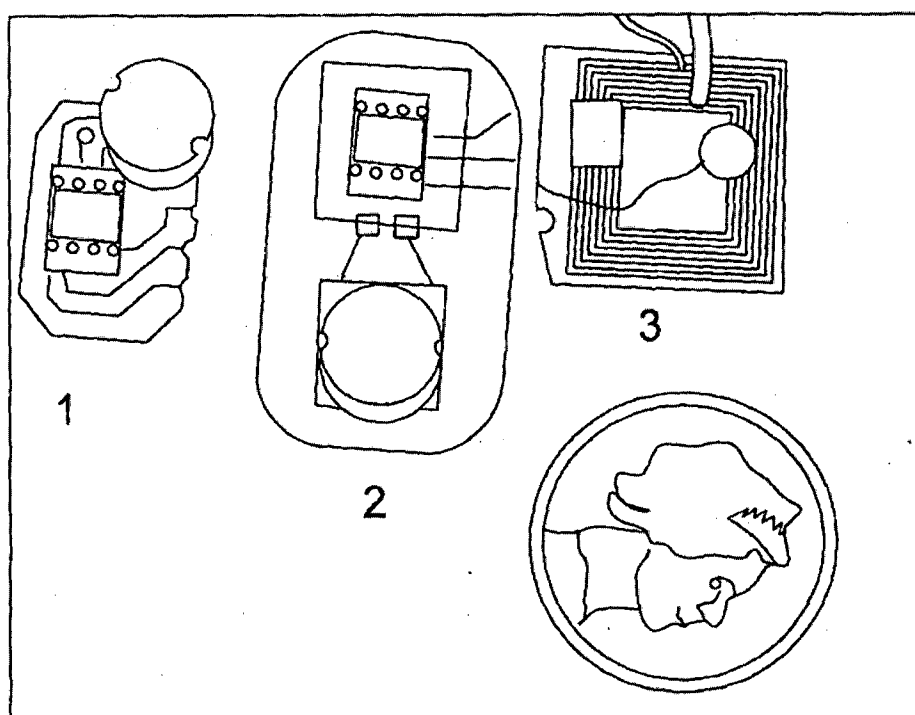


FIGURE 10

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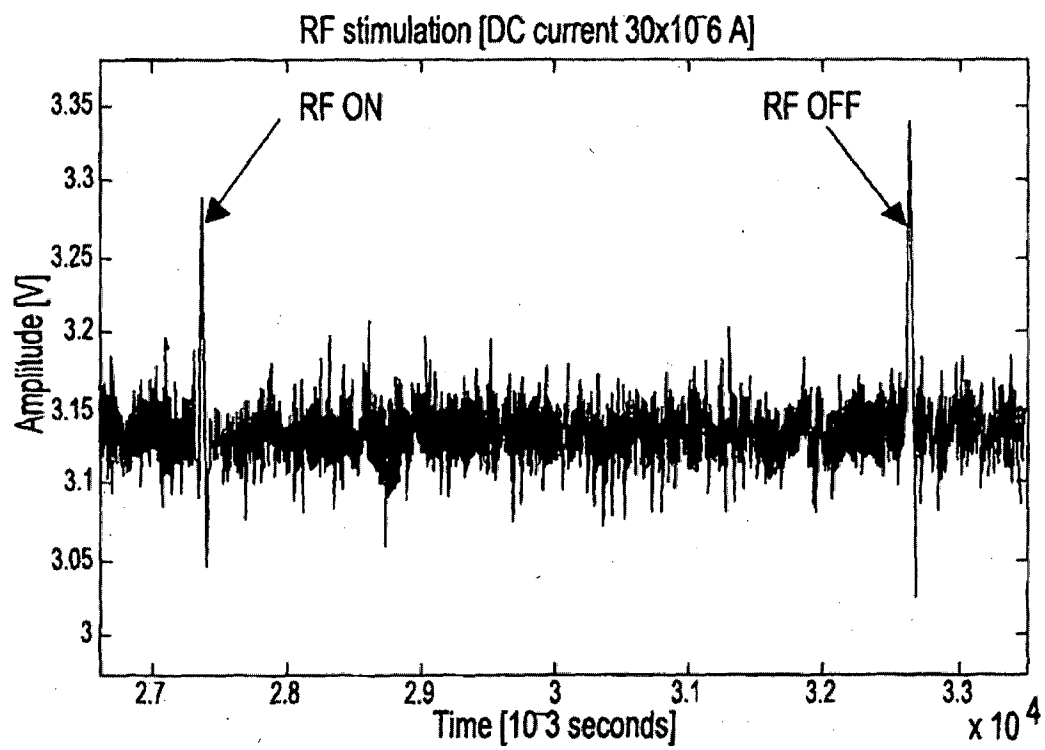


