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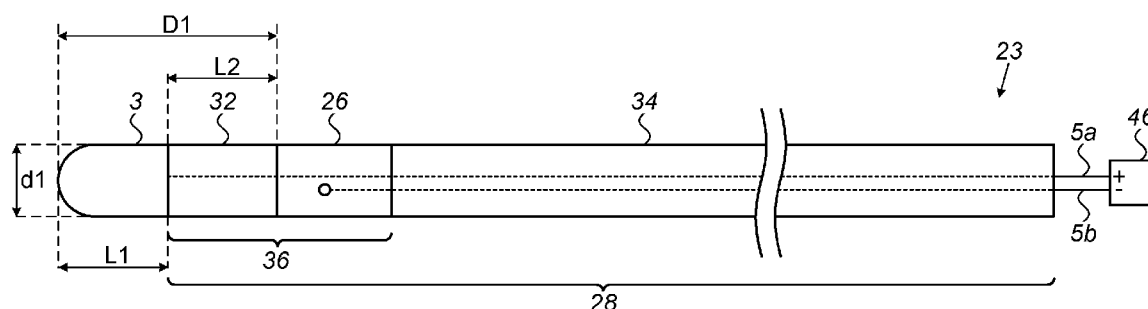


FIG. 2

(57) Abstract: Described embodiments include an apparatus (21) for removal of a thrombus from a body of a subject. The apparatus includes a first electrode (3), made of a first conductive metal having a first electronegativity, and a second electrode (26), made of a second conductive metal having a second electronegativity that is less than the first electronegativity. The apparatus further includes a voltage source (46), configured to apply a positive unipolar voltage between the first electrode and the second electrode while the first electrode is in contact with the thrombus, and while the second electrode is inside the body of the subject. Other embodiments are also described.



THROMBECTOMY DEVICES

CROSS-REFERENCE TO RELATED APPLICATIONS

The present application claims the benefit of (i) US Provisional Application 62/442,470, entitled "Thrombectomy device," filed January 5, 2017, and (ii) US Provisional Application
5 62/519,185, entitled "Electric thrombectomy device," filed June 14, 2017, the disclosures of which are incorporated herein by reference. The present application is also related to a US patent application (attorney ref. 1344-1003.2), entitled "Thrombectomy devices," filed on even date herewith.

FIELD OF THE INVENTION

10 The present application relates to the field of medical devices, particularly devices for thrombectomy, i.e., the removal of thrombi (blockages) from blood vessels.

BACKGROUND

US Patent Application Publication 2011/0301594, whose disclosure is incorporated herein by reference, describes a flexible catheter device capable of being introduced into body
15 passages, withdraw fluids therefrom or introduce fluids thereinto, and which includes electrodes configured to apply electrical signals in the body passage for carrying out thrombus dissolution and/or thrombectomy, wherein one of said electrodes is designed to contact the thrombus material and remove it or dissolve it, and wherein the electrical voltage signals are unipolar pulsatile voltage signals.

20 US Patent Application Publication 2004/0073243 describes devices and methods for removing an obstruction from a blood vessel. The devices are deployed in a collapsed condition and are then expanded within the body. The devices are then manipulated to engage and remove the obstruction.

US Patent 6,855,143 describes electrosurgical apparatus and methods for maintaining
25 patency in body passages subject to occlusion by invasive tissue growth. The apparatus includes an electrode support disposed at a shaft distal end having at least one active electrode arranged thereon, and at least one return electrode proximal to the at least one active electrode. In one embodiment, a plurality of active electrodes each comprising a curved wire loop portion are sealed within a distal portion of the electrode support.

30 US Patent 8,197,478 describes an apparatus and method for electrically induced

thrombosis. The surgical device includes a first electrode and a second electrode. The first electrode is for placement adjacent to, near, or within a treatment site of a patient. The second electrode can be movable with respect to the first electrode. When the electrodes are charged by an electricity source, negatively charged blood components are attracted to the positively charged electrode while being repelled from the negatively charged electrode. Due to the electric potential between the adjacent electrodes, thrombosis is induced. The negatively charged blood and components form a thrombus or a clot adjacent to the positively charged electrode. The surgical device can be used to induce the otherwise natural process of thrombosis. When the surgical device is used in a treatment site such as a puncture or incision, the thrombosis can seal the opening created by the treatment site.

US Patent Application Publication 2002/0133111 describes a microcatheter for removing thromboemboli from cerebral arteries in patients suffering from ischemic stroke. The microcatheter provides an extraction lumen that can be scaled to a very small diameter that is still capable of extracting and emulsifying thrombus without clogging the channel. The microcatheter uses a series of spaced apart energy application mechanisms along the entire length of the catheter's extraction lumen to develop sequential pressure differentials to cause fluid flows by means of cavitation, and to contemporaneously ablate embolic materials drawn through the extraction lumen by cavitation to thereby preventing clogging of the lumen. Preferred mechanisms for energy delivery are (i) a laser source and controller coupled to optic fibers in the catheter wall or (ii) an Rf source coupled to paired electrodes within the extraction lumen. Each energy emitter can apply energy to fluid media in the extraction channel of the catheter--wherein the intense energy pulses can be sequentially timed to cause fluid media flows in the proximal direction in the channel.

SUMMARY OF THE INVENTION

There is provided, in accordance with some embodiments of the present invention, apparatus for removal of a thrombus from a body of a subject. The apparatus includes a first electrode, made of a first conductive metal having a first electronegativity, a second electrode, made of a second conductive metal having a second electronegativity that is less than the first electronegativity, and a voltage source, configured to apply a positive unipolar voltage between the first electrode and the second electrode while the first electrode is in contact with the thrombus, and while the second electrode is inside the body of the subject.

In some embodiments, a distance between the first electrode and the second electrode is less than 3 mm.

In some embodiments, the distance is less than 0.7 mm.

In some embodiments, the apparatus further includes a tube, and the second electrode is shaped to define at least part of a wall of the tube.

In some embodiments, the first electrode is disposed at a distal end of the tube.

5 In some embodiments, the first electrode passes through a lumen of the tube.

In some embodiments, the second electrode is shaped to define a helix, and the first electrode passes through the second electrode.

In some embodiments, the first electrode and second electrode are coaxial with one another.

10 In some embodiments, a length of an exposed portion of the first electrode is between 0.1 and 50 mm.

In some embodiments, a diameter of the first electrode is between 0.01 and 4 mm.

In some embodiments, an amplitude of the unipolar voltage is between 1 and 100 V.

15 In some embodiments, in applying the unipolar voltage, the voltage source is configured to pass, between the first electrode and the second electrode, a current having an amplitude of between 0.1 and 4 mA.

In some embodiments, the first electrode includes a straight distal end.

In some embodiments, the apparatus further includes a balloon proximal to the first electrode, configured to center the first electrode with respect to the thrombus when inflated.

20 There is further provided, in accordance with some embodiments of the present invention, a method that includes applying a positive unipolar voltage between a first electrode, made of a first conductive metal having a first electronegativity, and a second electrode, made of a second conductive metal having a second electronegativity that is less than the first electronegativity, while the first electrode is in contact with a thrombus in a body of a subject,
25 and while the second electrode is inside the body of the subject. The method further includes, subsequently, removing the thrombus from the body of the subject.

In some embodiments, the method further includes, prior to applying the unipolar voltage, advancing the first electrode through the thrombus, at least until the thrombus contacts an electrical insulator that is disposed proximally to an exposed portion of the first electrode.

30 In some embodiments, the method further includes measuring an impedance between the

first electrode and the second electrode, and ascertaining that the thrombus has contacted the insulator, based on the measured impedance.

In some embodiments, the method further includes, prior to applying the unipolar voltage, advancing the first electrode through the thrombus until an entire length of the first
5 electrode contacts the thrombus.

In some embodiments, applying the unipolar voltage includes applying the unipolar voltage while a distance between a distal tip of the first electrode and a distal tip of the second electrode is between 1 and 100 mm.

In some embodiments, an electrical insulator is disposed proximally to an exposed
10 portion of the first electrode, and the method further includes, prior to applying the unipolar voltage, advancing the second electrode over the insulator.

In some embodiments, the second electrode is expandable, and the method further includes, prior to applying the unipolar voltage:

advancing a catheter, containing both the first electrode, and the second electrode in a
15 crimped position, through the thrombus; and

subsequently, withdrawing the catheter, such that the second electrode expands, from the crimped position, within the thrombus.

In some embodiments, the method further includes, prior to contacting the thrombus with the first electrode, centering the first electrode with respect to the thrombus, by inflating a
20 balloon that is proximal to the first electrode.

There is further provided, in accordance with some embodiments of the present invention, apparatus for removal of a thrombus from a body of a subject. The apparatus includes an outer electrode, shaped to define a helix, and an inner electrode, passing through the outer electrode, configured to attach to the thrombus when a positive unipolar voltage is applied
25 between the inner electrode and the outer electrode.

In some embodiments, the outer electrode is expandable.

In some embodiments, the apparatus further includes a voltage source configured to apply the positive unipolar voltage.

In some embodiments, the apparatus further includes an electrically-insulating cover over
30 both a proximal portion of the outer electrode and a distal portion of the outer electrode.

In some embodiments, the inner electrode is rod-shaped.

In some embodiments, the inner electrode passes through a center of the outer electrode.

In some embodiments, a distance between the inner electrode and a middle portion of the outer electrode is between 1 and 100 mm.

In some embodiments, the distance is between 2 and 30 mm.

5 In some embodiments, the inner electrode is made of a first conductive metal having a first electronegativity, and the outer electrode is made of a second conductive metal having a second electronegativity that is less than the first electronegativity.

There is further provided, in accordance with some embodiments of the present invention, a method that includes advancing a catheter, which contains both a crimped outer
10 electrode, and an inner electrode that passes through the outer electrode, through a thrombus in a body of a subject. The method further includes, subsequently to advancing the catheter through the thrombus, withdrawing the catheter, such that the outer electrode expands within the thrombus. The method further includes, subsequently to withdrawing the catheter, applying a
15 positive unipolar voltage between the inner electrode and the outer electrode, such that the thrombus becomes attached to the inner electrode, and, subsequently to the thrombus becoming attached to the inner electrode, withdrawing the inner electrode and the outer electrode from the
body of the subject.

In some embodiments, withdrawing the outer electrode includes, using the outer electrode, applying a mechanical force to the thrombus.

20 The present invention will be more fully understood from the following detailed description of embodiments thereof, taken together with the drawings, in which:

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a schematic illustration of apparatus for removal of a thrombus from a body of subject, in accordance with some embodiments of the present invention; and

25 Figs. 2-4 are schematic illustrations of electrode assemblies, in accordance with some embodiments of the present invention.

