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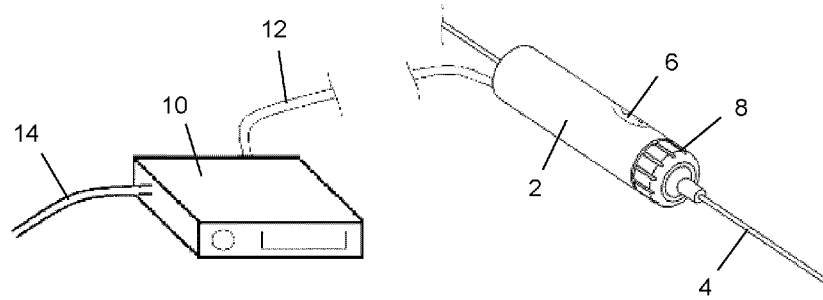


Figure 1

(57) Abstract: Endovascular apparatus for determining the condition of a vessel in a body comprises an elongate waveguide element such as a wire and an activation unit comprising a source of ultrasonic energy to activate the waveguide element, hence transmitting ultrasonic energy to an active distal section of the waveguide element. A signal acquisition system acquires feedback signals from the apparatus for interpretation of vessel condition. The signal acquisition system comprises at least one acoustic sensor for acquiring acoustic feedback signals generated by the apparatus when the waveguide element is activated and/or at least one inertial sensor for acquiring information representing orientation and/or acceleration of the activation unit. Data sets may be generated from acoustic and/or non-acoustic feedback signals, including inertial or electrical signals, and combinations of, or comparisons between, those data sets can characterise the condition of the vessel, including any lesion such as a blockage in the vessel.



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APPARATUS AND METHOD FOR DETERMINING THE CONDITION OF STRUCTURES IN THE BODY

This invention relates to techniques for determining the condition of vessels, cavities or other structures in the body, including characterising occlusions or obstructions in such
5 structures.

Embodiments of the invention employ active elongate elements such as wires and catheters. Some of those wires and catheters are adapted to pass through or to cross occlusions or obstructions in the body, for example to treat ischaemia, such elements
10 therefore being known in the art as crossing wires and crossing catheters. It should also be understood that crossing wires and crossing catheters may have additional functions such as to guide follow-on therapies once a blockage has been crossed.

Crossing wires will be used in this specification to exemplify the inventive concept but
15 it should be understood that the inventive concept can also be applied to crossing catheters. However, in other embodiments, active elongate elements such as wires or catheters do not necessarily cross through occlusions, meaning that the invention is not limited only to the use of crossing wires and crossing catheters.

20 Ischaemia is an inadequate supply of blood to an organ of the body. In atherosclerotic blood vessels, ischaemia occurs as a result of the blood vessels being blocked by obstructions that arise from lesions in the vessel wall, from atherosclerotic plaque, or from emboli arising from other sources. By partially or fully occluding a blood vessel, a blockage restricts blood flowing to tissues distal to the blockage, causing cell death
25 and a rapid deterioration in the health of those tissues.

Blockages such as chronic total occlusions (CTOs) result in an ischaemic response to wounds and trauma, leading to refractory ulceration of wounds and cuts and other insults to tissues. This anticipated response makes surgical intervention unattractive.
30 Thus, a preferred way to treat such blockages is by minimally invasive, endovascular procedures such as angioplasties. In such procedures, small-diameter therapeutic devices are introduced into the vasculature via guidewires or catheters, navigated to the blockage via the lumen of veins and arteries and deployed at the site of the lesion

to restore patency. Procedures used to revascularise occlusions in the coronary and peripheral arteries by treating chronic atherosclerotic plaques can also be used in the treatment of acute embolic occlusions, thrombi, or occlusive blood clots.

- 5 More generally, guidewires or catheters are used in other minimally-invasive procedures to introduce other devices and instruments into vessels or other cavities of the body to enable inspection, diagnosis and different types of treatment. Other medical procedures that use guidewires or catheters include gastrointestinal, urological and gynaecological procedures, all of which may require a passageway to
10 be formed through a blockage to facilitate the passage of often larger devices to the site of lesions or other targeted tissues distal to the lesions.

- In endovascular procedures, an artery is selected and recruited for use in obtaining access to the vasculature. The selection is based on the ability of the artery to
15 accommodate the passage of the intended diagnostic or therapeutic device to the target site and the extent to which it may minimise tissue and patient trauma.

- In revascularising procedures for peripheral arteries, access is often made by surgical cutdown and puncture to the femoral, popliteal and pedal arteries, commonly known in
20 medical terms as the Seldinger technique. Once access is made, an introducer wire and an introducer sheath are inserted into the vessel and secured at the site. The sheath acts as a port for the introduction, withdrawal and exchange of devices and to minimise abrasion of the arterial tissue. Then, catheters and guidewires are introduced into the artery to provide further protection and to assist in navigating a device to the
25 target site.

- A guidewire, for example, is pushed carefully along the lumen of the vessel to avoid trauma to the vessel wall and is navigated to the site of the occlusion. In successful procedures, the guidewire is then pushed across, or through, the occlusion and is kept
30 *in situ* to act as a guide over which a diagnostic or therapeutic device, such as a balloon catheter and/or a stent, is tracked to the site of the occlusion. Visualisation of the progression of guidewires, catheters and other diagnostic or therapeutic devices through the anatomy is typically done by X-ray, duplex ultrasound or MRI.

In the case of balloon angioplasty, a balloon catheter is introduced over the guidewire into the vessel and navigated to the site of the occlusion. The balloon is then dilated, pushing the occluding material outwardly to restore blood flow. Sometimes a stent is
5 placed within the lesion to act as a scaffold to maintain patency of the vessel.

Conventional endovascular wires are of various constructions and designs to facilitate access to, and crossing of, lesions in different anatomies and to support different devices. Such wires are available in a range of outer diameters and lengths associated
10 with the anatomies concerned and the distances over which they are expected to operate. They are made from various materials, most typically stainless steels or NiTi (Nitinol). Their manufacture typically involves cold-working the material while forming it into a wire and then machining or grinding the wire to different profiles to effect a desirable performance. As an example, specific tapers may be ground over the length
15 of a wire to produce differential degrees of flexibility along the length of the wire.

At its distal end in particular, the wire must have sufficient flexibility to conform to the tortuosity of a vessel and yet must also have sufficient axial and torsional strength to transmit force to the distal tip and to cross through a lesion. A balance is required
20 between flexibility expressed as 'trackability' and rigidity expressed as 'pushability' or 'steerability'. Pushability requires longitudinal, columnar stiffness whereas steerability requires torsional stiffness.

Conventional endovascular wires are operated by their proximal end being pushed,
25 pulled and torqued to navigate to the site of a blockage and are then pushed through the blockage. Thus, they are passive, in the sense that they do not transmit any energy other than that applied by the clinician.

The anatomies in which endovascular procedures may be conducted include, but are
30 not limited to, the coronary, neurovascular and the peripheral arteries that service the lower limbs. Different anatomies are associated with different types of lesions. For example, lesions found in the various peripheral vessels pose different challenges to those found in the coronary arteries.

In many instances, occlusions are too challenging for conventional endovascular elements such as guidewires to cross through. In this respect, atherosclerotic plaque is composed of materials whose constitution becomes progressively stiffer over time. For example, the iliac, femoral, popliteal and infra-popliteal arteries are susceptible to extensive calcification that poses a severe impediment to successful endovascular procedures. Conventional endovascular elements are limited when trying to cross nearly- or totally-occluding blockages that may also be significantly calcified.

For example, in peripheral infra-iliac procedures, an occlusion may have a calcified proximal cap that will be encountered in a preferred antegrade or femoral approach. Much time may be spent in attempting the conventional antegrade approach and escalating through different wires in further antegrade attempts before changing to a retrograde approach to cross the lesion. In a retrograde procedure, access is obtained through vessels distal to the lesion in the foot or ankle in the case of peripheral disease, or through collateral (typically septal) vessels in coronary anatomy. In this respect, retrograde techniques take advantage of occlusions sometimes having a softer distal cap that is easier to cross than a calcified proximal cap. However, retrograde procedures are more complex than antegrade procedures, requiring greater skill and taking much longer to do.

In over 50% of peripheral artery cases, particularly in the popliteal, tibial and peroneal arteries, the vessels are totally occluded by lesions; in approximately 30% of cases the target lesions are severely calcified. These calcified lesions are in effect composed of rigid inelastic segments that typically extend to a length of 3cm to 5cm within even longer extensive diffuse lesions that are, on average, of the order of 20cm to 25cm in length. Selecting a treatment for these lesions requires insight as to their length and composition that is not readily available from conventional imaging.

In the case of peripheral arteries, blockages are often too severely diseased and composed of materials too resistant to allow the ready passage of a guidewire. In such instances, the procedure takes substantially longer to complete and may require the use of additional devices to cross the lesion. Quite often, the procedure is eventually

abandoned entirely, which prevents preferred follow-on procedures such as balloon angioplasty and stenting and therefore limits the ability to treat the patient.

In view of these drawbacks, there have been several proposals for ultrasonically-
5 activated guidewires and catheters for use in atherectomy or thrombectomy
procedures, in which ultrasonic vibrations are transmitted along the element to the
distal tip to agitate and to ablate the material of a blockage. The element therefore
serves as a waveguide that conveys ultrasonic energy distally. Much of the prior art
relevant to the concept of ultrasonic activation in this context is discussed in our
10 previous patent applications published as WO 2020/094747, WO 2021/089847, WO
2021/089859 and WO 2021/224357, whose contents are incorporated herein by
reference.