FIGURE 11

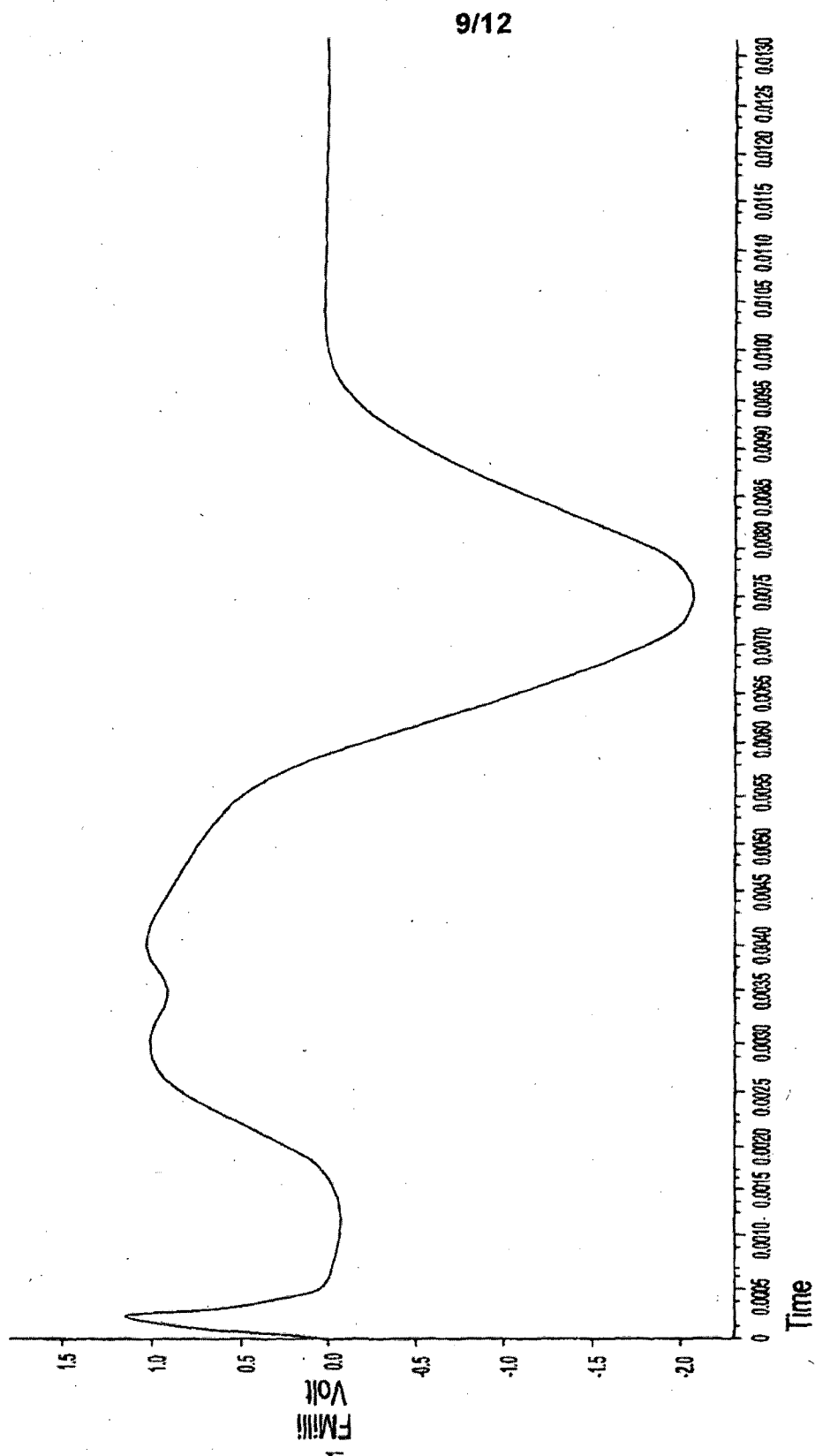
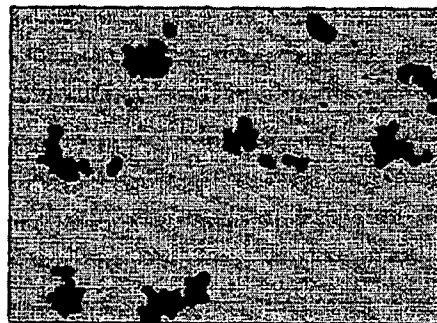