DETAILED DESCRIPTION OF EMBODIMENTS

OVERVIEW

Embodiments of the present invention provide apparatus and methods for removing a

thrombus from a blood vessel or other body passage, by application of a unipolar voltage between two electrodes in the body passage. For example, a positive unipolar voltage may be applied between a first electrode in contact with the thrombus, and a second electrode disposed proximally to the first electrode. The positive voltage causes the first electrode to attract the negatively-charged thrombus, such that the thrombus attaches to the first electrode. Subsequently, the thrombus may be removed by withdrawing the first electrode. Alternatively, a negative unipolar voltage may be applied between the first and second electrodes, causing dissolution of the thrombus. Subsequently, the disintegrated thrombus may be removed from the subject.

Advantageously, the electrodes may be made of different conductive metals having different respective electronegativities, such as to increase the effect of the applied unipolar voltage. For example, the first, thrombus-contacting electrode may have a higher electronegativity than that of the second electrode, such as to increase the attraction between the thrombus and the thrombus-contacting electrode.

In some embodiments, the thrombus-contacting electrode is advanced through the thrombus, at least until the thrombus contacts an electrical insulator that is disposed proximally to the exposed portion of the first electrode. This reduces, or eliminates, any exposed surface area of the electrode proximally to the thrombus, thus further increasing the effect of the applied unipolar voltage. To ascertain that the thrombus has contacted the insulator, the impedance between the first electrode and the second electrode may be measured, since the impedance between the electrodes changes as a function of the degree to which the electrode is covered by the thrombus.

In some embodiments, the second electrode is shaped to define a helix, and the first electrode passes through the helix. Advantageously, the helical second electrode helps withdraw the thrombus from the subject, by applying, to the thrombus, a mechanical force that complements the force of electrical attraction between the thrombus and the first electrode.

In general, in the context of the present application, including the claims, the term "unipolar voltage" may refer to any voltage signal that is mostly of a single polarity, even if the signal is not strictly unipolar. For example, a voltage signal that, during each five-minute interval of the signal, is positive for at least 80% of the interval, may be referred to as a positive unipolar voltage.

In general, in the context of the present application, including the claims, the term "thrombus" may refer to any combination of blood, fat, cholesterol, plaque, and/or foreign

materials originating from outside the body, which may possess an electric charge.

APPARATUS DESCRIPTION

Reference is initially made to Fig. 1, which is a schematic illustration of apparatus 21 for removal of a thrombus from a body of subject, in accordance with some embodiments of the present invention. (Fig. 1 generally corresponds to Fig. 2 of US Patent Application Publication 2011/0301594, whose disclosure is incorporated herein by reference.)

Apparatus 21 comprises a catheter 20, which has a proximal end 20p and a distal end 20d, and which is shaped to define a lumen 20a. Following the introduction of catheter 20 into the vascular system of the subject, e.g., using standard angiographic catheterization techniques, an electrode assembly 23 is passed through lumen 20a, and is subsequently used to remove a thrombus from the vascular system, as described in detail hereinbelow. In some embodiments, catheter 20 further comprises a proximal, lateral port 2 for withdrawing any debris (e.g., thrombus fragments) generated during the treatment process, using a syringe (not shown) or any other device suitable for this purpose. Alternatively or additionally, a second catheter, passing over catheter 20, may be positioned proximally to the thrombus, and subsequently used to aspirate such debris. Alternatively or additionally, a net disposed near the distal end of electrode assembly 23 may be used to catch and remove such debris.

In the particular embodiment shown in Fig. 1, electrode assembly 23 comprises a pair of coaxial electrodes: a first electrode 3, which is used to contact the thrombus, and a second electrode 26. First electrode 3 comprises a wire having a diameter d1 that may have any suitable value, such as between 0.01 and 4 mm. First electrode 3 comprises a distal end 3d. In some embodiments, as shown in subsequent figures, distal end 3d is straight. Alternatively, as shown in Fig. 1, distal end 3d may be curly, or may have any other suitable shape that increases the contact area between the electrode and the thrombus, relative to a straight distal end. For example, the surface of distal end 3d (or of the entire first electrode) may comprise a plurality of protrusions, or bumps, which increase the surface area available for contact with the thrombus. Alternatively or additionally, distal end 3d (or the entire first electrode) may be curved, such as to decrease the likelihood that the electrode will damage tissue of the subject.

In some embodiments, first electrode 3 is connected at its proximal end, at a connection point 4, to another wire 5, which passes through lumen 20a to proximal end 20p of the catheter. In other embodiments, instead of wire 5, first electrode 3 extends through the lumen of the catheter, to the proximal end of the catheter.

Typically, an electrically-isolating material separates the first electrode from the second electrode, such that the first and second electrodes are electrically isolated from one another. For example, an electrically-isolating layer 5i may cover wire 5, with second electrode 26, in turn, covering electrically-isolating layer 5i. For example, as shown in Fig. 1, second electrode 26 may comprise a multi-stranded wire, comprising a plurality of electrically-conducting strands 26s that are braided over, or wrapped around, electrically-isolating layer 5i. In some embodiments, an electrically-isolating cover 20c covers most of the second electrode, such that only a distal portion 26d of the second electrode remains exposed. In some embodiments, distal portion 26d is between 7 and 25 mm long, e.g., around 15 mm long.

Typically, the first electrode - or the exposed portion of the first electrode, which is the portion of the first electrode not covered by electrically-isolating layer 5i - has a length L1 that is between 0.1 and 150 mm (e.g., between 5 and 50 mm, such as between 5 and 25 mm). Alternatively, length L1 may have any other suitable value. The distal end of the first electrode is typically blunt, to help prevent any damage to the lumen through which the first electrode is passed.

Wire 5 terminates, at its proximal end, at a first terminal 3t. Similarly, the second electrode terminates, at its proximal end, at a second terminal 26t. Upon the first electrode contacting the thrombus, a unipolar voltage is applied between the electrodes, via first terminal 3t and second terminal 26t. A positive unipolar voltage between the first and second electrodes facilitates a thrombectomy (i.e., a removal of the thrombus), by causing the negatively-charged thrombus to become attached to the first electrode. Such a positive voltage may be obtained, for example, by grounding second terminal 26t, while applying a positive unipolar voltage signal to first terminal 3t. Conversely, a negative unipolar voltage between the first and second electrodes facilitates dissolution of the thrombus. Such a negative voltage may be obtained, for example, by grounding first terminal 3t, while applying a positive unipolar voltage signal to second terminal 26t.

In general, the unipolar voltage signal applied to the terminals may have any suitable form, such as any of the forms described in US Patent Application Publication 2011/0301594, whose disclosure is incorporated herein by reference. For example, the unipolar voltage signal may be a periodic signal that includes a sequence of pulses, each of these pulses, for example, being shaped as the positive half-wave of a sinusoidal signal, or having a trapezoidal shape. Alternatively, the unipolar voltage signal may be a direct current (DC) voltage signal.

Although the amplitude of the unipolar voltage may have any suitable value, this

amplitude is typically between 0.1 and 100 V, e.g., between 1 and 100 V, such as between 1 and 50 V, or between 4 and 40 V. Such an amplitude is large enough to be effective, yet small enough such as to avoid damaging the tissue near the thrombus. For example, as described in US Patent Application Publication 2011/0301594 with reference to Fig. 1D thereof, each trapezoidal pulse of the applied voltage signal may (i) linearly ramp up from ground level (0 volts) to an amplitude of around 40 volts, over a time period of around 5 milliseconds, (ii) remain constant over a time period of around 5 milliseconds, and then (iii) linearly ramp down to ground level over a time period of around 5 milliseconds. Before the beginning of the subsequent pulse, the voltage may remain at ground level for another time period of around 5 milliseconds. In general, the applied unipolar voltage signal, if pulsatile, may have any suitable frequency, such as between 0.1 Hz to 100 MHz, e.g., around 50 Hz, as in the example immediately above. Typically, the unipolar voltage is applied such that a current having an amplitude of between 0.1 and 4 mA (e.g., 1-3 mA) is passed between the first electrode and the second electrode.

In some embodiments, the voltage source that applies the unipolar voltage is current-regulated, e.g., to between 0.1 and 4 mA. In other embodiments, the voltage source is voltage-regulated, e.g., to between 1 and 50V. Typically, the voltage is applied for a duration of more than 1 second, to facilitate attachment of the thrombus to the first electrode, but less than 10 minutes, to prevent risk to the patient. For example, the duration may be more than 5 seconds but less than 5 minutes, e.g., more than 10 seconds but less than 2 minutes.

Typically, the unipolar voltage is applied while the first electrode is in contact with the thrombus, and while the second electrode is inside the body of the subject, e.g., within the catheter lumen, but not in contact with the thrombus. (Notwithstanding the above, it is noted that in some embodiments, e.g., as described below with reference to Fig. 4, both of the electrodes may contact the thrombus.) For example, prior to applying the unipolar voltage, the electrode assembly may be advanced, such that the first electrode pierces the thrombus (i.e., passes through the thrombus in contact therewith). Alternatively, as described below with reference to Fig. 3, catheter 20, with the two electrodes appropriately positioned within the catheter lumen, may be advanced through the thrombus and then withdrawn from over the first electrode, such that the first electrode is positioned within the thrombus.

In some cases, it may be advantageous for the position of the catheter to remain as distal as possible during the application of the unipolar voltage, to facilitate the collection of any bubbles or debris generated during the procedure. Hence, the second electrode, and even the first electrode and the thrombus with which it is in contact, may be partly or fully contained

within the catheter lumen while the unipolar voltage is applied. For example, following, or together with, the advancement of the electrode assembly as described in the paragraph above, the catheter may also be advanced, such that the second electrode and/or the first electrode are contained within the catheter lumen during the subsequent application of the unipolar voltage.

5 Typically, while the unipolar voltage is applied, the respective distal tips of the electrodes are spaced apart from each other by a distance D1 of between 1 and 100 mm, such as between 2 and 30 mm. Such a distance facilitates suitable electrical conductivity between the electrodes via the blood at the treatment site, while maintaining the second electrode at a sufficient distance from the thrombus such as to prevent contact of the second electrode with the thrombus.
10 Alternatively, distance D1 may be less than 1 mm (in which case the second electrode may contact the thrombus), or more than 100 mm.