Among other concepts, our previous patent application published as WO 2020/094747
15 discloses a system that comprises an ultrasonic source, an active crossing wire and a
signal acquisition, processing and communication chipset or control circuit. The
chipset or circuit can generate signals for controlling the system and can provide
outputs to users and/or external data acquisition systems. In particular, a controller
monitors measurements of frequency and amplitude of current and voltage at the
20 source and of incident, reflected and standing waveforms in the wire and thereby
estimates displacement of the distal tip. Modulation of those variables is monitored as
the wire transits through the anatomy and crosses through different types of
occlusions, including calcified CTOs. This enables determination of calcific versus non-
calcific lesions and of the duration or length of a calcified segment of a lesion. A user
25 can then react to control the system or the system can control itself accordingly, for
example by increasing input power on encountering a lesion that is determined to be
calcific.

WO 2020/094747 proposes that a digital signal processor interrogates the
30 measurements made, provides feedback and interprets and compares the relative
contributions of losses from anatomical tortuosity in navigating to the site versus those
arising from passage through the occlusion. The system processes data obtained from
measurements that are indicative of the ultrasonic waveform as transformations of the

resonant vibrations occur while passing through the vasculature and through occlusions. Algorithms transform the raw data into procedurally relevant outputs. The system can compare and interpret the difference between calculated values from the active system and a prescribed set of values to characterise the nature of a material
5 occluding the vessel.

Thus, the system of WO 2020/094747 considers variations in characteristic losses that are typical of engagement of the active wire with different healthy and diseased tissue types. There is differentiation between losses in the vessel and losses associated with
10 lesions and between lesions of different composition, especially between calcified and non-calcified lesions. The characteristic response to differential changes occurring in different media and in the passage or navigation of the endovascular wire through different anatomies is used to create distinct algorithms that are used to: 1) determine the source of, and to compensate for, losses in the system; 2) assess the tone of
15 arterial vessels; and 3) determine the composition detail of a lesion. These algorithms may, for example, provide compensation to the tip of the wire as it comes into contact with compliant, non-compliant and calcific material and in the latter case may amplify the energy input to the system accordingly.

20 The present invention takes WO 2020/094747 as its starting point and further develops concepts disclosed in our International patent application published as WO 2022/129623, whose content is also incorporated herein by reference. The invention seeks to improve the quality of feedback concerning the behaviour of an ultrasonically-energised elongate waveguide element, such as a wire, as the element traverses and
25 interacts with the anatomy and with any obstructions or other lesions encountered in the anatomy. In this respect, it has been found that when *in situ* and activated, the element will produce characteristic acoustic signatures indicative of different properties that characterise a lesion, the tissue of a vessel and possibly also the flow of blood along a vessel.

30

WO 2019/152898 discloses an ultrasonically activated tubular element that is advanced along a passive guidewire. The tubular element of WO 2019/152898 may be able to treat clots but even if it would be able to cross a calcific CTO, it is to be

contrasted with a wire as contemplated in preferred embodiments of the invention. A wire can be configured to convey ultrasonic energy effectively to the distal end portion and to cause the active distal end portion to oscillate with desirable characteristics. However, a tubular element cannot be made flexible enough to track to the site of a lesion along a tortuous and narrow path without losing the stiffness and uniformity that is desirable to transmit signals along the element to the distal end portion and back. There is also a significant risk that a tubular or columnar element would break under ultrasonic excitation due to changes in its material properties when bent. Nevertheless, in the invention, it may be convenient for a catheter or tube surrounding a wire to support acoustic sensors if desired.

Whilst WO 2019/152898 recites sensing ultrasound characteristics such as power, frequency, amplitude, phase and/or stroke length, it does not disclose an independent acoustic sensor as contemplated by the invention. Implicitly, these ultrasound characteristics would be measured directly from the transducer in WO 2019/152898 by measuring its driving inputs and mechanical properties rather than by listening to the transducer or the active element.

A wide range of different sensors and sensed parameters are proposed in WO 2019/152898 but there is no mention of where the sensors may be located, or of acoustic sensors or listening to sound. The sensors are not concerned with interactions between a wire and a vessel wall or surrounding tissues or blockages and do not allow the device to serve as a diagnostic aid for a clinician. Instead, the sensors suggested by WO 2019/152898 are dedicated to controlling the device during a crossing procedure. There is no mention of monitoring acoustic outputs independent of control of the device or the use of data as a clinical diagnostic as envisaged by the invention.

US 5284148 discloses an ultrasound diagnostic probe that can scan radially but not longitudinally and cannot cross a blockage if one is encountered.

US 2017/215837 discloses a passive guidewire in which an acoustic sensor is located proximally with respect to the guidewire. This can only listen to interactions with

structures immediately distal of the guidewire, such as a calcific cap of a blockage, and not with a surrounding vessel wall or with the internal structure of a blockage, which could for example have a gel-like consistency behind a stiffer cap. Thus, there is no possibility of further characterising a lesion, or a vessel, as the wire passes through
5 and beyond that initial encounter.

US 2004/260180 discloses a transceiver that both transmits and receives signals in duplex fashion. A transceiver and its supporting electronics can only detect and process reflections of the signals that it itself transmits, and so cannot detect and
10 process signals driven from another source, such as a transducer acting on a crossing wire whose distal end is active in a structure within the body.

Thus, the invention resides in endovascular apparatus for determining the condition of a vessel, cavity or other structure in a body, including any lesion in such a structure.
15 The apparatus comprises: an elongate waveguide element; an activation unit comprising a source of ultrasonic energy and a coupling for coupling the source to the waveguide element to activate the waveguide element, thereby transmitting ultrasonic energy from the source along the waveguide element to an active distal section of the waveguide element; and a signal acquisition system that is configured to acquire
20 feedback signals from the apparatus for use in interpreting vessel condition. The signal acquisition system comprises at least one acoustic sensor for acquiring acoustic feedback signals generated by the apparatus when the waveguide element is activated. At least two acoustic sensors may be spaced longitudinally from each other.

25 At least one acoustic sensor may be mounted in or on the activation unit, for example in longitudinal alignment with, or proximally relative to, or distally relative to, the coupling of the activation unit. At least one acoustic sensor may be mounted on or parallel with the waveguide element, for example proximally or distally relative to the length of the waveguide element.

30

The waveguide element may be, or may comprise, or may be surrounded by a catheter, in which case at least one acoustic sensor may be mounted on the catheter.

Additionally, or alternatively, the waveguide element may be or may comprise a wire, in which case at least one acoustic sensor may be mounted on the wire. A strain gauge may be fixed to the waveguide element, such as a wire, to acquire operational feedback signals from the waveguide element. Such a strain gauge could serve as an
5 acoustic sensor.

A least one acoustic sensor may be an extra-corporeal sensor arranged to lie against a part of the body or may be an intra-corporeal sensor arranged to be inserted into the
10 body.

In preferred embodiments, the signal acquisition system further comprises at least one electronic sensor that is configured to acquire operational feedback signals representing operational parameters of the source of ultrasonic energy. Those operational parameters could be frequency and/or amplitude and/or phase of current
15 drawn by, or voltage dropped across, the source of ultrasonic energy. The signal acquisition system may be configured to monitor variations in frequency or amplitude of vibration of the waveguide element via the coupling.

The apparatus may further comprise a signal processing system for processing
20 feedback signals acquired by the signal acquisition system. Such a signal processing system could, for example, be configured to employ numerical algorithms selected for specific types of the waveguide element.

The signal processing system may be configured to determine characteristics of an
25 obstruction in a vessel from the acquired feedback signals. The signal processing system may also be configured to compare relative contributions of losses from anatomical tortuosity in navigating the active distal section to an obstruction versus losses arising from the passage of the active distal section through the obstruction.

30 The signal processing system may be configured to compare the acquired feedback signals with stored data that characterises known obstructions, and to characterise an obstruction with reference to that comparison.

The signal processing system may further comprise an output to a user interface and/or to an external data acquisition system, and/or an input from a user interface and/or from an external data network.

- 5 The apparatus may further comprise a controller that is responsive to the signal processing system. Such a controller could be configured to modulate excitation voltage applied to, or excitation current supplied to, the source of ultrasonic energy. The controller may, in particular, be configured to control the source of ultrasonic energy by varying frequency and/or amplitude of the excitation voltage applied to the
- 10 source of ultrasonic energy. The controller could also be configured to drive the frequency of the excitation voltage by employing a phase difference between the excitation voltage and the excitation current in conjunction with amplitude of the excitation voltage.
- 15 The controller may comprise an amplitude feedback controller and may be configured to use a resonant frequency as an operating point of control. The controller may be configured to pulse or vary a drive signal to the source of ultrasonic energy.

- The controller may be configured: to monitor modulation of transmitted signals and to
- 20 control the source of ultrasonic energy automatically to compensate for background energy loss encountered in the waveguide element as the active distal section approaches an obstruction; and to distinguish the background energy loss from additional energy loss as the active distal section passes through the obstruction and to compensate for the background energy loss to sustain displacement at the active
- 25 distal section.

- The controller could be configured to modify or change a control algorithm in response to variation in operational parameters of the source of ultrasonic energy arising from interaction of the active distal section with an obstruction in use.

30

The inventive concept embraces a communication system comprising the apparatus of the invention in data communication with a computer system that is arranged to receive data from the apparatus, to optimise and update control algorithms accordingly

and to output the optimised, updated control algorithms to the apparatus. Optimally, two or more such apparatuses are in data communication with the computer system, which is therefore arranged to optimise control algorithms in accordance with data received from multiple procedures performed using the apparatuses and to output the
5 optimised, updated control algorithms to the apparatuses.