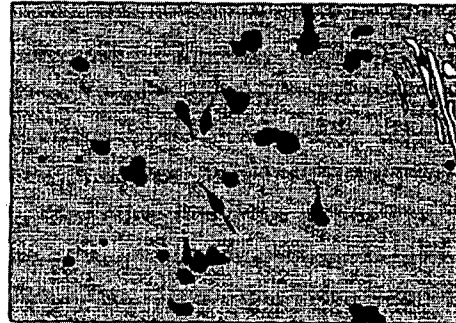
FIGURE 12

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No Current

FIGURE 13A



30 μ A Current

FIGURE 13B

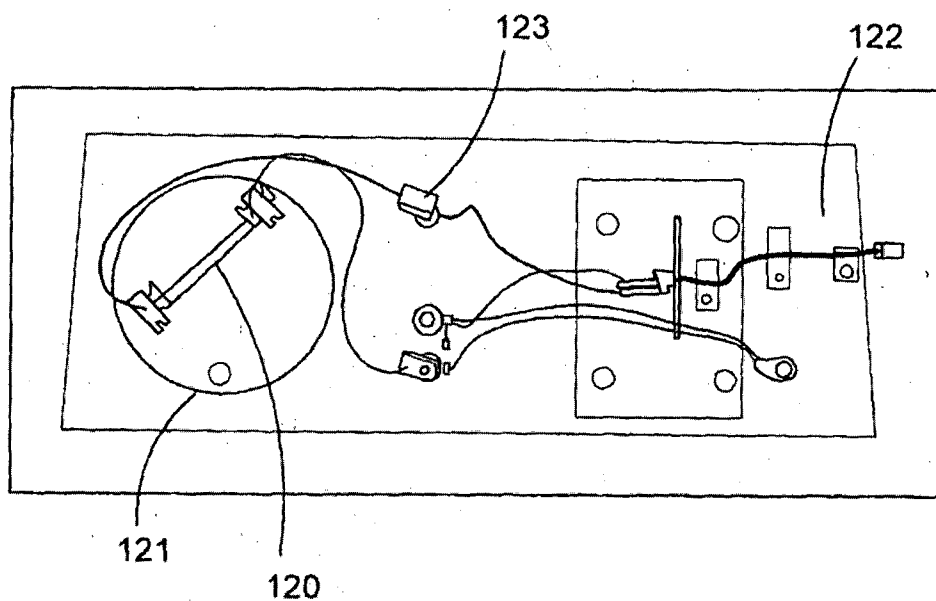


FIGURE 14A

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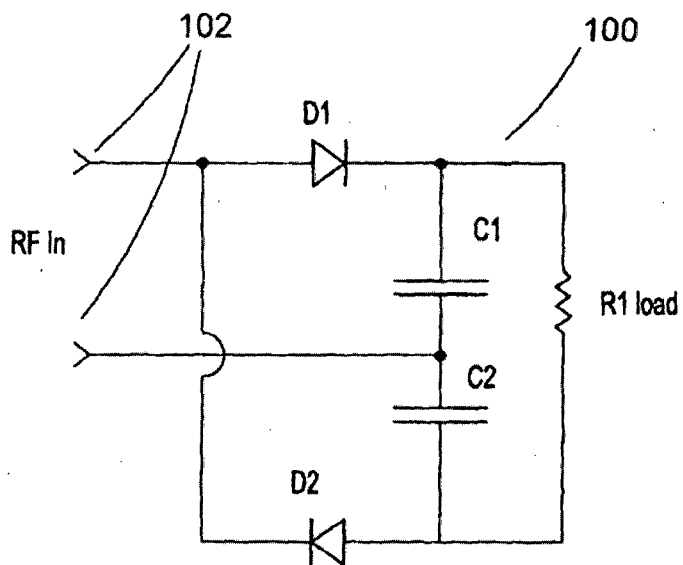


FIGURE 14B

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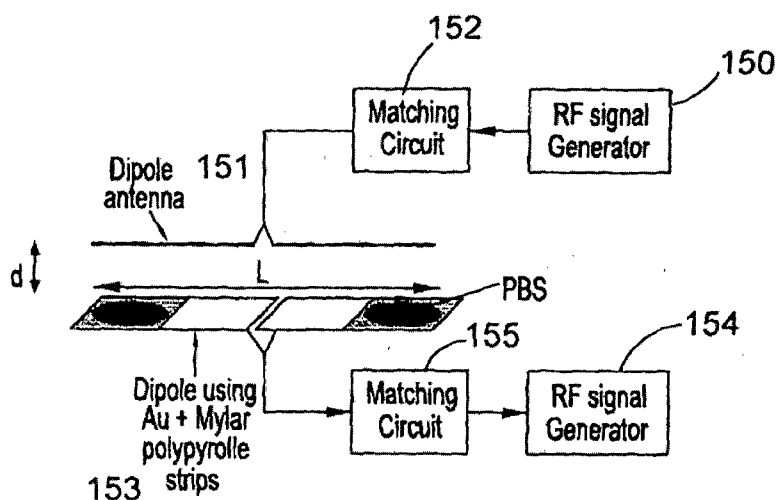