In some embodiments, the separation distance L2 between the first electrode and the second electrode (i.e., the distance between the proximal tip of the first electrode and the distal tip of the second electrode) is relatively small, such as to reduce the amount of electric current
15 that passes through the tissue surrounding the blood vessel in which the thrombus is located. For example, assuming the total diameter of (i) the blood vessel, and (ii) the tissue surrounding the blood vessel, is D2, such that the total transverse cross-sectional area A2 of the blood vessel and the surrounding tissue is $\pi(D2/2)^2$, L2 may satisfy the relation $L2 \cdot (1 \text{ mm}) \ll A2$, where " $\ll$ " implies "at least one order of magnitude smaller than." (The above assumes L2 is given in mm,
20 and A2 in mm^2 .) In some embodiments, L2 is even smaller, in that L2 satisfies the relation $L2 \cdot (1 \text{ mm}) \ll A1$, where A1 is the transverse cross-sectional area of the blood vessel.

In general, the ease of manufacture increases with L2. Hence, for ease of manufacture, embodiments of the present invention typically set L2 in accordance with the blood-vessel dimensions, rather than always making L2 as small as possible. In other words, for a relatively
25 large blood vessel, since it may not be necessary to have such a small separation between the electrodes, a larger separation distance may be used, relative to a smaller blood vessel. Some embodiments of the present invention define a range of suitable separations for each particular application, where the upper limit of the range is one order of magnitude less than $A1/(1 \text{ mm})$, and the lower limit of the range is two orders of magnitude smaller than $A1/(1 \text{ mm})$.

30 For example, in neurovascular applications, a relatively large vessel may be around 6 mm in diameter, such that the vessel has a cross-sectional area of around 30 mm^2 . Hence, for such application, distance L2 may be between 0.3 mm and 3 mm. Smaller vessels, such as in the more distal segments of the middle cerebral artery (MCA) in the brain, have a cross-sectional

area of around 7 mm^2 . Hence, for such applications, L2 may be between 0.07 mm and 0.7 mm. For the treatment of other conditions, such as deep vein thrombosis, pulmonary embolisms, or coronary artery occlusions, L2 may likewise be set in accordance with the blood-vessel diameter (or cross-sectional area), as described above.

5 Typically, the electrodes are made of different respective conductive metals. Typically, when performing a thrombectomy (by applying a positive voltage between the first and second electrodes), the first electrode has a higher electronegativity than that of the second electrode. For example, the first electrode may be made of gold or platinum, with the second electrode made of titanium or stainless steel. Conversely, when performing thrombus dissolution (by
10 applying a negative voltage between the first and second electrodes), the first electrode typically has a lower electronegativity than that of the second electrode.

(It is noted that, in the context of the present description and claims, an electrode may be considered to be "made of" a particular material, even if it is only coated by this material. For example, an electrode "made of" titanium may comprise any suitable material that is coated by a
15 layer of titanium.)

In some embodiments, apparatus 21 comprises radiopaque markers, which facilitate visualization of the apparatus using x-ray imaging. For example, one or more radiopaque gold rings or coatings may cover a portion of the second electrode, if the second electrode is made of titanium, or any other material that is generally not radiopaque.

20 In some embodiments, apparatus 21 comprises a balloon, disposed proximally to the first electrode. Prior to the first electrode contacting the thrombus, the balloon is inflated, such as to center the first electrode relative to the thrombus. The first electrode may then pass through the center of the thrombus, thus increasing the effectiveness of the subsequently applied unipolar voltage.

25 Reference is now made to Fig. 2, which is a schematic illustration of electrode assembly 23, in accordance with some embodiments of the present invention.

In some embodiments, as shown in Fig. 2, electrode assembly 23 comprises a (hollow) tube 28, second electrode 26 being shaped to define part of the wall of tube 28. (Tube 28 may alternatively be referred to as a "hollow shaft.") As further shown, first electrode 3 may be
30 disposed at the distal end of the tube. As described above with reference to Fig. 1, first electrode 3 may comprise a straight wire (that is not hollow), having any suitable diameter and length. For example, the diameter d1 of the first electrode may be between 0.01 and 4 mm, and/or the length

L1 of the first electrode may be between 0.1 and 50 mm (e.g., between 5 and 25 mm). In some embodiments, as shown, the diameter of tube 28 is the same as the diameter of the first electrode.

For example, tube 28 may comprise a proximal portion 34, made of any suitable conductive or non-conductive material, and a distal portion 36, comprising a tubular second electrode 26, along with an electrical insulator 32, which typically is also tubular, that separates the second electrode from the first electrode. A first wire 5a, which passes through the lumen of the tube, may be connected at its distal end to the first electrode. Likewise, a second wire 5b, also passing through the lumen of the tube, may be connected at its distal end to the second electrode. In such embodiments, a voltage source 46 may apply a unipolar voltage between the electrodes by applying the unipolar voltage between first wire 5a and second wire 5b.

Alternatively, in place of proximal portion 34 of the tube wall, second electrode 26 may extend to the proximal end of the tube. In such embodiments, second wire 5b may not be needed. Rather, a unipolar voltage may be applied between the electrodes by applying the unipolar voltage between first wire 5a and second electrode 26 directly, or between first wire 5a and an external wire connected to second electrode 26.

In general, the distance D1 between the respective distal tips of the electrodes may have any suitable value. Typically, however, distance D1 is between 1 and 100 mm, such as between 2 and 30 mm, as described above with reference to Fig. 1. For example, if L1 is 15 mm, the length of insulator 32 may likewise be 15 mm, such that D1 is 30 mm. Likewise, separation distance L2 (which is equivalent to the length of insulator 32) may be relatively small, and may be set in accordance to the dimensions of the blood vessel in which the thrombus is contained, as described above with reference to Fig. 1.

Insulator 32 may be made of any suitable biocompatible insulating material, such as Polyimide, Silicone, PolyUrethane, PolyEthylene, or Teflon. In some embodiments, insulator 32 comprises a glue or adhesive, such as a cyanoacrylate adhesive. In other embodiments, instead of insulator 32, an air gap (of length L2) separates the two electrodes from one another.

Reference is now made to Fig. 3, which is a schematic illustration of electrode assembly 23, in accordance with other embodiments of the present invention.

In Fig. 3, as in Fig. 2, second electrode 26 is tubular, and is coaxial with first electrode 3, in that the two electrodes share a common longitudinal axis 27. Fig. 3 differs from Fig. 2, however, in that first electrode 3 passes through the lumen of second electrode 26. In particular, first electrode 3 passes through the lumen of tubular insulator 32, which in turn passes through the lumen of second electrode 26. Insulator 32 is thus disposed proximally to the exposed

portion of the first electrode, and the second electrode, in turn, is disposed proximally to the exposed portion of the insulator.

In some embodiments, first electrode 3, tubular insulator 32, and second electrode 26 are fixed in place, relative to each other. In other embodiments, at least one of these elements is slideable with respect to the others. For example, the first electrode may be slideable within the tubular insulator, and/or the second electrode may be slideable over the tubular insulator. Thus, for example, prior to applying the unipolar voltage, the second electrode may be advanced over the insulator, until the distance D1 between the respective distal tips of the electrodes is less than a predefined target (such 100 mm or 30 mm, as described above with reference to Fig. 1), and/or until the distance between the two electrodes (i.e., the exposed length of insulator 32) is less than a predefined target separation distance L2 (such as 3 mm or 0.7 mm). Alternatively or additionally, prior to applying the unipolar voltage, the first electrode may be advanced through the lumen of the insulator, until the length between the respective distal tips of the electrodes reaches a predefined target, and/or until the distance between the two electrodes reaches a predefined target.

In some embodiments, second electrode 26 is shaped to define only the distal portion of the wall of tube 28 (i.e., the second electrode does not extend to the proximal end of tube 28), and is therefore connected to the proximal end of electrode assembly 23 via a wire, as in Fig. 2. Alternatively or additionally, first electrode 3 may not extend to the proximal end of the electrode assembly; rather, a wire, passing through the lumen of insulator 32, may connect the first electrode 3 to the proximal end of electrode assembly, as in Fig. 2.

In some embodiments, the exposed portion of the first electrode is straight, as shown in Fig. 3. In other embodiments, the exposed portion of the first electrode is curved, such as to decrease the likelihood that the electrode will damage tissue of the subject.

As described above with reference to Fig. 1, radiopaque markers may be disposed at any suitable location on electrode assembly 23. For example, Fig. 3 shows an embodiment in which the distal portion of the second electrode comprises a radiopaque marker 38, comprising a ring of radiopaque material.

In some embodiments, a second tube, concentric with tube 28, is disposed within, or around the outside surface of, tube 28. Such a second tube may be radiopaque, thus facilitating visibility of the electrode assembly under fluoroscopy, and/or may impart particular mechanical properties (e.g., rigidity) to the electrode assembly.

Reference is now made to Figs. 1-3, collectively.

Typically, prior to applying the unipolar voltage for thrombectomy or thrombus dissolution, the first electrode is advanced through the thrombus, at least until the thrombus contacts the electrical insulator (e.g., insulator 32) that is disposed proximally to the exposed portion of the first electrode. For example, the first electrode may be advanced through the thrombus until the entire length of the first electrode (or the entire length of the exposed portion of the first electrode) contacts the thrombus. This increases the effect of the applied voltage, by reducing, or eliminating, any exposed portion of the first electrode that is proximal to the thrombus. The first electrode may be advanced through the thrombus by distally pushing the entire electrode assembly through the lumen of catheter 20; alternatively, for embodiments in which the first electrode is slideable with respect to other elements belonging to the electrode assembly, the first electrode may be pushed, while holding the remainder of the electrode assembly in place.

Although the thrombectomy or thrombus-dissolution procedure described herein is, typically, performed under fluoroscopy, it may be difficult, based on fluoroscopy alone, to ascertain that the thrombus has contacted the insulator. Hence, in some embodiments, the impedance between the first electrode and the second electrode is measured as the first electrode is advanced through the thrombus, as this measured impedance indicates the extent to which the first electrode is exposed proximally to the thrombus. (The impedance increases as more of the electrode becomes covered by the thrombus.) Based on the measured impedance, it may be ascertained that the thrombus has contacted the insulator.

In some embodiments, to measure the impedance, a voltage, which is lower than the unipolar voltage applied for treatment, is applied between the electrodes, and the resulting current is then measured. The impedance is then the voltage divided by the measured current. (Since the actual value of the impedance is not necessarily of interest, the impedance may be "measured" by measuring the current, even without computing the actual impedance value. For example, once the current reaches a minimum, it may be ascertained that the thrombus has contacted the insulator, even without computing any impedance values.) In other embodiments, the impedance is measured by passing a low current between the electrodes, and then measuring the resulting voltage.