The inventive concept also embraces a corresponding method for determining the condition of a vessel in a body. The method comprises: navigating a distal section of an elongate waveguide element to a site in the vessel; activating the waveguide
10 element by transmitting ultrasonic energy to the distal section; acquiring acoustic feedback signals generated when the waveguide element is activated; and interpreting the acoustic feedback signals to characterise the condition of the vessel.

The method of the invention can assess decay in amplitude of, or a shift of frequency
15 of, displacement of the waveguide element caused by losses resulting from contact with a wall of the vessel or with material in the vessel such as an occluding lesion.

The distal section of the activated waveguide element can be engaged with a lesion in the vessel, and consequential changes in the acoustic feedback signals can then be
20 interpreted to characterise the lesion. Conveniently, the distal section of the activated waveguide element can also disrupt the lesion.

The method may further comprise comparing sensed data representing the response of the activated waveguide element to the lesion with stored data representing the
25 response of a corresponding activated waveguide element to interaction with a known lesion.

Acoustic feedback signals may be acquired in an extra-corporeal activation unit disposed proximally of the waveguide element, and/or at one or more locations along
30 the waveguide element, and/or at an intra-corporeal distal location along the waveguide element, and/or at one or more locations outside the vessel, and/or at two or more locations longitudinally spaced from each other.

Preferably, the method further comprises acquiring non-acoustic feedback signals representing operational parameters of a source of ultrasonic energy coupled with the waveguide element, or more generally obtained by monitoring variations in frequency or amplitude of vibration of the waveguide element. It can be determined from the operational parameters how the source responds to the waveguide element encountering the vessel and any lesion in the vessel. For example, the non-acoustic feedback signals may be electrical feedback signals represent variations of frequency and/or amplitude and/or phase of current drawn by, or voltage dropped across, the source of ultrasonic energy. Conveniently, damping of the waveguide element can be determined by monitoring decay of a current signal over time. Non-acoustic feedback signals can also be inertial signals representing orientation and acceleration of an activation unit.

Data sets can be generated from the acoustic and non-acoustic feedback signals, allowing combinations of, or comparisons between, the respective data sets to be used characterise the condition of the vessel. Amplitude or frequency of the ultrasonic energy transmitted to the distal section along the waveguide element may be adjusted in response to the non-acoustic feedback signals. Also in response to the non-acoustic feedback signals, the source may be controlled to maintain a resonant frequency in the waveguide element.

The method of the invention may comprise: outputting data to an external data network; receiving data from the network in response; and, on receiving data from the network, modifying or changing a control algorithm accordingly. The method may also comprise: outputting data to an external computer system; in the external computer system, optimising and updating a control algorithm in accordance with that data; outputting the optimised, updated control algorithm from the external computer system; and using the optimised, updated control algorithm to control activation of the waveguide element. Preferably, the computer system can optimise the control algorithm in accordance with data received from multiple procedures.

Two or more different waveforms can be applied sequentially to a source of the ultrasonic energy, those waveforms being selected from, for example, sinusoidal, pulsed, multi-tone, chirp or noise waveforms.

- 5 To improve sensitivity, the method can comprise: advancing the distal section of the activated waveguide element close to a lesion in the vessel; acquiring baseline feedback signals; advancing the distal section of the activated waveguide element into engagement with the lesion; acquiring operational feedback signals; and subtracting the baseline feedback signals from the operational feedback signals.

10

- In summary, the invention involves acoustic characterisation of the effects of intraluminal elements such as ultrasonically activated wires. In particular, the invention employs an ultrasonic waveguide device such as a crossing wire not only to excavate a lesion and to disrupt calcified intraluminal or intramural plaques within the vessel but
15 to determine the characteristics of a vascular lumen. Those characteristics may include the internal diameter of the vessel, the vascular tone of the vessel and the mechanical characteristics and composition of any material blocking the vessel.

- In WO 2020/094747, the inventors proposed that different wires having known
20 characteristics, such as specific combinations of ground tapered profile, land length and diameter, will respond to a lesion in a way that can discriminate between lesions of a calcific or non-calcific nature. The inventors have now determined that further analysis and processing of spectra can provide for more sensitive assessment of a lesion and/or of other surfaces that the wire may contact within the vasculature. More
25 specifically, the invention aims to allow assessment of the internal diameter of a vessel and to characterise, through interpolation, the mechanical properties of the vessel wall and any materials that may be blocking the vessel. Thus, the invention enables identification of whether a blockage is composed of a gelatinous plaque, calcific material, a thrombus or some other form of embolic material. Of particular interest is to
30 determine whether the blockage is of a vulnerable soft plaque or a calcified plaque or, if the blockage is a thrombus, to characterise what type of thrombus is present.

In examples to be described, a system of the invention comprises a wire that is manufactured with a specific ground profile toward its distal end and whose longitudinally successive sections have specific diameters and lengths. Examples of such wire characteristics are taught in our aforementioned prior patent applications.

- 5 They enable a distal end portion of the wire to activate in a particular way, at the resonant frequency (and harmonic frequencies associated with or consistent with the resonant frequency) of the piezo-electric ultrasonic transducer that activates the wire.

- 10 A coupling mechanism enables the wire to be coupled to the transducer. The transducer is driven by an ultrasonic signal generator that can excite the transducer and hence the wire at a desired frequency and amplitude. A control circuit monitors and controls the electrical load across the transducer to effect the desired actuation.

- 15 In accordance with the invention, at least one acoustic sensor detects, and so in effect listens to, acoustic emissions from the wire, the coupler and/or the transducer. The system can monitor and analyse the detected acoustic spectra and can present processed information to the user in a meaningful way. Acoustic information may be used in conjunction with other information, such as inputs to or outputs from the control circuit, to improve the quality of analysis, detection and determination. Processed
20 information may also be stored in and shared from an external database, such as in the cloud, the better to educate physicians and to perfect analytical algorithms with a growing sample size representing use of the invention in actual procedures.

- 25 The invention exploits the insight that interpretation of acoustic spectra emitted during the passage of a vibrating wire or other waveguide through vascular anatomies can provide a means to interpret characteristics of tissues. This is possible because when the wire comes, forcefully, into contact with any surface, such as the inner surface of a vessel or a lesion blocking the vessel, that contact will modulate the frequency and/or the amplitude of the acoustic waveform travelling through the wire. It is possible to
30 associate those modulations with particular characteristics of the vascular anatomy. It is also the case that at such ultrasonic high frequency, interactions with the vessel wall will disrupt calcified materials within the wall, thus at once assessing vascular hardness as well as softening plaque.

It is also possible through interrogation of the acoustic spectra alone, and/or through other inputs from the environment, to interpret from transformations in the wire what structures or materials the wire may be contacting as it passes through the internal morphology of a vascular lumen. This includes any blockage that may be in the lumen, or, if the wire is excavating or removing any such blockages, the character of the blockage.

A basis for making such an assessment is that the amplitude of any axial or radial displacement associated with resonance in the system varies with input amplitudes and its decay, or displacement of frequency, is associated with losses resulting from the wire coming into contact with other materials or surfaces at its end or along its length. These changes in the acoustics detected along the wire can be used to characterise the vessel, its lumen and any obstruction. Further, as impedance in the transducer may also modulate as a result of changes in the losses in the system as the wire is damped or becomes more or less constrained, superimposition of this electrical response can be used to analyse and describe the characteristics of the vessel, its lumen and any obstruction more accurately.

One or more acoustic sensors may, for example, be positioned on, in, or close to a housing of the transducer, or on a wire, or on a catheter, or in, or in contact with, the patient's body in order to detect sounds being emitted and to subtract surrounding noise. The resulting acoustic spectra are processed and analysed by an algorithm that recognises sound spectra characteristic of specific types of interference and resonant and sub-harmonic frequencies. As noted above, the sensitivity of the acoustic algorithm may be increased by interrogating variations in electrical signals used to drive the transducer at its resonant frequency.

The acoustic spectra are compared by the system to the ultrasound spectra in a device that employs an intravascular waveguide, such as a wire, resonating at a frequency and amplitude that allows the distal end portion of the wire to resonate with axial and radial displacement. In the context of a crossing wire, the primary purpose of those displacements is to excavate through materials occluding a vessel. The

invention uses those displacements for another or additional purpose, namely to generate an acoustic signal that varies in different ways on travelling through the vasculature and on encountering and engaging with a lesion. The acoustic signal also varies in different ways on engaging with different types of lesion, hence serving as an
5 acoustic signature that characterises the lesion.

As explained in our aforementioned previous patent applications, the dimensions and profile of a crossing wire allow the wire to resonate at harmonic and sub-harmonic frequencies with various modes of displacement, particularly in its distal end portion.
10 Modulation occurs as the wire comes into contact with different surfaces. For example, when the distal tip of the wire encounters a calcified blockage that restrains its lateral displacement, the mode of displacement of the wire will transition from 'fixed to free' to 'fixed to fixed'. 'Fixed to free' may be visualised as a node at the proximal end of the wire and an antinode at the distal end of the wire whereas 'fixed to fixed' may be
15 visualised as a node at both the proximal and distal ends. This modulation will shift the wavelength slightly and therefore change the acoustic signal transmitted by the wire.