FIGURE 15

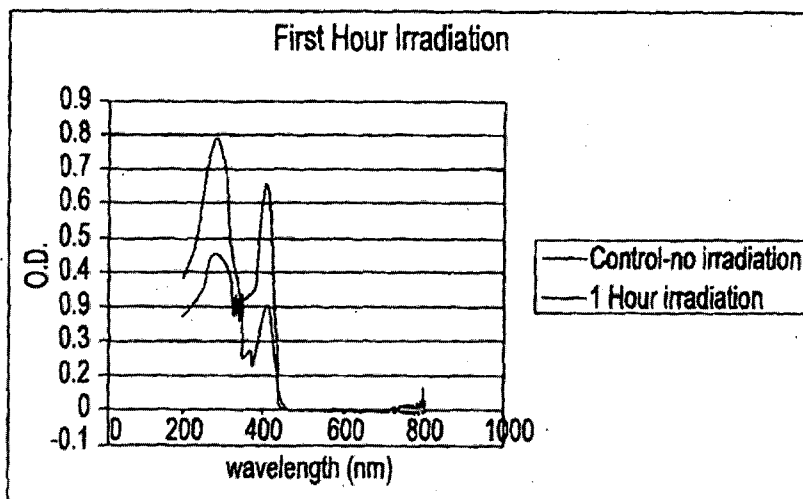


FIGURE 16

INTERNATIONAL SEARCH REPORT

 International application No.
PCT/AU2013/000028

A. CLASSIFICATION OF SUBJECT MATTER

A61N 1/18 (2006.01) A61N 1/05 (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPI and EPODOC and A61N 1/- and keywords: nerve and repair and antenna and stimulate and electrical and similar terms.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Documents are listed in the continuation of Box C	



Further documents are listed in the continuation of Box C



See patent family annex

* "A"	Special categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E"	earlier application or patent but published on or after the international filing date	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed		
Date of the actual completion of the international search 19 February 2013		Date of mailing of the international search report 19 February 2013	
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA Email address: pct@ipaustalia.gov.au Facsimile No.: +61 2 6283 7999		Authorised officer David Melhuish AUSTRALIAN PATENT OFFICE (ISO 9001 Quality Certified Service) Telephone No. 0262832426	

INTERNATIONAL SEARCH REPORT		International application No.
C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		PCT/AU2013/000028
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2006/0194724 A1 (WHITEHURST et al.) 31 August 2006 paragraphs 27, 29, 30, 36, 41 to 44, 46, 47 and 51	1 to 6, 9 to 11, 15 to 20, 22, 24 to 28, 30 to 41, 43 and 45 to 52
Y	paragraphs 27, 29, 30, 36, 41 to 44, 46, 47 and 51	12 to 14
X	WO 2008/005843 A2 (CYBERKINETICS NEUROTECHNOLOGY SYSTEMS, INC.) 10 January 2008 paragraphs 151 to 161, 47, 58, 65 and 140	1 to 7, 9 to 11 and 15 to 52
X	WO 2002/047757 A2 (ALFRED E. MANN INSTITUTE FOR BIOMEDICAL ENGINEERING AT THE UNIVERSITY OF SOUTHERN CALIFORNIA) 20 June 2002 paragraphs 31 to 34 and 24	1 to 3, 6, 9, 10, 15 to 17, 20, 22, 25 to 28, 30 to 36, 38, 39, 41, 43, 45, 46 and 51
X	WO 2010/135634 A2 (ARIZONA BOARD OF REGENTS FOR AND ON BEHALF OF ARIZONA STATE UNIVERSITY) 25 November 2010 page 7 line 25 to page 8 line 27, page 14 lines 1 to 7 and 28	1 to 3, 6 to 9, 15, 16, 20 to 36, 38 and 41 to 45
Y	page 7 line 25 to page 8 line 27, page 14 lines 1 to 7 and 28	12 to 14
X	US 2008/0319506 A1 (CAULLER) 25 December 2008 paragraphs 17, 18, 23, 27, 41 and 42	1 to 3, 6, 9 to 11, 15 to 20, 22, 24 to 28, 30 to 36, 38 to 41, 43 and 45 to 51

INTERNATIONAL SEARCH REPORT		International application No.	
Information on patent family members		PCT/AU2013/000028	
This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.			
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		AU 2008268368 B2	10 Nov 2011
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		US 2010069994 A1	18 Mar 2010
		US 2012065701 A1	15 Mar 2012
		WO 2009003025 A2	31 Dec 2008
End of Annex			
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