In other embodiments, catheter 20, while containing the two electrodes, is advanced through the thrombus. Subsequently, the catheter is withdrawn from over the first electrode (and, optionally, from over the second electrode), such that the first electrode remains positioned within the thrombus, with the second electrode being positioned proximally thereto. Subsequently, the unipolar voltage is applied.

Reference is now made to Fig. 4, which is a schematic illustration of electrode assembly 23, in accordance with yet other embodiments of the present invention.

In some embodiments, second electrode 26 wraps around first electrode 3, with a radial gap separating between the two electrodes. For example, second electrode 26 may be shaped to define a helix, and first electrode 3, which is typically rod-shaped, may pass through the second electrode, along the longitudinal axis of the second electrode. Typically, in such embodiments, the proximal and distal portions of the second electrode are covered by an insulating cover 42, such that only the middle portion 44 of the second electrode is exposed. (Middle portion 44 includes the portion of the second electrode having a maximum radius, relative to other portions of the second electrode.) Insulating cover 42 helps prevent unwanted electrical contact between the two electrodes. (In these embodiments, the first electrode may be referred to as an "inner electrode," and the second electrode may be referred to as an "outer electrode," or as a "stent.")

Typically, the first electrode passes through the center of the second electrode, such that the distance D1 between the first electrode and middle portion 44, which is approximately equal to the radius of middle portion 44, is between 1 and 100 mm, such as between 2 and 30 mm. Alternatively, distance D1 may have any other suitable value.

Typically, the second electrode is expandable. Prior to applying the unipolar voltage, catheter 20 (Fig. 1), which contains both the first electrode, and the second electrode in a crimped position, is advanced through the thrombus. Subsequently, the catheter is withdrawn from over the two electrodes, such that the second electrode expands, from the crimped position, within the thrombus. Subsequently, a positive unipolar voltage is applied between the first and second electrodes, causing the thrombus to become attached to the first electrode. During the application of the voltage, the first electrode may protrude distally from the second electrode. Alternatively, the distal end of the first electrode may remain inside of the second electrode.

During, and/or following, the application of the unipolar voltage, the electrode assembly is withdrawn. During withdrawal of the electrode assembly, the second electrode, which is positioned within the thrombus, helps remove the thrombus, by applying, to the thrombus, a mechanical force that complements the attractive force between the thrombus and the first electrode.

For any of the configurations described above with reference to Figs. 1-4, a negative unipolar voltage may be applied between the first and second electrodes, causing the thrombus to dissolve. In yet other embodiments, an alternating voltage, instead of a unipolar voltage, may be applied, to cause thermal coagulation.

Although Figs. 1-4 show embodiments in which the two electrodes are coaxial with one another, in that they share a common longitudinal axis (as explicitly indicated in Fig. 3), it is noted that other embodiments are also within the scope of the present invention. For example, as described in US Patent Application Publication 2011/0301594 with reference to Figs. 1A-C thereof, the two electrodes may pass through separate lumens of catheter 20, or may pass, side by side (but separated by an insulator), through a common lumen of catheter 20.

It is noted that any of the tubes and catheters described herein may comprise a wall that is at least partly solid, coiled, braided, or meshed. Likewise, any of the electrodes described herein may be shaped to define a tube, a coil (which may have a constant or variable pitch), a braid, or a mesh.

It will be appreciated by persons skilled in the art that the present invention is not limited to what has been particularly shown and described hereinabove. Rather, the scope of embodiments of the present invention includes both combinations and subcombinations of the various features described hereinabove, as well as variations and modifications thereof that are not in the prior art, which would occur to persons skilled in the art upon reading the foregoing description. Documents incorporated by reference in the present patent application are to be considered an integral part of the application except that to the extent any terms are defined in these incorporated documents in a manner that conflicts with the definitions made explicitly or implicitly in the present specification, only the definitions in the present specification should be considered.

CLAIMS

1. Apparatus for removal of a thrombus from a body of a subject, the apparatus comprising:
a first electrode, made of a first conductive metal having a first electronegativity;
a second electrode, made of a second conductive metal having a second electronegativity
5 that is less than the first electronegativity; and
a voltage source, configured to apply a positive unipolar voltage between the first
electrode and the second electrode while the first electrode is in contact with the thrombus, and
while the second electrode is inside the body of the subject.
2. The apparatus according to claim 1, wherein a distance between the first electrode and
10 the second electrode is less than 3 mm.
3. The apparatus according to claim 2, wherein the distance is less than 0.7 mm.
4. The apparatus according to any one of claims 1-3, further comprising a tube, wherein the
second electrode is shaped to define at least part of a wall of the tube.
5. The apparatus according to claim 4, wherein the first electrode is disposed at a distal end
15 of the tube.
6. The apparatus according to claim 4, wherein the first electrode passes through a lumen of
the tube.
7. The apparatus according to any one of claims 1-6, wherein the second electrode is shaped
to define a helix, and wherein the first electrode passes through the second electrode.
- 20 8. The apparatus according to any one of claims 1-7, wherein the first electrode and second
electrode are coaxial with one another.
9. The apparatus according to any one of claims 1-8, wherein a length of an exposed portion
of the first electrode is between 0.1 and 50 mm.
10. The apparatus according to any one of claims 1-9, wherein a diameter of the first
25 electrode is between 0.01 and 4 mm.
11. The apparatus according to any one of claims 1-10, wherein an amplitude of the unipolar
voltage is between 1 and 100 V.
12. The apparatus according to any one of claims 1-11, wherein, in applying the unipolar
voltage, the voltage source is configured to pass, between the first electrode and the second
30 electrode, a current having an amplitude of between 0.1 and 4 mA.
13. The apparatus according to any one of claims 1-12, wherein the first electrode comprises

a straight distal end.

14. The apparatus according to any one of claims 1-13, further comprising a balloon proximal to the first electrode, configured to center the first electrode with respect to the thrombus when inflated.

5 15. A method, comprising:

applying a positive unipolar voltage between a first electrode, made of a first conductive metal having a first electronegativity, and a second electrode, made of a second conductive metal having a second electronegativity that is less than the first electronegativity, while the first electrode is in contact with a thrombus in a body of a subject, and while the second electrode is
10 inside the body of the subject; and

subsequently, removing the thrombus from the body of the subject.

16. The method according to claim 15, further comprising, prior to applying the unipolar voltage, advancing the first electrode through the thrombus, at least until the thrombus contacts an electrical insulator that is disposed proximally to an exposed portion of the first electrode.

15 17. The method according to claim 16, further comprising measuring an impedance between the first electrode and the second electrode, and ascertaining that the thrombus has contacted the insulator, based on the measured impedance.

18. The method according to any one of claims 15-17, further comprising, prior to applying the unipolar voltage, advancing the first electrode through the thrombus until an entire length of
20 the first electrode contacts the thrombus.

19. The method according to any one of claims 15-18, wherein an amplitude of the unipolar voltage is between 1 and 100 V.

20. The method according to any one of claims 15-19, wherein applying the unipolar voltage comprises applying the unipolar voltage such that a current having an amplitude of between 0.1
25 and 4 mA is passed between the first electrode and the second electrode.

21. The method according to any one of claims 15-20, wherein applying the unipolar voltage comprises applying the unipolar voltage while a distance between a distal tip of the first electrode and a distal tip of the second electrode is between 1 and 100 mm.

22. The method according to any one of claims 15-21, wherein an electrical insulator is
30 disposed proximally to an exposed portion of the first electrode, and wherein the method further comprises, prior to applying the unipolar voltage, advancing the second electrode over the

insulator.

23. The method according to any one of claims 15-22, wherein the second electrode is expandable, and wherein the method further comprises, prior to applying the unipolar voltage:

advancing a catheter, containing both the first electrode, and the second electrode in a
5 crimped position, through the thrombus; and

subsequently, withdrawing the catheter, such that the second electrode expands, from the crimped position, within the thrombus.

24. The method according to any one of claims 15-23, further comprising, prior to contacting the thrombus with the first electrode, centering the first electrode with respect to the thrombus,
10 by inflating a balloon that is proximal to the first electrode.

25. Apparatus for removal of a thrombus from a body of a subject, the apparatus comprising:
an outer electrode, shaped to define a helix; and
an inner electrode, passing through the outer electrode, configured to attach to the
thrombus when a positive unipolar voltage is applied between the inner electrode and the outer
15 electrode.

26. The apparatus according to claim 25, wherein the outer electrode is expandable.

27. The apparatus according to any one of claims 25-26, further comprising a voltage source configured to apply the positive unipolar voltage.

28. The apparatus according to claim 27, further comprising an electrically-insulating cover
20 over both a proximal portion of the outer electrode and a distal portion of the outer electrode.

29. The apparatus according to any one of claims 25-28, wherein the inner electrode is rod-shaped.

30. The apparatus according to any one of claims 25-29, wherein the inner electrode passes through a center of the outer electrode.

25 31. The apparatus according to any one of claims 25-30, wherein a distance between the inner electrode and a middle portion of the outer electrode is between 1 and 100 mm.

32. The apparatus according to claim 31, wherein the distance is between 2 and 30 mm.

33. The apparatus according to any one of claims 25-32, wherein the inner electrode is made of a first conductive metal having a first electronegativity, and wherein the outer electrode is
30 made of a second conductive metal having a second electronegativity that is less than the first electronegativity.

34. A method, comprising:

advancing a catheter, which contains both a crimped outer electrode, and an inner electrode that passes through the outer electrode, through a thrombus in a body of a subject;

subsequently to advancing the catheter through the thrombus, withdrawing the catheter,

5 such that the outer electrode expands within the thrombus;

subsequently to withdrawing the catheter, applying a positive unipolar voltage between the inner electrode and the outer electrode, such that the thrombus becomes attached to the inner electrode; and

10 subsequently to the thrombus becoming attached to the inner electrode, withdrawing the inner electrode and the outer electrode from the body of the subject.

35. The method according to claim 34, wherein withdrawing the outer electrode comprises, using the outer electrode, applying a mechanical force to the thrombus.