Analysing changes in wavelength allows the system to sense what type of materials have disturbed its wavelength and frequency and therefore to determine the type of
20 materials with which the distal end portion of the wire is in contact. Thus, interpretation of the acoustic spectra emitted during the passage of waveguides through vascular anatomies can provide a means to interpret characteristics of the tissue with which the wire comes into contact. It can also interpolate, through mathematical transformations, features of acoustic spectra or electrical signals indicating how the wire is responding
25 to the internal morphology of the lumen in removing any blockages in the vessel.

As the system is dynamic, characterisation of the manner in which the system responds needs to be done dynamically to be true to comparisons between electronic control and acoustically-emitted variables. The dynamic interrogation and subtraction
30 of features, or addition in the case of patterned excitation, needs be monitored in time. In this respect, feedback may be interrogated from compared programmed inputs such as pulses or patterns to seek variations of specific features. Feedback may also be

interrogated from compared variations over time, such as a quality factor or Q factor representing damping.

Thus, the invention embodies principles of acoustic characterisation, proposing that an
5 active element such as a wire *in situ* within a vessel will produce characteristic
acoustics as it comes into contact with the vessel wall and with any blockage, whether
a thrombus, soft or fibrous, or an atherosclerotic lesion, hard or soft, in the lumen or in
the wall of the vessel. The captured acoustic signature will be characteristic of the
lumen of the vessel and the surrounding tissues. It is proposed that through direct
10 comparative measurements interpolated or extrapolated, it will be possible with post-
processing analysis and suitable algorithms to produce a reliable diagnostic output to
associate these characteristic acoustic spectra with the nature and integrity of the
tissues.

15 Preferred embodiments of the invention employ two sensors in operation
simultaneously, namely an electrical or electronic sensor and an acoustic sensor.

The electronic sensor acts on features such as the transducer that generates
ultrasonic energy and determines how the transducer is operating, setting the scope of
20 its ability to sense and produce data that may be interrogated. The electronic sensor
also detects the electrical drive frequency and the ways in which the system responds
to variability or instability introduced by the wire moving through tortuous vessels up to
the point of the lesion. The electrical drive frequency is modulated by encounters with
vessel walls and blockages in the lumen. Driver electronics respond to this by tracking
25 variables of phase angle, current and/or voltage. The invention contemplates
interrogation of this dynamic control variation in the main variables, to provide
characteristic features that can be associated with the physical characteristics a vessel
and any blockage within it.

30 One or more acoustic sensors, or microphones, listen for all, or a portion of, the
acoustic emissions through and from biological tissues when the active wire is *in vivo*,
whether intramurally, intraluminally or extra-corporeally. The acoustic sensor, in
particular, listens for acoustic emissions from the wire actuated internally within the

lumen of a vessel. The invention enables interrogation of variations in acoustic emissions affected by interference between the wire and the vessel or anything in the vessel, such as a CTO.

- 5 The data set from acoustic sensors is much richer than the data set from the small range of operational frequencies used in activating the wire, even though the acoustic emissions are created by that small actuating range. The result is a huge amount of additional data that can be mined using various mathematical instruments to find features and then to associate those features with the nature of the vessel and its
10 contents, the behaviour of the wire and the nature of a new channel excavated by use of the wire. Thus, the electronic data set can be enormously enhanced by the integration of acoustic data.

- Interrogating the full range and the spectrum all of the different frequencies that are
15 being expressed requires significant post-processing assessment, hence a preference for a cloud-based, machine-learning approach to operation, development and updating of advanced algorithms. However, a suitably programmed on-board processor facility, in the local device, would be able to manipulate the data through suitable algorithms to provide at least 'binary' feedback, such as whether a lesion is calcified or non-calcified
20 or hard or soft. It is emphasised that post-processing of any form, whether in the cloud or otherwise, is not a requirement. Such processing may be performed locally, in real time.

- Disclosed, therefore, is an ultrasonic system that induces vibrations in customised
25 endovascular surgical wire devices and interrogates and applies artificial intelligence to acoustic feedback and optionally also other feedback in the system. The feedback can be used to optimise the performance of the system in navigating to, crossing through and characterising and modifying the structure and properties of endovascular occlusions.

30

A programmable circuit system for data acquisition and processing and for controlling activation of the system may include an integrated, or on-board, programmable digital signal processing chipset. This processes the monitored, transmitted and received or

incoming acoustic and/or electrical or electronic signals using algorithms to: interrogate the response; compare the ultrasonic feedback and the effect on the resonant frequency standing wave; estimate the size of the opening tunnelled through the lesion by the activated tip; and modulate the power in the system via voltage amplitude and
5 system frequency.

Analog and digital signal analysis and power control of the device as well as communications modules enable wired and wireless connection of the device and its data to wider data networks and the internet. This may, for example, facilitate
10 development of more intelligent algorithms to manage the system.

As ultrasonic vibrations are transmitted via the transmission member serving as a waveguide, the distal tip of the transmission member vibrates at a prescribed frequency and amplitude with the capability of beneficially disrupting the diseased
15 tissue or other material. The digital signal processing and control circuitry responds to acoustic and other feedback to allow semi-autonomous gross characterisation of the lesion, power control and the estimated size of opening in the system.

When the ultrasonic system is activated, the emitted waves travel along the wire to its
20 distal tip where they are reflected or transmitted through to neighbouring materials. Reverberations created in the wire at different transitional points establish a series of secondary and tertiary reflections. These waves are characteristic of different wire designs and features and they can be optimised to heighten the difference in the features of their signals. The reflections are determined to be composed of a specific
25 pattern of response in the waveform at any time for a given input and their variation is associated with perturbations or differences in the ambient environment. The waveforms give rise to characteristic acoustic emissions that can be used in isolation or in addition to other feedback signals.

30 The amplitude of displacement along the wire, at specific frequencies, varies through the course of a procedure as a result of damping from contact with surrounding tissues, either during navigation to the site of a lesion or in contact with diseased, non-compliant or calcified tissues in a lesion. The reverberations in the system and

resulting acoustic emissions are similarly affected, in characteristic ways, that allows their use in characterising the source and the nature of whatever is causing damping.

5 To effect a constant vibration amplitude, the ultrasonic transducer is controlled by a suitable feedback controller. In the case of the ultrasonic waveform, phase feedback control and comparison can be made by an electrical equivalent model such as the Butterworth-vanDyke model.

10 The ultrasonic transducer can be controlled by the frequency and the amplitude of the excitation voltage. Changing the frequency may influence the phase between the voltage and the current. The amplitude of the excitation voltage that controls the current is proportional to the vibration amplitude in resonance. This allows control algorithms to employ only phase and amplitude to drive frequency.

15 In a preferred embodiment, the approach is to drive the system using the resonance frequency as the operating point of control, in conjunction with an amplitude feedback controller, managing this operation through the use of customised programmed control algorithms that are unique for each wire type.

20 The advantages of a resonant driven, low damped system are the low voltages necessary and the high values of effective power. This solution also offers advantages in controlling the response of a Nitinol wire to ultrasonic activation.

25 Temperature effects in Nitinol and changing load conditions during a procedure due to interaction with surrounding tissues that can potentially result in a change of resonant frequency and vibration amplitude can be compensated for, within a range, for a given transducer.

30 Thus, in terms of the use of voltage and current, control and analysis through the resonant frequency may be used to monitor differential changes, over time and length, and this interrogation and compensation may be used to characterise the nature of the endovascular anatomy. The ability to capture the acoustic emissions from the interaction of the system with the neighbouring tissues provides for an additional and

separate means of inferring the nature of, or characterising, the tissues, as their response to the interaction with the wire will be determined by their structural properties.

- 5 The comparison and analysis of and between the primary emitted signal and the tertiary feedback responses in the wire considers variations in characteristic losses, typical with the engagement of the active member with different, healthy and diseased, tissue types. It differentiates between these types of losses in the vessel and those associated with lesions between lesions of different composition, for example between
10 calcified and non-calcified lesions.

- The resistance load encountered and the acoustic emissions recorded by the system vary. As the active member passes through different anatomies, analog signals may be interrogated by an on-board digital signal processor, conditioned and the parametric
15 output processed by algorithms to add to data from acoustic feedback to characterise response, to define feedback and to effect control.

- Algorithms may be customised to attune to the wire type. The range and the rate of change and the differential order of the change, filtered by the signal processing
20 circuit, may be used by an algorithm to characterise the nature of the material through which the wire passes. This may then be communicated to the physician as the procedure is being undertaken to assist in defining therapy.

- To improve performance, algorithms may be trained by bench ex-vivo and in-vivo data.
25 The latter possibility is enabled by a communications model that provides for the transportation of data to and from the device. The system can enable wired or wireless communication of data between the device and another device or cloud service for analysis and storage.

- 30 Thus, the quality of the operation and interpretation by the device can be improved over time by the interpolation of more data sets from additional procedures that builds upon the use experience. Such data can inform the design of iterative generations of control and interpretation algorithms. Consequently, on-board, local and/or cloud-

based refinement of algorithms can improve the design and operational interface of a treatment device and can provide more detailed feedback to a physician using the device, in addition to customising the operation of the device to suit different wire geometries and anatomies.

5

The frequency at which the transducer generates a mechanical signal may be at a set short-range frequency sweep, over a short range of frequencies, to accommodate losses from interaction and impingement by different forces over the length of the wire. The speed of the microprocessor allows the device to process small fluctuations in resonance in real time.

10

The signal used to drive the ultrasonic generator may be pulsed or varied to reduce heating and to optimize analysis and matching of offsets at the resonant frequency.

For example, a pulsed modulation of voltage, over a small frequency range, can

15

activate the crossing wire and a digital signal processor unit can interrogate the measurements made, provide feedback and interpret and compare the relative contributions of losses from anatomical tortuosity in navigating to the site versus those arising from passage through the occlusion.