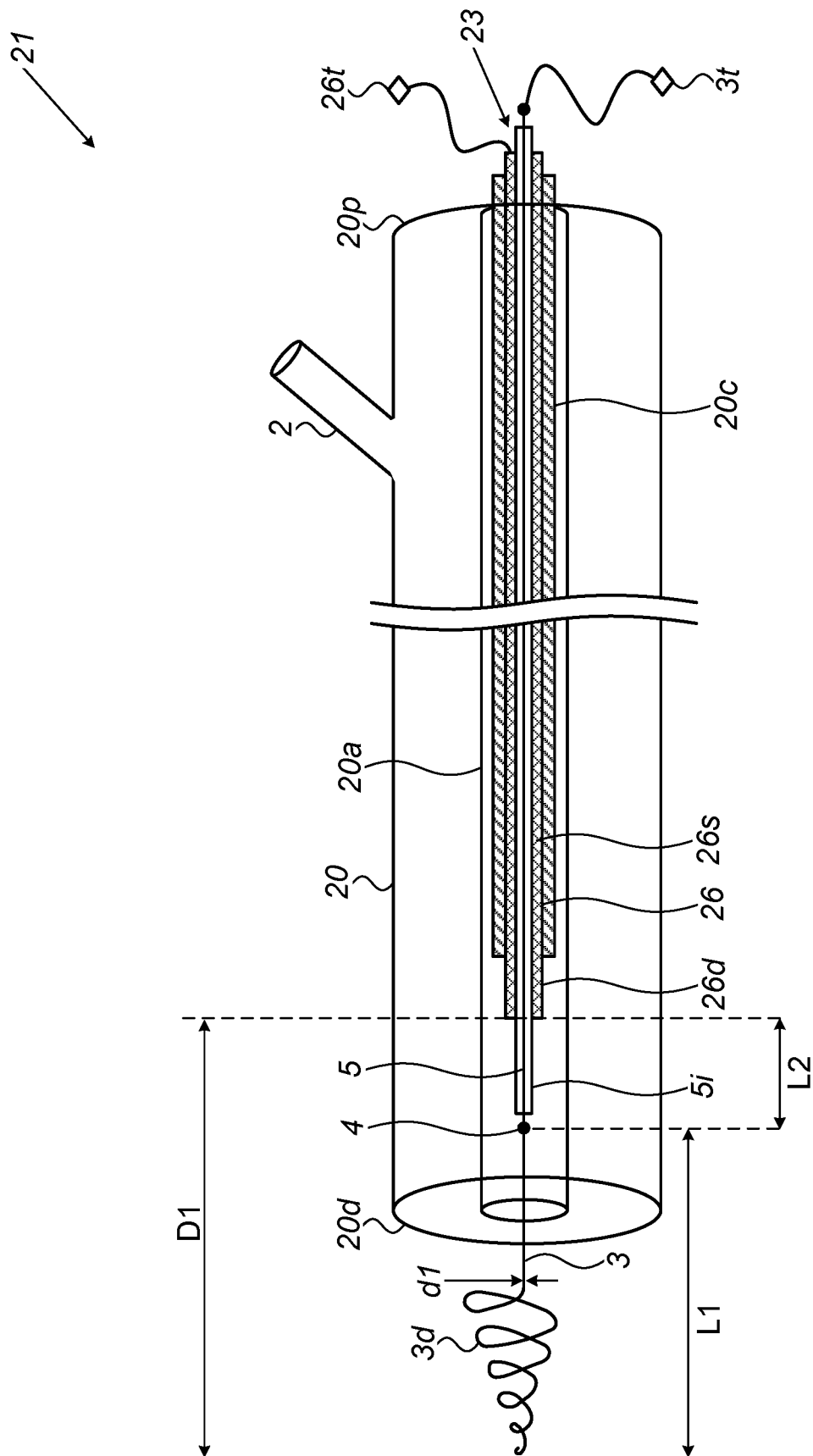


FIG. 1

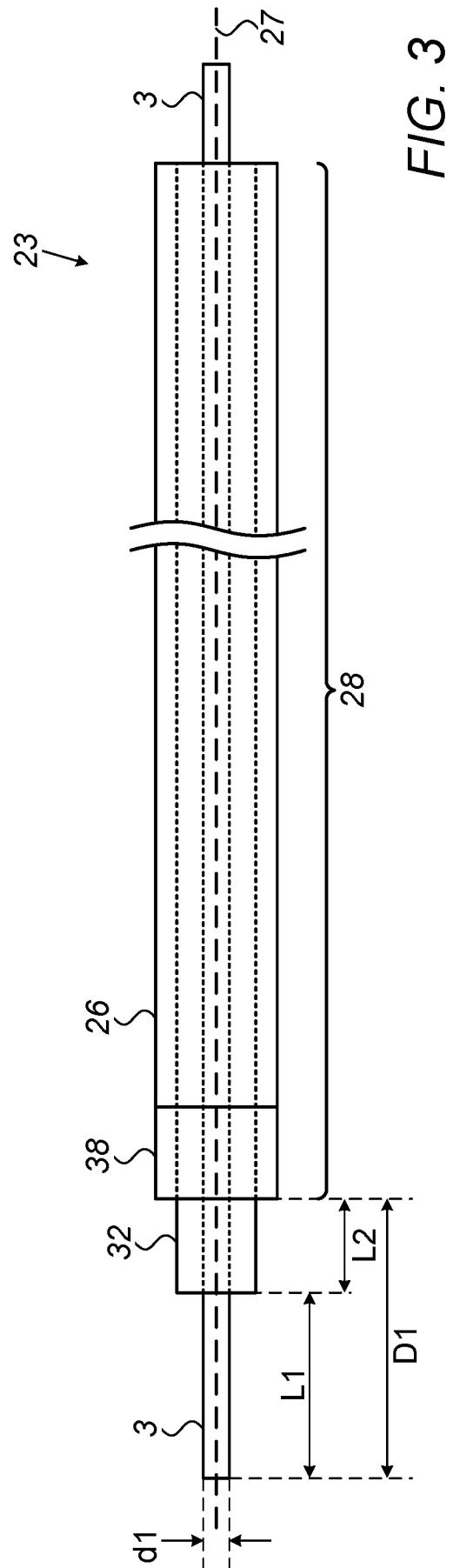
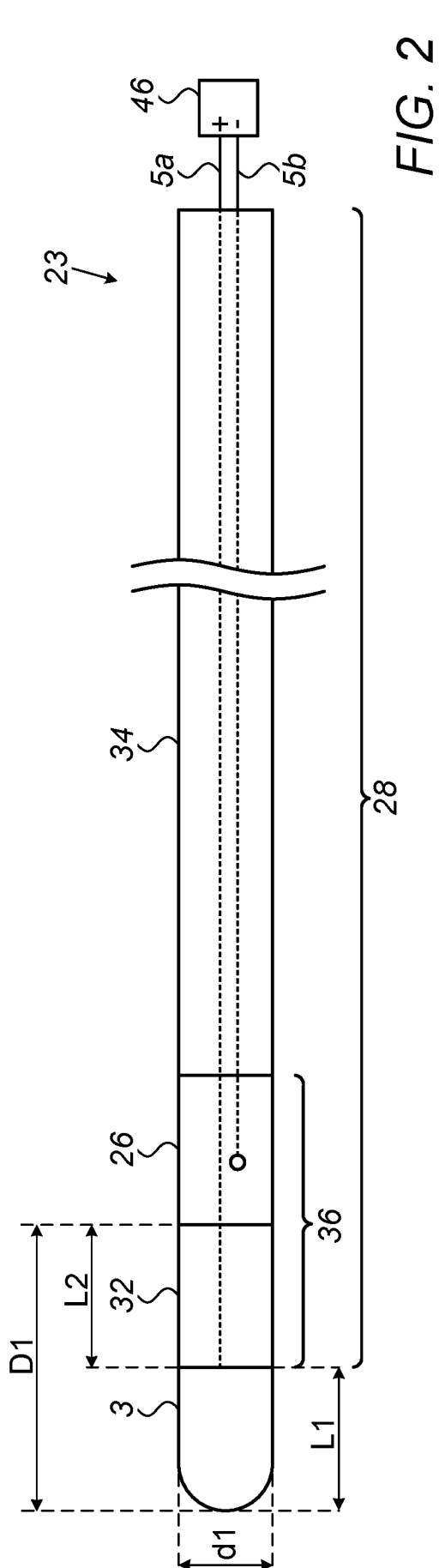
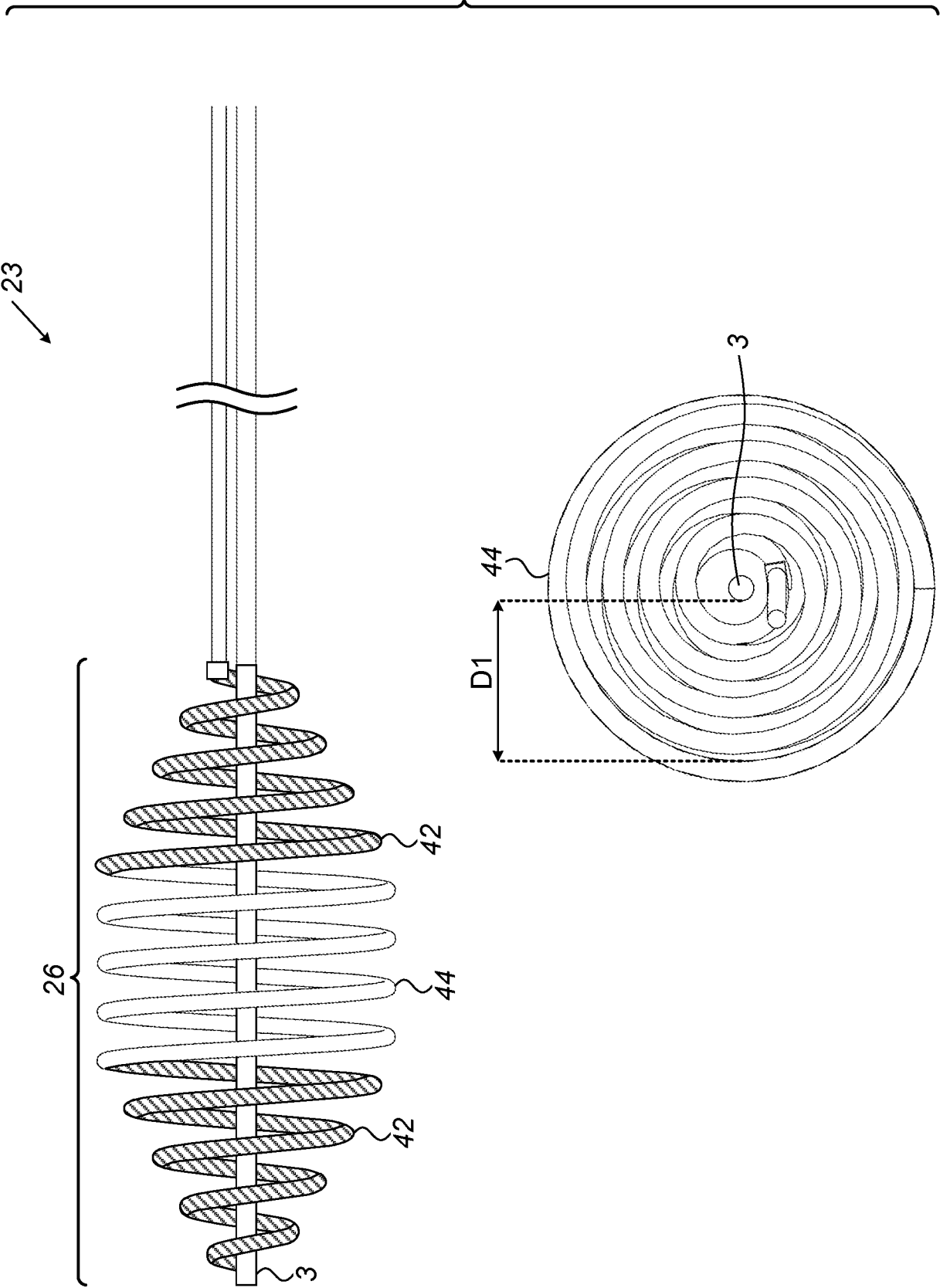