20

The invention employs methods to interrogate feedback signals to characterise the vessel or lesion through which the wire is crossing and to collect data on the lesion being crossed, such as its length and composition which are facets that inform the manner in which the target lesion may be treated by the physician. This data may also be provided as feedback to the physician in a haptic and/or visual and/or audio form on a display to help the physician to operate the device. For example, this feedback could allow the physician to monitor a crossing procedure, using a simple backlit screen on the compact activation unit to display and assess the character of the lesion.

25

In another embodiment, where a user has access to a network, data from the procedure may be captured anonymously to protect patient confidentiality and communicated from the device to a data storage and processing platform where it may be analysed in real time or later. Characterisation of the lesion may also be presented to the user for their analysis and interpretation while conducting the procedure.

30

An attachment may be used to record and measure displacement of the wire as it traverses the vasculature and to map that data against lesion composition from feedback to characterise the properties of the lesion as a function of displacement
5 through the lesion.

The variation in the magnitude of the input and control parameters of current, voltage and frequency with the characteristic capacitance of the converter provide a matrix of measurements and controls that can be used in conjunction with acoustic feedback to
10 determine the power and characterise the lesion being crossed.

Monitoring acoustic emissions and electronic response such as current may support interpretation of the lesion and modulation of voltage allows for the amplification of power and the recovery of frequency as the device actuates the contact surface and
15 reduces offset. This array of measurements in the small frequency range then allows for gross characterisation of the composition of the lesion, be it calcified, fibrous or gelatinous over all or part of its length. These interpolated characteristic components are not absolute characteristics of the lesion but are instead indicative of: composition; degree of calcification; and whether the lesion is rigid, compacted or disaggregated.
20 This can be indicative of the nature of the lesion and inform the physician of the optimal therapy to consider. This may, for example, help to determine whether the composition or consistency of the lesion is compacted calcific particulate, or non-compacted fibrotic, or hard or soft gelatinous.

25 A specific algorithm, for each standard wire type, could be employed to estimate the diameter mapped out by deflection of the distal tip when excited at different levels of frequency and power and device configuration in the conditions pertaining to the procedure. This provides an estimate of the diameter of a resulting tunnelled channel through the occlusion.

30

The system may process data obtained from measurements of the ultrasonic waveform as it is generated, as the waveform passes through the wire or other transmission member, as transformations of the resonant vibrations occur, and as the

reflected waveform is attenuated by a transmission member, while passing through the vasculature and through occlusions.

Monitoring and analysing modulation of transmitted signals can automatically adjust for
5 energy losses in the system through voltage control to increase power in the system
and compensate for energy losses encountered in the wire as it is passes through the
vasculature to the occlusion. Monitoring and analysing modulation of transmitted
signals can also distinguish these losses from additional losses as the wire passes
through the occlusion and to compensate those additional losses to sustain the
10 displacement at the distal tip.

The measured parameters and variables may be operated on numerically to determine
their rate of change relative to each other and other parameters. Differences between
these calculated values from the active system and a prescribed set of values can be
15 compared and interpreted numerically to characterise the nature of a material
occluding a vessel.

In summary, the invention relates to endovascular apparatus for determining the
condition of a vessel in a body. The apparatus comprises an elongate waveguide
20 element such as a wire and an activation unit comprising a source of ultrasonic energy
to activate the waveguide element, hence transmitting ultrasonic energy to an active
distal section of the waveguide element. In accordance with the invention, a signal
acquisition system acquires feedback signals from the apparatus for interpretation of
condition of a vessel, cavity or structure of the body. The signal acquisition system
25 comprises at least one acoustic sensor for acquiring acoustic feedback signals
generated by the apparatus when the waveguide element is activated and/or at least
one inertial sensor for acquiring information representing orientation and/or
acceleration of the activation unit. Data sets may be generated from acoustic and/or
non-acoustic feedback signals, including inertial or electrical signals, and combinations
30 of, or comparisons between, those data sets can characterise the condition of the
vessel, cavity or structure, including any lesion such as a blockage in the vessel, cavity
or structure.

In order that the invention may be more readily understood, reference will now be made, by way of example, to the accompanying drawings in which:

5 Figure 1 is a perspective view of apparatus that implements the invention;

Figure 2 is a schematic side view of a crossing wire of the apparatus, when active;

10 Figure 3a represents first, second, third and fourth harmonic waveforms, the wavelength of the second, third and fourth waveforms being half that of the preceding waveform;

Figure 3b represents fundamental complex waveforms generated from the harmonic waveforms of Figure 3a;

15 Figure 4 is a detail side view of an active wire of the apparatus protruding distally from a catheter;

20 Figure 5 is a series of drawings showing the wire when active, excavating a tunnel in a lesion that was blocking a blood vessel;

Figures 6, 7 and 8 are a sequence of views that show an active wire excavating a tunnel in a lesion;

25 Figure 9 is a diagram of an acoustic signal over time, showing the response of an active wire to encountering a calcium sample representing a lesion;

Figure 10 is a block diagram of an embodiment of the invention;

30 Figure 11 is a block diagram of another embodiment of the invention;

Figure 12 shows a typical oscilloscope image of voltage and current waveforms applied to a transducer of apparatus like that shown Figure 1;

Figure 13 is a side view in longitudinal section of a crossing wire and catheter coupled to an activation unit, showing possible acoustic sensor locations within the activation unit;

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Figure 14 is a side view of a crossing wire and catheter coupled to an activation unit, showing possible acoustic sensor locations on the catheter;

10

Figure 15 is a perspective view of a catheter containing a crossing wire, showing a possible acoustic sensor location on the catheter;

Figure 16 is a perspective view of a crossing wire, showing a possible acoustic sensor location on the wire;

15

Figure 17 is a schematic sectional view of a patient's leg, showing an acoustic sensor of the invention incorporated into an adhesive patch applied to the leg close to the site of a lesion in the patient's vasculature;

20

Figure 18 corresponds to Figure 17 but shows an acoustic sensor unit held against the leg near the lesion instead of the adhesive patch;

Figure 19 corresponds to Figure 18 but shows the acoustic sensor in the form of a hand-held scanner being swept over the leg near the lesion;

25

Figure 20 is a schematic side view of a patient's leg, showing acoustic sensors of the invention implanted under the skin of the leg;

30

Figure 21 is a schematic sectional view corresponding to Figure 19, showing one of the acoustic sensors embedded close to the site of a lesion in the patient's vasculature;

Figure 22 shows an acoustic signal emitted, in a frequency range up to 125kHz, when an active wire crosses a sample of chalk;

Figure 23 corresponds to Figure 22 but focuses on a range up to 10kHz;

5 Figure 24 shows an acoustic signal emitted, in a frequency range up to 125kHz, when an active wire crosses a sample of BegoStone plaster;

Figure 25 corresponds to Figure 24 but focuses on a range up to 10kHz;

10 Figure 26 shows an acoustic signal emitted, in a frequency range up to 125kHz, when an active wire is not crossing a sample but is instead active in water;

Figure 27 corresponds to Figure 26 but focuses on a range up to 10kHz;

15 Figure 28 is a schematic view of a device of the invention engaging and forming an opening in an obstruction in a blood vessel;

Figure 29 is a flowchart of a data acquisition and processing technique of the invention;

20 Figure 30 is a power spectrum plot of an activated wire captured by an external microphone;

25 Figure 31 is a plot of power in a range of power bands expressed as amplitude versus time;

Figure 32 is a plot of total power plotted against time in a particular frequency band;

30 Figure 33 is a spectrogram of the frequency of an electrical current signal as the amplitude of a driving current is varied;

Figure 34 shows impedance amplitude and impedance phase of a transducer plotted against frequency;

5 Figure 35 is a side view in longitudinal section of a crossing wire and catheter coupled to an activation unit, showing the further option of inertial sensors within the activation unit;

10 Figure 36 is a perspective view from below of an activation unit of the invention showing X, Y, Z axes along which linear acceleration can be measured, and about which changes in pitch, roll and yaw movement of the activation unit can be measured by an inertial measurement system within the unit; and

Figure 37 is a block diagram of an embodiment of the invention that implements inertial sensing as illustrated in Figures 35 and 36.

15

Figure 1 of the drawings shows the overall configuration of a system that implements the invention and illustrates some major components of such a system. This example features a handheld ultrasonic activation unit 2 through which a flexible transmission member in the form of an endovascular waveguide or wire 4 extends, in central
20 alignment. In this example, portions of the wire 4 extend both proximally and distally from the activation unit 2. This arrangement is advantageous for various reasons as explained in our previous patent applications but is described here to exemplify, and not to limit, the present invention. The invention can be used with benefit in conjunction with more conventional activated crossing elements that may, for example, extend only
25 distally from an ultrasonic actuator.

The wire 4 can be inserted into a patient's vasculature and traversed to bring its distal end to the location of a lesion. Once a complex lesion is encountered that resists the wire 4 crossing it, or before, the activation unit 2 can be coupled to the wire 4 at a
30 suitable longitudinal location. When activated, the activation unit 2 transmits ultrasonic vibrations to and along the wire 4, enhancing the ability of the wire 4 to cross the lesion through ablation and other mechanisms. The wire 4 thereby serves as a crossing wire

for crossing through an occlusion in a blood vessel and can then remain in situ to serve as a guide wire for delivering subsequent therapeutic devices to treat the lesion.