FIG. 4



INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER IPC (2018.01) A61B 18/14 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) IPC (2018.01) A61B 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) Databases consulted: Esp@cenet, Google Patents, Derwent Innovation Search terms used: Electrode, expand, dilate, deploy, thrombus, removal, voltage, thrombectomy		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011301594 A1 ORION 08 Dec 2011 (2011/12/08) para.[0018], [0020], [0021], [0022], [0024], [0028], [0031], [0052]-[0055], [0061], [0068], [0072], [0073], ; fig. 1A, 2	1-22,24,25,27-33
Y		23,26,34,35
X	US 2001001314 A1 ARTHROCARE CORP 17 May 2001 (2001/05/17) * the whole document *	1,8,11,13,15,19,21, 25,27-30,33
Y	US 2012296262 A1 OGATA et al. 22 Nov 2012 (2012/11/22) para.[0080]; fig. 9A, 9B	23,26,34,35
☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "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) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "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 "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 "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 "&" document member of the same patent family		
Date of the actual completion of the international search 08 May 2018		Date of mailing of the international search report 10 May 2018
Name and mailing address of the ISA: Israel Patent Office Technology Park, Bldg.5, Malcha, Jerusalem, 9695101, Israel Facsimile No. 972-2-5651616		Authorized officer AHARONY Meytal Telephone No. 972-2-5657820

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report			Publication date	Patent family member(s)			Publication Date
US	2011301594	A1	08 Dec 2011	US	2011301594	A1	08 Dec 2011
				EP	2346431	A1	27 Jul 2011
				EP	2346431	A4	03 Oct 2012
				EP	3184067	A1	28 Jun 2017
				IL	212516	D0	30 Jun 2011
				IL	212516	A	28 Nov 2013
				WO	2010061376	A1	03 Jun 2010
US	2001001314	A1	17 May 2001	US	2001001314	A1	17 May 2001
				US	6855143	B2	15 Feb 2005
				AT	173903	T	15 Dec 1998
				AT	207331	T	15 Nov 2001
				AT	208589	T	15 Nov 2001
				AT	222079	T	15 Aug 2002
				AT	222732	T	15 Sep 2002
				AT	234592	T	15 Apr 2003
				AT	262837	T	15 Apr 2004
				AT	299355	T	15 Jul 2005
				AT	304830	T	15 Oct 2005
				AT	309769	T	15 Dec 2005
				AT	357185	T	15 Apr 2007
				AT	375126	T	15 Oct 2007
				AT	381296	T	15 Jan 2008
				AT	395873	T	15 Jun 2008
				AT	423523	T	15 Mar 2009
				AT	435610	T	15 Jul 2009
				AT	442094	T	15 Sep 2009
				AT	485781	T	15 Nov 2010
				AT	519440	T	15 Aug 2011
				AT	522178	T	15 Sep 2011
				AT	524128	T	15 Sep 2011

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
	AT 544391	T	15 Feb 2012
	AU 3335793	A	03 Aug 1993
	AU 674664	B2	09 Jan 1997
	AU 6829694	A	12 Dec 1994
	AU 676329	B2	06 Mar 1997
	AU 1054597	A	11 Jun 1997
	AU 702687	B2	04 Mar 1999
	AU 6026696	A	30 Dec 1996
	AU 706294	B2	10 Jun 1999
	AU 1057197	A	11 Jun 1997
	AU 709928	B2	09 Sep 1999
	AU 2472497	A	14 Aug 1997
	AU 711197	B2	07 Oct 1999
	AU 1112499	A	10 May 1999
	AU 1194099	A	10 May 1999
	AU 1332101	A	23 Apr 2001
	AU 1464099	A	15 Jun 1999
	AU 1633400	A	19 Jun 2000
	AU 1999099	A	05 Jul 1999
	AU 3296199	A	06 Sep 1999
	AU 3601797	A	10 Feb 1998
	AU 3663597	A	10 Feb 1998
	AU 3912900	A	09 Oct 2000
	AU 3975899	A	23 Nov 1999
	AU 4223300	A	02 Nov 2000
	AU 4315101	A	27 Aug 2001
	AU 4650700	A	02 Nov 2000
	AU 4842999	A	17 Jan 2000
	AU 5142900	A	12 Dec 2000
	AU 5255499	A	28 Feb 2000
	AU 5276596	A	30 Oct 1996

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
	AU 5385496	A	30 Oct 1996
	AU 5773699	A	06 Mar 2000
	AU 6163701	A	18 Feb 2002
	AU 6172601	A	24 Dec 2001
	AU 7141198	A	30 Dec 1998
	AU 9035898	A	16 Mar 1999
	AU 9782998	A	27 Apr 1999
	AU 2002329212	A1	29 Jan 2003
	AU 2002332012	A1	14 Apr 2003
	AU 2002332031	A1	14 Apr 2003
	AU 2002336575	A1	01 Apr 2003
	AU 2002362310	A1	01 Apr 2003
	AU 2003215263	A1	04 Sep 2003
	AU 2003215263	A8	04 Sep 2003
	AU 2003218050	A1	04 Sep 2003
	AU 2003218050	A8	04 Sep 2003
	AU 2003237102	A1	10 Nov 2003
	AU 2003248766	A1	19 Jan 2004
	AU 2003248766	A8	19 Jan 2004
	BR 9604831	A	05 Jan 1999
	CA 2129745	A1	08 Jul 1993
	CA 2129745	C	20 Feb 2001
	CA 2162395	A1	24 Nov 1994
	CA 2162395	C	18 Jan 2000
	CA 2217540	A1	17 Oct 1996
	CA 2221330	A1	19 Dec 1996
	CA 2221330	C	15 Feb 2000
	CA 2237795	A1	29 May 1997
	CA 2237947	A1	29 May 1997
	CA 2237947	C	15 Feb 2000
	CA 2287206	A1	17 Dec 1998

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
	CA	2318891 A1	26 Aug 1999
	CZ	9703245 A3	14 Jan 1998
	DE	9422383 U1	22 Mar 2001
	DE	19513990 A1	17 Oct 1996
	DE	29623990 U1	08 Feb 2001
	DE	29624229 U1	23 Aug 2001
	DE	60045154 D1	09 Dec 2010
	DE	69227783 D1	14 Jan 1999
	DE	69227783 T2	20 May 1999
	DE	69232735 D1	19 Sep 2002
	DE	69232735 T2	07 Aug 2003
	DE	69431246 D1	02 Oct 2002
	DE	69431246 T2	30 Apr 2003
	DE	69431246 T3	27 Dec 2007
	DE	69616327 D1	29 Nov 2001
	DE	69616327 T2	27 Jun 2002
	DE	69617047 D1	20 Dec 2001
	DE	69617047 T2	11 Jul 2002
	DE	69626841 D1	24 Apr 2003
	DE	69626841 T2	18 Dec 2003
	DE	69634929 D1	18 Aug 2005
	DE	69637965 D1	20 Aug 2009
	DE	69638343 D1	28 Apr 2011
	DE	69739572 D1	22 Oct 2009
	DE	69822877 D1	06 May 2004
	DE	69822877 T2	05 Jan 2005
	DE	69831682 D1	02 Feb 2006
	DE	69831682 T2	22 Jun 2006
	DE	69838555 D1	22 Nov 2007
	DE	69838555 T2	24 Jul 2008
	DE	69839526 D1	03 Jul 2008

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
	DE 69840602	D1	09 Apr 2009
	DE 69928370	D1	22 Dec 2005
	DE 69928370	T2	03 Aug 2006
	DE 69935586	D1	03 May 2007
	DE 69937788	D1	31 Jan 2008
	DE 69937788	T2	11 Dec 2008
	EP 0624076	A1	17 Nov 1994
	EP 0624076	A4	28 Jun 1995
	EP 0624076	B1	02 Dec 1998
	EP 0697841	A1	28 Feb 1996
	EP 0697841	A4	18 Dec 1996
	EP 0697841	B1	28 Aug 2002
	EP 0697841	B2	23 May 2007
	EP 0820249	A1	28 Jan 1998
	EP 0820249	A4	18 Nov 1998
	EP 0820249	B1	13 Jul 2005
	EP 0820457	A1	28 Jan 1998
	EP 0837647	A1	29 Apr 1998
	EP 0837647	A4	01 Jul 1998
	EP 0837647	B1	24 Oct 2001
	EP 0865256	A1	23 Sep 1998
	EP 0865256	A4	07 Oct 1998
	EP 0865256	B1	19 Mar 2003
	EP 0882430	A2	09 Dec 1998
	EP 0882430	A3	20 Jan 1999
	EP 0882430	B1	14 Aug 2002
	EP 0886493	A1	30 Dec 1998
	EP 0886493	A4	03 Feb 1999
	EP 0886493	B1	14 Nov 2001
	EP 0917482	A1	26 May 1999
	EP 0917482	A4	22 Dec 1999