Typically, the wire 4 may be more than 2m and up to 3m in length. For example,
5 access to a lesion in or through the foot may involve the wire travelling a distance of typically 1200mm to 2000mm within the vasculature depending on whether an ipsilateral, contralateral or radial approach is chosen. In this respect, a wire 4 tapering distally to a fine wire at its tip can navigate to the pedal arteries and around the pedal arch between the dorsal and plantar arteries. However, the invention is not limited to
10 pedal infra-inguinal or peripheral vessels and could, for example, be used in coronary applications, where the ability of the wire 4 to navigate to and to excavate within tortuous small-diameter arteries is also beneficial.

The activation unit 2 may include user controls 6 and optionally also a display. The
15 activation unit 2 further comprises a distal hand toggle 8 that a user can turn about the central longitudinal axis of the unit 2 and of the wire 4. In particular, the activation unit 2 can slide over the wire 4 and can be coupled to the wire 4 at a plurality of longitudinally spaced locations by applying torque to turn the toggle 8.

20 To effect coupling, as will be shown in a later drawing, the toggle 8 acts on a collet within the activation unit 2 that surrounds and is coaxial with the wire 4. When the toggle 8 is tightened, the collet grips the wire 4 to transmit ultrasonic energy from an integrated ultrasonic transducer within the activation unit 2, optionally via an amplifier horn that is coupled to the transducer. The wire 4 could be coupled directly to the
25 transducer in some embodiments, in which case the horn may be omitted.

Rotation of the toggle 8 is reversible to release the activation unit 2 from the wire 4. Provision is thereby made to interchange wires 4 of different dimensions, configurations or materials for different purposes. There is also the possibility of
30 interchanging the transducer, the horn and/or the collet within the activation unit 2.

In the disaggregated arrangement exemplified in Figure 1, an ultrasonic signal generator 10 is separate from the activation unit 2 and connected to the activation unit

2 by a connector cable 12. Integrated arrangements are also possible in which the ultrasonic signal generator 10 is incorporated into the housing of the activation unit 2.

The example shown in Figure 1 has an externally-powered ultrasonic signal generator
5 10 and therefore comprises a power cable 14 that connects to an external source of electrical power. Other examples may be powered by internal batteries, which may be incorporated into the ultrasonic signal generator unit 10 or into the activation unit 2.

In general, the components of the system are preferably portable and are more
10 preferably hand-held. The components may be wireless, rechargeable, reusable and recyclable. Any external cable 12, 14 for conveying power or signals may be coupled through a slip ring to allow free rotation of the cable 12, 14 and to avoid entanglement with the wire 4.

15 The diameter of the distal section of the wire 4 determines the flexibility of that distal section and its ability easily to conform to the shape of the anatomy through which it is intended to pass. For example, for certain Nitinol's with particular thermal transition temperatures, a distal section of an appropriate length and with a diameter of, for example, 0.005" to 0.007" combines appropriate flexibility with the ability to excavate
20 occlusive material in a tortuous (pedal or coronary) anatomy.

When using ultrasonic energy to excite the wire 4, it is desirable to optimise displacement amplitude in and around the distal tip of the wire to excavate and cross a lesion. Conversely, it is desirable to minimise displacement or movement of the
25 proximal end portion of the wire 4, which is outside the patient's body and part of which may hang freely from the proximal side of the activation unit 2. To achieve this, the distal length of the wire 4 from the distal tip to where the activation unit 2 is coupled to the wire 4 should be an odd multiple of a quarter wavelength of the ultrasonic wave. This creates a standing wave in the wire with a vibrating antinode at the distal tip,
30 hence maximising the amplitude of vibration at the distal tip.

With reference now also to Figure 2, the wire 4 includes regions where the geometry tapers to effect a change in diameter. Specifically, the wire 4 shown in Figure 2

comprises a substantially straight proximal section 16 and a substantially straight distal tip section 18 providing an excavating part for crossing a lesion. The distal section 18 is narrower than the proximal section 16 and can be tapered or can be uniform in diameter along its length.

5

The distal section 18 is joined to the proximal section 16 by a distally tapering transition 20. The proximal section 16, the distal section 18 and the transition 20 are in mutual coaxial alignment along a central longitudinal axis of the wire 4, albeit substantially flexible to be bent along their length.

10

The purpose of the tapered transition 20 is to provide gain and to sustain the transmission of ultrasonic energy through the wire 4. For the purpose of amplification, the change in the cross-sectional area represents a level of gain in both lateral and longitudinal displacement amplitudes in the wire 4. The length and the diameter of the distal section 18 will determine the mode and magnitude of displacement in axial and radial directions. The transition 20 will also affect how a lateral mode of displacement may be established in the distal section 18 of the wire.

15

As with all endovascular wires, a balance is required between flexibility expressed as 'trackability' and rigidity expressed as 'pushability' or 'steerability'. As noted previously, pushability requires longitudinal, columnar stiffness whereas steerability requires torsional stiffness. However, unlike passive wires, the wire 4 must also be able to transmit ultrasonic energy to the distal section 18 to assist in crossing lesions. In this way, the wire 4 functions as an excavator, not just at its tip but also along part of its length. In particular, the distal section 18 acts radially as a lateral excavation device for opening an aperture in a lesion within a blood vessel. The wire 4 may also have distal portions shaped to amplify radial excavation.

20

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As the goal of the activated wire 4 is to cross through a lesion, its dimensions are optimised with the purpose of excavating as large an aperture as possible for a given input. Specifically, the distal section 18 of the wire 4, once activated with ultrasonic energy as shown in Figure 2, moves in a primary longitudinal mode, moving in and out, and also in a radial direction that maps out and excavates a greater volume at the

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distal end through lateral movement or radial displacement along the wire 4. The distal section 18 of the wire 4 is also seen to move through lateral and undulating movements at or near the drive frequency under the resonant wave and secondary modes of differential harmonics, dependent on the activating frequency, the length of the distal section 18 and the tortuosity of the anatomy. These waveforms may interfere with each other and be more or less effective in excavating material at different moments.

Figures 3a and 3b illustrate one of the reasons for these complex movements of the distal section 18 when the wire 4 is activated. Figure 3a represents first, second, third and fourth harmonic waveforms 22A, 22B, 22C and 22D. It will be noted that the wavelength of each of the second, third and fourth subharmonic waveforms 22B, 22C and 22D is half that of the preceding waveform. Figure 3b represents complex waveforms 24A, 24B, 24C generated from combinations or superpositions of the subharmonic waveforms 22B, 22C and 22D with the harmonic waveform 22A of Figure 3a.

Where the distal section 18 of the wire 4 emerges from a surrounding sheath or catheter 26 as shown in Figure 4 of the drawings, additional lower-frequency lateral vibrations may arise. Freedom of movement enables the lateral component to be expressed and some component of movement may arise from a cantilever effect. In this respect, Figure 4 shows how sleeving the wire 4 in this way leaves a desired distal length free to oscillate laterally as shown. The distal extent of sleeving, and hence the length of the free end of the wire 4, controls excavation by the distal section 18 of the wire 4. Sleeving or jacketing the wire 4 up to a resonant or harmonic length, so that the distal end of the catheter 26 substantially coincides with a resonant or harmonic length, allows the wire 4 to excavate a larger aperture.

Optionally, the catheter 26 and/or the wire 4 can be moved longitudinally relative to each other in distal and proximal directions as shown, for example by turning a thumbwheel on the activation unit 2 that acts on an outer sleeve of the catheter 26. The behaviour of the wire 4 can also be influenced by adjusting radial clearance between the catheter 26 and the wire 4 or by applying radially inward force from the

catheter 26 around the wire 4 as also shown schematically in Figure 4. Squeezing or forceful radial constraint of the wire using a collar such as a balloon has a variable effect depending on the frequency at the time as well as the relative location of the acoustic source and where it is coupled to the wire.

5

The diameters of the various sections 16, 18, 20 of the wire 4 are chosen for an optimal balance between pushability and trackability, in addition to being able to allow follow-on devices of standard dimensions to use the wire 4 as a guidewire. By way of example, the proximal section 16 may have a diameter of 0.43mm and the distal
10 section 18 may have a diameter of 0.18mm or 0.25mm. The taper in the intermediate transition 20 is slight and so is greatly exaggerated in Figure 2. The transition 20 may extend over a multiple of λ in length or a fraction of λ in length, that fraction preferably having with a numerator of 1 and an even denominator - for example in the sequence 1/2, 1/4, 1/8... - whereas the distal section 18 may have a length of $\lambda/2$ or a multiple of
15 $\lambda/2$ or a fraction of $\lambda/2$ such as $\lambda/4$. The optimal lengths we have found for the materials being considered for the sections 18 and 20 are λ , $\lambda/2$ and potentially $\lambda/4$ at lower sub harmonics and for fine wires.

The overall geometry of the wire 4 including its nominal diameter and length and the
20 driving frequency of the system are determined by the characteristic speed of sound in the material of the wire. This characteristic is a function of the properties of that material and its geometry. The chosen frequency will produce harmonics along the length of the wire and the loading of the tip of the wire 4 will assist in establishing standing waves. The system may produce lateral and longitudinal displacements over
25 a range of frequencies away from that of the drive frequency, often occurring at sub-harmonics of the frequency in the distal section 18.

In one example, which does not preclude other dimensions, a wire 4 with a core cross section diameter of 0.43 mm defining the proximal section 16 has a tapered transition
30 section 20 optimally located to transition to a distal section 18 of 0.18 mm in diameter. The lengths of each section 16, 18, 20 of the wire 4 can be chosen to have a longitudinal resonant mode at or near the driving frequency, such as 40kHz, with strong sub-harmonics at or near 20kHz, 10kHz or others. Through appropriate design,

there are neighbouring lateral modes near 40khz and 20khz or others. There may be amplification across the tapered transition 20 by a factor of approximately 2.4 or other suitable value.