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
	EP 0917482	B1	09 Sep 2009
	EP 0921759	A1	16 Jun 1999
	EP 0921759	A4	07 Feb 2001
	EP 0921759	B1	31 Aug 2011
	EP 0998248	A1	10 May 2000
	EP 0998248	A4	21 Mar 2001
	EP 1009343	A1	21 Jun 2000
	EP 1009343	A4	10 Jan 2001
	EP 1018994	A1	19 Jul 2000
	EP 1018994	A4	17 Jan 2001
	EP 1018994	B1	21 Sep 2005
	EP 1024769	A1	09 Aug 2000
	EP 1024769	A4	12 Sep 2001
	EP 1024769	B1	25 Feb 2009
	EP 1026996	A1	16 Aug 2000
	EP 1026996	A4	12 Sep 2001
	EP 1026996	B1	10 Oct 2007
	EP 1027020	A1	16 Aug 2000
	EP 1027020	A4	21 Nov 2001
	EP 1027020	B1	16 Nov 2005
	EP 1036547	A2	20 Sep 2000
	EP 1036547	A3	27 Dec 2000
	EP 1039862	A1	04 Oct 2000
	EP 1039862	A4	03 Jan 2001
	EP 1039862	B1	21 May 2008
	EP 1041933	A1	11 Oct 2000
	EP 1041933	A4	27 Dec 2000
	EP 1041933	B1	31 Mar 2004
	EP 1061857	A1	27 Dec 2000
	EP 1061857	A4	21 Nov 2001
	EP 1061857	B1	19 Dec 2007

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
	EP 1079746	A1	07 Mar 2001
	EP 1079746	A4	12 Sep 2001
	EP 1079746	B1	21 Mar 2007
	EP 1080680	A1	07 Mar 2001
	EP 1080682	A1	07 Mar 2001
	EP 1080682	B1	08 Jul 2009
	EP 1174093	A1	23 Jan 2002
	EP 1178757	A1	13 Feb 2002
	EP 1178758	A1	13 Feb 2002
	EP 1178758	A4	09 Apr 2008
	EP 1178758	B1	27 Oct 2010
	EP 1179320	A2	13 Feb 2002
	EP 1179320	A3	03 Dec 2003
	EP 1187570	A1	20 Mar 2002
	EP 1187570	A4	09 Apr 2008
	EP 1257221	A1	20 Nov 2002
	EP 1289438	A1	12 Mar 2003
	EP 1289438	A4	07 Sep 2005
	EP 1309282	A1	14 May 2003
	EP 1309282	A4	08 Mar 2006
	EP 1404236	A1	07 Apr 2004
	EP 1404236	A4	05 Jan 2005
	EP 1404236	B1	14 Sep 2011
	EP 1411847	A2	28 Apr 2004
	EP 1411847	A4	05 Jan 2005
	EP 1411847	B1	06 Jun 2012
	EP 1437977	A2	21 Jul 2004
	EP 1437977	A4	21 Mar 2007
	EP 1437977	B1	21 May 2014
	EP 1460945	A2	29 Sep 2004
	EP 1460945	A4	21 Jan 2009

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
	EP 1460945	B1	09 Jan 2013
	EP 1474203	A2	10 Nov 2004
	EP 1474203	B1	15 Jun 2016
	EP 1503688	A1	09 Feb 2005
	EP 1503688	A4	29 Jul 2009
	EP 1571969	A2	14 Sep 2005
	EP 1571969	A4	05 Jul 2006
	EP 1571969	B1	08 Feb 2012
	EP 1637087	A2	22 Mar 2006
	EP 1637087	A3	10 May 2006
	EP 1637087	B1	10 Aug 2011
	EP 1880686	A2	23 Jan 2008
	EP 1880686	A3	26 Jan 2011
	EP 1880686	B1	21 Jun 2017
	EP 2055253	A2	06 May 2009
	EP 2055253	A3	03 Feb 2010
	EP 2055253	B1	08 Mar 2017
	EP 2055254	A2	06 May 2009
	EP 2055254	A3	10 Feb 2010
	EP 2055254	B1	14 Jan 2015
	EP 2057954	A1	13 May 2009
	EP 2057954	B1	16 Mar 2011
	HU 9801565	A2	28 Sep 1998
	HU 9801565	A3	28 Nov 2001
	JP H10510745	A	20 Oct 1998
	JP 2912023	B2	28 Jun 1999
	JP H09501328	A	10 Feb 1997
	JP 2931102	B2	09 Aug 1999
	JP H11502144	A	23 Feb 1999
	JP 3033848	B2	17 Apr 2000
	JP H11501555	A	09 Feb 1999

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
		JP 3215434 B2	09 Oct 2001
		JP 2000515798 A	28 Nov 2000
		JP 3391466 B2	31 Mar 2003
		JP 2002541904 A	10 Dec 2002
		JP 4261070 B2	30 Apr 2009
		JP 2003500099 A	07 Jan 2003
		JP 4290894 B2	08 Jul 2009
		JP 2008220988 A	25 Sep 2008
		JP 4713613 B2	29 Jun 2011
		JP 2001522252 A	13 Nov 2001
		JP 4756179 B2	24 Aug 2011
		JP 2004505663 A	26 Feb 2004
		JP 4986006 B2	25 Jul 2012
		JP 2014217780 A	20 Nov 2014
		JP 6110343 B2	05 Apr 2017
		JP H11503725 A	30 Mar 1999
		JP 2000060868 A	29 Feb 2000
		JP 2001513395 A	04 Sep 2001
		JP 2001518352 A	16 Oct 2001
		JP 2001520081 A	30 Oct 2001
		JP 2001523513 A	27 Nov 2001
		JP 2002503508 A	05 Feb 2002
		JP 2002508214 A	19 Mar 2002
		JP 2002513619 A	14 May 2002
		JP 2002514097 A	14 May 2002
		JP 2002541902 A	10 Dec 2002
		JP 2003527875 A	24 Sep 2003
		JP 2008296034 A	11 Dec 2008
		JP 2011045756 A	10 Mar 2011
		JP 2016195852 A	24 Nov 2016
		MX 9707835 A	31 Jan 1998

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
		MX PA00008132 A	21 Jun 2002
		MX PA01011647 A	30 Jul 2002
		NZ 246503 A	26 Jul 1996
		NZ 266678 A	19 Dec 1997
		NZ 323589 A	29 Jul 1999
		PL 322721 A1	16 Feb 1998
		PL 185393 B1	30 May 2003
		RU 2159242 C2	20 Nov 2000
		SK 137197 A3	06 May 1998
		US RE40156 E	18 Mar 2008
		US 5366443 A	22 Nov 1994
		US 5419767 A	30 May 1995
		US 5681282 A	28 Oct 1997
		US 5683366 A	04 Nov 1997
		US 5697281 A	16 Dec 1997
		US 5697536 A	16 Dec 1997
		US 5697882 A	16 Dec 1997
		US 5697909 A	16 Dec 1997
		US 5766153 A	16 Jun 1998
		US 5810764 A	22 Sep 1998
		US 5843019 A	01 Dec 1998
		US 5860951 A	19 Jan 1999
		US 5871469 A	16 Feb 1999
		US 5873855 A	23 Feb 1999
		US 5888198 A	30 Mar 1999
		US 5891095 A	06 Apr 1999
		US 5902272 A	11 May 1999
		US 5925663 A	20 Jul 1999
		US 6024733 A	15 Feb 2000
		US 6032674 A	07 Mar 2000
		US 6045532 A	04 Apr 2000

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
		US 6053172 A	25 Apr 2000
		US 6063079 A	16 May 2000
		US 6066134 A	23 May 2000
		US 6080776 A	27 Jun 2000
		US 6086585 A	11 Jul 2000
		US 6102046 A	15 Aug 2000
		US 6105581 A	22 Aug 2000
		US 6109268 A	29 Aug 2000
		US 6113597 A	05 Sep 2000
		US 6117109 A	12 Sep 2000
		US 6142992 A	07 Nov 2000
		US 6149620 A	21 Nov 2000
		US 6159194 A	12 Dec 2000
		US 6159208 A	12 Dec 2000
		US 6179824 B1	30 Jan 2001
		US 6179836 B1	30 Jan 2001
		US 6183469 B1	06 Feb 2001
		US 6190381 B1	20 Feb 2001
		US 6203542 B1	20 Mar 2001
		US 6210402 B1	03 Apr 2001
		US 6224592 B1	01 May 2001
		US 6228078 B1	08 May 2001
		US 6228082 B1	08 May 2001
		US 6235020 B1	22 May 2001
		US 6235765 B1	22 May 2001
		US 6238391 B1	29 May 2001
		US 6254600 B1	03 Jul 2001
		US 6264650 B1	24 Jul 2001
		US 6264651 B1	24 Jul 2001
		US 6264652 B1	24 Jul 2001
		US 6277112 B1	21 Aug 2001

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
	US 6283961	B1	04 Sep 2001
	US 6296636	B1	02 Oct 2001
	US 6296638	B1	02 Oct 2001
	US 6309387	B1	30 Oct 2001
	US 6312408	B1	06 Nov 2001
	US 6322549	B1	27 Nov 2001
	US 6355032	B1	12 Mar 2002
	US 6363937	B1	02 Apr 2002
	US 6379351	B1	30 Apr 2002
	US 6391025	B1	21 May 2002
	US 6416507	B1	09 Jul 2002
	US 6416508	B1	09 Jul 2002
	US 6432103	B1	13 Aug 2002
	US 6461350	B1	08 Oct 2002
	US 6461354	B1	08 Oct 2002
	US 2001029370	A1	11 Oct 2001
	US 6464695	B2	15 Oct 2002
	US 6468270	B1	22 Oct 2002
	US 6468274	B1	22 Oct 2002
	US 6482201	B1	19 Nov 2002
	US 2001056280	A1	27 Dec 2001
	US 6500173	B2	31 Dec 2002
	US 6540741	B1	01 Apr 2003
	US 2001025176	A1	27 Sep 2001
	US 6544261	B2	08 Apr 2003
	US 6557559	B1	06 May 2003
	US 6575968	B1	10 Jun 2003
	US 6582423	B1	24 Jun 2003
	US 2001051802	A1	13 Dec 2001
	US 6589237	B2	08 Jul 2003
	US 6595990	B1	22 Jul 2003

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
		US 6602248 B1	05 Aug 2003
		US 2002151885 A1	17 Oct 2002
		US 6620155 B2	16 Sep 2003
		US 6623454 B1	23 Sep 2003
		US 6632193 B1	14 Oct 2003
		US 6632220 B1	14 Oct 2003
		US 6659106 B1	09 Dec 2003
		US 2003040742 A1	27 Feb 2003
		US 6712811 B2	30 Mar 2004
		US 2002193789 A1	19 Dec 2002
		US 6719754 B2	13 Apr 2004
		US 6726684 B1	27 Apr 2004
		US 2002052600 A1	02 May 2002
		US 6746447 B2	08 Jun 2004
		US 6749604 B1	15 Jun 2004
		US 2003055418 A1	20 Mar 2003
		US 6763836 B2	20 Jul 2004
		US 2001020167 A1	06 Sep 2001
		US 6770071 B2	03 Aug 2004
		US 2001032001 A1	18 Oct 2001
		US 6772012 B2	03 Aug 2004
		US 2001049522 A1	06 Dec 2001
		US 6773431 B2	10 Aug 2004
		US 2002068930 A1	06 Jun 2002
		US 6805130 B2	19 Oct 2004
		US 2002026186 A1	28 Feb 2002
		US 6832996 B2	21 Dec 2004
		US 2003009164 A1	09 Jan 2003
		US 6837887 B2	04 Jan 2005
		US 2002095152 A1	18 Jul 2002
		US 6837888 B2	04 Jan 2005