- 5 As a result, through appropriate selection of material, geometry and distal design features, desirable lateral modes will be energised as shown in Figure 2 even when the wire 4 is driven with longitudinal vibrations. In unison, both the longitudinal and lateral vibrations contribute to excavation of a lesion and result in the wire 4 opening an aperture or lumen in the lesion whose internal diameter is substantially greater than
10 the diameter of the wire 4.

Thus, when activated, the wire 4 serves as an excavation tool that tunnels its way by excavating material distal to the tip 18 of the wire 4 by virtue of longitudinal movement of the wire 4 and then through the offset translation or lateral motion of the wire 4
15 within the vasculature, which provides a lateral offset that opens up the diameter of the tunnel. Consequently, the wire 4 abrades the inner surface of the occlusion not just at its distal tip but also along some of its length extending proximally from the distal tip and forms a wider aperture for the passage of follow-on therapeutic devices over the wire 4. This effect is shown in Figures 5 to 8 of the drawings.

20 Figure 5 shows how the distal section 18 of the wire 4 may excavate an aperture 28 in the lesion 30 whose diameter is greater than the diameter of the wire 4 and so create a larger lumen through which therapies may be introduced to the lesion 30. The active wire 4 performs both longitudinal, axial or directional excavation as well as radial,
25 lateral or orbital excavation through orbiting of the wire 4 out of the axial plane of the wire 4 at different harmonics in a consistent, monotonic manner.

The wire 4 can be navigated along a vessel 32 to the lesion 30 in an active or passive mode. Once activated and brought into contact with the lesion 30, the wire 4 moves
30 from a 'fixed to free' state to a 'fixed to fixed' state, which to some extent attenuates the expressed amplitude in the wire 4. As the wire 4 passes through the lesion 30, subharmonic displacements are expressed and then as the wire 4 returns to a 'fixed to free' state, lateral subharmonic components are expressed to excavate the larger

aperture 28. Thus, lateral oscillation of the wire 4 carves out a channel through the lesion 30 in the lumen of the vessel 32.

Figures 6, 7 and 8 exemplify how the ability to alter the relative longitudinal position of the wire 4 and the catheter 26 can be exploited to affect the lateral motion of the distal end of the wire 4, thereby influencing secondary or lateral excavation, burrowing or tunnelling of the lesion 30 by the wire 4 within the lesion 30. In particular, Figures 6, 7 and 8 show, schematically, how the distal end of the wire 4 firstly penetrates the lesion 30, as shown in Figure 6, to create a longitudinal aperture 28 and then, with lateral oscillation of the wire 4 optimised, widens the aperture 28 to create a lumen of the desired diameter as shown in Figures 7 and 8.

When a sufficient free end length of the wire 4 extends distally beyond the lesion 30, lateral oscillation in that free end portion begins lateral excavation of the distal segment of the lesion 30 as shown in Figure 7. Then, drawing the activated wire 4 back proximally through the lesion 30 extends and widens the aperture 28 as shown in Figure 8, aided by lateral oscillation being optimised in the portion of the wire 4 between the catheter 26 and the lesion 30. If required, the activated wire 4 can then be pushed distally back through the lesion 30 to widen the aperture 28 further.

Referring back to Figures 2 to 8, it will be apparent that the behaviour of the active wire 4, and particularly its distal tip section 18, will change as the wire 4 is influenced by its changing surroundings in use within the anatomy. Thus, the behaviour of the wire 4 will depend upon the position of the distal tip section 18 in the anatomy, the medium in which the distal tip section 18 moves, and especially the materials and structures with which the distal tip section 18 comes into contact. These behaviours, and changes between them, will be expressed in terms of wavelength, frequency, amplitude and the expression of subharmonic and complex waveforms.

The invention embodies a principle, which is that these characteristics of the behaviour of an active wire 4 produce distinctive acoustic emissions that can be detected and analysed to determine that behaviour and thereby to infer the factors that produce that behaviour. Thus, it is possible to use an acoustic signature to infer information such as

the medium in which the distal tip section 18 is moving and the materials and structures with which the distal tip section 18 is in contact.

To illustrate this principle, Figure 9 shows an acoustic signature of an active wire 4 before contact with a lesion 30, on the left, and during contact with a lesion 30, on the right. Two acoustic signatures are shown on the right of Figure 9: one from an acoustic sensor positioned distally, close to the active tip of the wire 4 and the other from an acoustic sensor positioned proximally, for example in or adjacent to an activation unit 2. The acoustic signature is plotted as frequency on the vertical axis against time on the horizontal axis. In this example, the lesion 30 was represented by a sample of calcium carbonate in the form of chalk. The wire 4 was driven at a frequency of 40kHz.

It will be apparent that before contact with the lesion 30, as shown on the left of Figure 9, the wire 4 predominantly expresses vibrations around the sub-harmonic of 20kHz. Conversely, during contact with the lesion 30 as shown on the right of Figure 9, the wire 4 begins to express vibrations at various subharmonic frequencies below 20kHz, as marked by the ellipse A. The acoustic signature therefore reflects that the wire 4 is now in the process of crossing through the lesion 30. Moreover, aspects of the acoustic signature, when analysed and compared with known signatures, can characterise the lesion 30 itself. For example, the onset of cavitation is typically marked by an increase in broadband noise.

Figure 10 illustrates the components and elements of a system 34 for detecting and acting on acoustic feedback from the active wire 4. Figure 10 also shows the flow of data through the system, including communications. A controller 36, which may be in the housing of the activation unit 2, controls an ultrasonic generator 38 to generate a signal that is converted to ultrasonic energy by a transducer 40. The ultrasonic energy is fed via a coupling 42 such as the aforementioned collet and an optional acoustic horn to the active wire 4 that navigates the vasculature and crosses a blockage such as a CTO.

Acoustic feedback from the active wire 4 is received by one or more acoustic sensors 44 such as microphones or other transducers, amplified by an amplifier 46 and filtered

by a series of bandpass filters 48 before undergoing analog-to-digital conversion 50 to generate feedback data that is sent to a processor 52. The controller 36 controls a preferably wireless communications system 54, for example using a Wi-Fi network or a Bluetooth connection, to receive data from the processor 52 and to communicate that data to local storage 56 and/or to the cloud 58. Figure 10 also shows a means for providing feedback to a user, such as the aforementioned display 60 and/or a haptic feedback system.

The system 62 shown in Figure 11 is a refinement of the system 34 of Figure 10. Like numerals are used for like features. In the system 62 of Figure 11, non-acoustic feedback is obtained from a second, additional source, namely an electrical feedback receiver 64. Signals from the electrical feedback receiver 64 are amplified by an amplifier 46 and filtered by bandpass filters 48 before undergoing analog-to-digital conversion 50 to generate additional, auxiliary feedback data that is sent to the processor 52.

The electrical feedback receiver 64 may, for example, detect changes in impedance in the transducer 40 that drives the wire 4, those changes being attributed to changing losses in the system as the wire 4 is damped or becomes more or less constrained. For example, increased damping lowers the Q factor of the system.

Q factor can be measured as shown in Figure 12. The upper trace in Figure 12 shows voltage applied by the ultrasonic generator 38 to the transducer 40. The lower trace shows current through the transducer, as measured by the electrical feedback receiver 64. When the voltage signal is stopped abruptly, the system continues to resonate for a length of time proportional to Q. By curve-fitting an exponential decay function to the current signal, the processor 52 may derive a value for Q and hence damping. This value is influenced by the nature of the lesion 30.

Characterisation of impedance changes may involve separating out differences based on location or dynamic variations and comparison of variations in voltage, current and phase angle between different times. Superimposition of data representing this electrical response with data representing the corresponding acoustic response at a

given point in time can be used to analyse and describe the characteristics of a vessel 32, its lumen and any lesion 30 more accurately.

Similarly, it would be possible to employ two or more acoustic sensors 44 at different positions in the system or relative to a lesion 30 to provide additional acoustic data to corroborate and confirm the measured characteristics of a vessel 32, its lumen and any lesion 30. Figures 12 to 20 show various possibilities in this respect, it being understood that one, two or more acoustic sensors 44 could be employed at or near any of the positions described and illustrated.

In general, acoustic sensors 44 can be placed at any of various positions in the system. Different sensor positions will produce different acoustic signatures. Locating multiple acoustic sensors around the transducer 40 and an associated collet can produce different relative patterns of characteristic spectra that can be subject to interrogation for association with different features. An external acoustic sensor could also integrate lighting such as an LED to provide visual feedback in respect of the performance of the system. This could be interpolated from changes in the acoustic signature or an overlay of the acoustic response over the electronic or electrical response of the system.

Turning next, then, to Figure 13, this shows an ultrasonic activation unit 2 through which a wire 4 extends longitudinally. In this example, the activation unit 2 is powered externally and is optionally supplied with an ultrasonic signal through a cable 12.

Figure 13 shows that the activation unit 2 contains an ultrasonic transducer 40 and a distally tapering acoustic horn 66 attached to the distal face of the transducer 40. A collet 68 couples the wire 4 to the distal end of the horn 66. The transducer 40, the horn 66 and the collet 68 are penetrated by a central lumen to allow for the through-passage of the wire 4. The wire 4 thereby extends though the full length of the activation unit 2 to emerge proximally from the activation unit 2. The activation unit 2 can be moved along the wire 4 and then can be coupled to transmit ultrasonic energy to the wire 4 at any of a various locations along the wire 4. In other arrangements, the

wire 4 could instead emerge from the activation unit 2 laterally at a proximal location with respect to the collet 68.