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
		US 6896672 B1	24 May 2005
		US 6896674 B1	24 May 2005
		US 2003084907 A1	08 May 2003
		US 6915806 B2	12 Jul 2005
		US 6929640 B1	16 Aug 2005
		US 2003097129 A1	22 May 2003
		US 6949096 B2	27 Sep 2005
		US 2004087939 A1	06 May 2004
		US 6960204 B2	01 Nov 2005
		US 2003097126 A1	22 May 2003
		US 6974453 B2	13 Dec 2005
		US 2003225403 A1	04 Dec 2003
		US 6991631 B2	31 Jan 2006
		US 7070596 B1	04 Jul 2006
		US 2004006339 A1	08 Jan 2004
		US 7090672 B2	15 Aug 2006
		US 2003163178 A1	28 Aug 2003
		US 7094215 B2	22 Aug 2006
		US 2004024398 A1	05 Feb 2004
		US 7104986 B2	12 Sep 2006
		US 7131969 B1	07 Nov 2006
		US 2006041255 A1	23 Feb 2006
		US 7169143 B2	30 Jan 2007
		US 2002120259 A1	29 Aug 2002
		US 7179255 B2	20 Feb 2007
		US 2002099366 A1	25 Jul 2002
		US 7186234 B2	06 Mar 2007
		US 2003216726 A1	20 Nov 2003
		US 7192428 B2	20 Mar 2007
		US 7201750 B1	10 Apr 2007
		US 2004087937 A1	06 May 2004

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
	US 7217268	B2	15 May 2007
	US 2004153057	A1	05 Aug 2004
	US 7241293	B2	10 Jul 2007
	US 2003212395	A1	13 Nov 2003
	US 7270658	B2	18 Sep 2007
	US 2006095026	A1	04 May 2006
	US 7270659	B2	18 Sep 2007
	US 2002095151	A1	18 Jul 2002
	US 7270661	B2	18 Sep 2007
	US 2004054366	A1	18 Mar 2004
	US 7276063	B2	02 Oct 2007
	US 2006129145	A1	15 Jun 2006
	US 7297145	B2	20 Nov 2007
	US 2004024399	A1	05 Feb 2004
	US 7318823	B2	15 Jan 2008
	US 2007010809	A1	11 Jan 2007
	US 7331956	B2	19 Feb 2008
	US 2003216725	A1	20 Nov 2003
	US 7331957	B2	19 Feb 2008
	US 2004049180	A1	11 Mar 2004
	US 7357798	B2	15 Apr 2008
	US 2005010205	A1	13 Jan 2005
	US 7387625	B2	17 Jun 2008
	US 2003014047	A1	16 Jan 2003
	US 7393351	B2	01 Jul 2008
	US 2005131402	A1	16 Jun 2005
	US 7419488	B2	02 Sep 2008
	US 7422585	B1	09 Sep 2008
	US 2007112346	A1	17 May 2007
	US 7429260	B2	30 Sep 2008
	US 2001025177	A1	27 Sep 2001

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
	US 7429262	B2	30 Sep 2008
	US 2003028189	A1	06 Feb 2003
	US 7435247	B2	14 Oct 2008
	US 2003208194	A1	06 Nov 2003
	US 7442191	B2	28 Oct 2008
	US 2007112348	A1	17 May 2007
	US 7445618	B2	04 Nov 2008
	US 2005187543	A1	25 Aug 2005
	US 7449021	B2	11 Nov 2008
	US 2008004615	A1	03 Jan 2008
	US 7462178	B2	09 Dec 2008
	US 2007129715	A1	07 Jun 2007
	US 7468059	B2	23 Dec 2008
	US 7505812	B1	17 Mar 2009
	US 2007179497	A1	02 Aug 2007
	US 7507236	B2	24 Mar 2009
	US 7572251	B1	11 Aug 2009
	US 7678069	B1	16 Mar 2010
	US 2008119844	A1	22 May 2008
	US 7717912	B2	18 May 2010
	US 7758537	B1	20 Jul 2010
	US 2008243117	A1	02 Oct 2008
	US 7794456	B2	14 Sep 2010
	US 2009069807	A1	12 Mar 2009
	US 7819863	B2	26 Oct 2010
	US 2003130655	A1	10 Jul 2003
	US 7824398	B2	02 Nov 2010
	US 2008132890	A1	05 Jun 2008
	US 7824405	B2	02 Nov 2010
	US 2010324553	A1	23 Dec 2010
	US 7951141	B2	31 May 2011

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
	US	2008004621 A1	03 Jan 2008
	US	7988689 B2	02 Aug 2011
	US	2008021447 A1	24 Jan 2008
	US	8663216 B2	04 Mar 2014
	US	2001029373 A1	11 Oct 2001
	US	2002026059 A1	28 Feb 2002
	US	2003158545 A1	21 Aug 2003
	US	2003171743 A1	11 Sep 2003
	US	2003212396 A1	13 Nov 2003
	US	2004215184 A1	28 Oct 2004
	US	2004230190 A1	18 Nov 2004
	US	2005004634 A1	06 Jan 2005
	US	2005261754 A1	24 Nov 2005
	US	2006189971 A1	24 Aug 2006
	US	2006253117 A1	09 Nov 2006
	US	2007149966 A1	28 Jun 2007
	US	2008009847 A1	10 Jan 2008
	US	2008015565 A1	17 Jan 2008
	US	2011028970 A1	03 Feb 2011
	WO	0000098 A1	06 Jan 2000
	WO	0007507 A1	17 Feb 2000
	WO	0009053 A1	24 Feb 2000
	WO	0009053 A9	22 Aug 2002
	WO	0032127 A1	08 Jun 2000
	WO	0056229 A1	28 Sep 2000
	WO	0062685 A1	26 Oct 2000
	WO	0062698 A1	26 Oct 2000
	WO	0062698 A9	13 Jun 2002
	WO	0071043 A1	30 Nov 2000
	WO	0126570 A1	19 Apr 2001
	WO	0160273 A1	23 Aug 2001

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
	WO 0195819	A1	20 Dec 2001
	WO 0211635	A1	14 Feb 2002
	WO 9313816	A1	22 Jul 1993
	WO 9426228	A1	24 Nov 1994
	WO 9632051	A1	17 Oct 1996
	WO 9632395	A1	17 Oct 1996
	WO 9639914	A1	19 Dec 1996
	WO 9718765	A1	29 May 1997
	WO 9718768	A1	29 May 1997
	WO 9803117	A1	29 Jan 1998
	WO 9803220	A1	29 Jan 1998
	WO 9856324	A1	17 Dec 1998
	WO 9909919	A1	04 Mar 1999
	WO 9917690	A1	15 Apr 1999
	WO 9920185	A1	29 Apr 1999
	WO 9920213	A1	29 Apr 1999
	WO 9926546	A1	03 Jun 1999
	WO 9930655	A1	24 Jun 1999
	WO 9942037	A1	26 Aug 1999
	WO 9956646	A1	11 Nov 1999
	WO 9956646	A9	16 Nov 2000
	WO 02102255	A1	27 Dec 2002
	WO 03005882	A2	23 Jan 2003
	WO 03005882	A3	06 Nov 2003
	WO 03024305	A2	27 Mar 2003
	WO 03024305	A3	15 Jul 2004
	WO 03024506	A2	27 Mar 2003
	WO 03024506	A3	30 Oct 2003
	WO 03028540	A2	10 Apr 2003
	WO 03028540	A3	12 Sep 2003
	WO 03028540	A9	27 May 2004

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
		WO 03028542 A2	10 Apr 2003
		WO 03028542 A3	06 Nov 2003
		WO 03068055 A2	21 Aug 2003
		WO 03068055 A3	24 Dec 2003
		WO 03068311 A2	21 Aug 2003
		WO 03068311 A3	25 Mar 2004
		WO 03090638 A1	06 Nov 2003
		WO 03090638 A9	03 Feb 2005
		WO 2004002293 A2	08 Jan 2004
		WO 2004002293 A3	28 Jul 2005
US 2012296262 A1	22 Nov 2012	US 2012296262 A1	22 Nov 2012
		US 9561073 B2	07 Feb 2017
		AU 2008304599 A1	02 Apr 2009
		AU 2008304599 B2	22 Nov 2012
		CA 2700968 A1	02 Apr 2009
		CA 2795256 A1	06 Oct 2011
		CA 2795256 C	03 Oct 2017
		CN 103037795 A	10 Apr 2013
		CN 103037795 B	25 Nov 2015
		CN 105250022 A	20 Jan 2016
		EP 2197383 A1	23 Jun 2010
		EP 2197383 A4	22 Aug 2012
		EP 2197383 B1	31 Jan 2018
		EP 2552336 A1	06 Feb 2013
		EP 2552336 A4	11 Sep 2013
		EP 2552336 B1	10 Feb 2016
		EP 3045137 A1	20 Jul 2016
		EP 3045137 B1	14 Feb 2018
		JP 2010540099 A	24 Dec 2010
		JP 5618332 B2	05 Nov 2014

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/IB2018/050010

Patent document cited search report	Publication date	Patent family member(s)	Publication Date
		JP 2013523285 A	17 Jun 2013
		JP 5917487 B2	18 May 2016
		JP 2014208263 A	06 Nov 2014
		JP 6050283 B2	21 Dec 2016
		JP 2016052601 A	14 Apr 2016
		JP 6211576 B2	11 Oct 2017
		JP 2017094092 A	01 Jun 2017
		KR 20100075528 A	02 Jul 2010
		KR 101228879 B1	05 Feb 2013
		KR 20130041800 A	25 Apr 2013
		KR 101671333 B1	01 Nov 2016
		US 2010292685 A1	18 Nov 2010
		US 8911435 B2	16 Dec 2014
		US 2013131513 A1	23 May 2013
		US 9271787 B2	01 Mar 2016
		US 2010256616 A1	07 Oct 2010
		US 9283034 B2	15 Mar 2016
		US 2016135881 A1	19 May 2016
		US 2017100192 A1	13 Apr 2017
		WO 2009042614 A1	02 Apr 2009
		WO 2011123834 A1	06 Oct 2011