5 In Figure 13, the catheter 26 that surrounds and supports the wire 4 can be coupled to a distal region of the wire 4. In this example, coupling is effected by a distal annular balloon 70 within the catheter 26, which expands into the distal inner lumen of the catheter 26 around the wire 4. The balloon 36 may be inflated via an inflation port 38 on the catheter 26. Additional ports and lumens may be included in the catheter 26, for example to provide for aspiration of embolus or of fragments or particles generated
10 during excavation.

Optionally, the balloon 70 or other coupling may be configured to grip the wire 4, applying inward clamping force to the distal portion of the wire 4. In this way, ultrasonic energy could be coupled through waveguide elements of the catheter 26, transmitting
15 electromechanical energy from the catheter 26 through to the distal tip region of the wire 4 via the coupling through the balloon 70.

The proximal end of the catheter 26 is coupled to the transducer 40 by an adapter element 72. The proximal end of the adapter element 72 abuts the distal end of the
20 horn 66 around the collet 68 and is thereby coupled to the transducer 40 to receive ultrasonic energy. In principle, the adapter element 72 can facilitate transmission of energy from the transducer 40 in any of three modes of operation, namely: the wire 4 being activated independently; the catheter 26 being activated independently; or the catheter 26 and the wire 4 being activated simultaneously.

25 Acoustic sensors 44 may be placed on the outside of the activation unit 2, in the body of the activation unit 2 or on different sections of the catheter 26. Differential placement of acoustic sensors can provide for distinctive interference and characteristic patterns in the acoustic spectra.

30 In the example shown in Figure 13, acoustic sensors 44 are disposed on the adapter element 72 adjacent to the collet 68 and proximally relative to the collet 68, here being mounted on the housing of the activation unit 2.

In addition to locating an acoustic sensor 44 in the housing or casing of the activation unit 2, an option would be to house the acoustic sensor 44 outside the housing, for example along a catheter 26. In this respect, Figure 14 shows the exterior of an activation unit 2 with a catheter 26 extending distally from the unit 2. Here, various acoustic sensors 44 are disposed distally relative to the collet 68. One acoustic sensor 44 is positioned at the distal end of the unit 2, specifically on or in the toggle 8 that acts on the collet 68 within. Two more acoustic sensors 44 are shown on the catheter 26, one near the proximal end and the other near the distal end of the catheter 26.

Figure 15 shows a catheter 26 and the wire 4 within, separately from the activation unit 2. An acoustic sensor 44 is shown near the distal end of the catheter 26. Thus, the catheter 26 provides a means to introduce an acoustic sensor intravascularly.

Incorporation of an acoustic sensor 44 in a catheter 26 and its introduction over a wire 4 to the location of a blockage or the distal end of the wire 4 provides a way of measuring the manner of the interaction between the wire 4, the blood and any acoustic effects created by the interaction between the wire 4 and the vessel 32 or any blockage 30 within it. As noted previously, it is possible to adjust and control the distance by which the wire 4 extends beyond a microcatheter sleeve, hence the length of wire 4 that is exposed into the lumen of the vessel 32. This adds additional control over how the wire 4 is excited and how acoustic emissions may be created from within the vessel 32.

Housing the acoustic sensor 44 in or on the catheter 26 makes the entire system more efficient. The proximity of the wire 4 to the acoustic sensor 44 and the ability to capture emissions from the catheter 26 increase the reliability of acoustic sensing and reduce variability that might otherwise arise from variations in the tissues while being more sensitive to the variations that might arise in the patterns of acoustic emissions that would arise from interaction between the wire 4 and the catheter 26.

Figure 16 shows that a sensor could even be applied to the wire 4 itself, for example in the form of an electrical or optical strain gauge 74. In this example, the strain gauge is

affixed to the proximal section 16 of the wire 4, close to the tapered transition 20 that leads to the thinner distal section 18 of the wire 4. Such a sensor could serve as an acoustic sensor or could more directly determine the behaviour of the wire 4 from strains experienced by the wire 4 when activated. For example, integrating an acoustic emitter or a micro array on the surface of the wire 4 can provide a means to optimise the emissions in specific ranges of interest. Signals from the strain gauge 74 could further corroborate data received from acoustic sensors 44, in addition to or instead of non-acoustic feedback from an electrical feedback receiver 64 such as that shown in Figure 11.

10

Figures 17 to 21 show various ways of positioning acoustic sensors on or in a patient's body, exemplified here by the patient's leg 76. In each case, an active wire 4 has been advanced through the patient's vasculature and into a vessel 32 blocked by a lesion 30, shown here in the lower leg 76. The distal tip of the wire 4 has engaged the lesion 30 and is about to be activated with ultrasonic energy to begin excavating a channel through the lesion 30.

15

Figures 16 to 19 show extra-corporeal positioning of acoustic sensors 44. Positioning acoustic sensors 44 externally of the body allows for the interrogation of acoustic emissions from the wire 4 and the vessel 32 through the surrounding tissues.

20

In Figure 16, the acoustic sensor 44 is integrated into a surgical patch or embodied in a surgical band or the like to bring the acoustic sensor 44 into close proximity to the tissue. The acoustic sensor 44 is located close to the area of interest, be that along the length of the vessel 32 or otherwise in a region of the patient's body affected by the disease of the vessel 32. Alternatively, an ultrasonic probe could serve as an acoustic sensor 44 to detect acoustic emissions as shown in Figure 17 as a stationary unit and in Figure 18 as a hand-held unit that can be swept over the patient's skin close to the lesion 30. The data from the probe can then be used directly to interpolate the location and proximity to the lesion 30 and the manner in which movement of the wire is disturbed, characterising whatever blockages may be present.

25

30

Figures 20 and 21 show intra-corporeal positioning of acoustic sensors 44 on probes 78 positioned internally of the body. This allows the acoustic sensors 44 to be introduced through the tissues into the compartment surrounding the vessel 32, getting closer to the region of the vessel 32 where the lesion 30 is being treated or the region of the vessel 32 to be assessed for diseased medial tissue.

Surgical insertion into the tissue of a probe 78 carrying an acoustic sensor 44 at its distal tip provides a way of getting closer to the region of the lesion 30 or the vessel 32. This enables detection of acoustic emissions from the interaction between the wire 4 and its surroundings and its transmission through the vessel 32, without losses and aberrations to the acoustic spectra that could arise from passage through a significant thickness of muscle and skin.

Figures 22 to 27 show acoustic signals emitted, and especially how specific frequencies are expressed, as an active wire crosses through different materials. The materials chosen were chalk (Figures 22 and 23), BegoStone (Figures 24 and 25) and water (Figures 26 and 27). BegoStone (registered trade mark) is a commercially available super-hard plaster originally developed for dental applications. In each case, the signals were obtained with the wire and samples in a bath of water, using a hydrophone positioned near the distal tip of the wire. The signals were captured on an oscilloscope and were not post-processed.

For each material, the acoustic signal is shown across a wide frequency range of up to 125kHz (in Figures 22, 24 and 26) and in a narrower low (audible) resonance range of up to 10kHz (in Figures 23, 25 and 27). The lower range is taken from the larger data set, itself a sample in time.

Nominally, the system is designed to drive at 40kHz but with the wire 4 and collet 68 in place, the system actually resonates at (and therefore the electronics drive the system at) a slightly different frequency of about 38kHz. Consequently, if all other acoustic influences were subtracted, it would be expected only to see a line at a frequency of around 38kHz. Such a line is evident and can also be measured electronically by the electrical feedback receiver 64, as is a line at 40kHz at which the wire 4 is designed to

resonate. However, several additional emitted resonant frequencies are observed as features appearing at different frequencies, notably at the harmonics of the drive frequency of the system, but also at others. Thus, in addition to the line at 38kHz, high amplitudes of acoustic emissions can be seen at the harmonics 8kHz, 19kHz and
5 76kHz and at even higher frequencies such as 114kHz. Other characteristic features establish themselves around and between these harmonics of the drive frequency. In the lower range shown in Figures 23, 25 and 27, characteristic emissions are also expressed at different frequencies.

10 To recap, preferred embodiments of the invention comprise an ultrasonic generator, a transducer, an active elongate element such as a wire and/or catheter, a signal processing system and a controller. The controller monitors the sensor data output of the signal processing system, which includes both electrical feedback signals and acoustic signals from a microphone.

15

The sensor data, whether in a raw or processed form, can provide real-time information to the controller for autonomous and adaptive control of the system. The sensor data can also provide real-time or follow-up information to a user about the condition of vessels or cavities in the body, such as the nature of an obstruction being
20 crossed by the active element. The sensor data may also be transmitted to secondary systems via wired or wireless interfaces for further processing.

In an embodiment shown in Figure 28, a vibration or acoustic sensor such as a surface microphone 80 is placed externally to the patient's body. For example, a piezoelectric
25 contact microphone 80 may be adhered to the patient's skin in a position best suited to detect emissions from the active element. The active element is exemplified here as a wire 82 protruding distally from within a surrounding catheter 84 and being driven by a handheld activation unit 86, external to the body 88, to excavate an opening 90 in an obstruction 92 blocking a blood vessel 94.

30

The controller 96 shown in Figure 28 comprises a processor 98, a user interface 100 and an integrated data acquisition system 102. The controller 96 is shown here as a unit separate from the activation unit 86 but could instead be incorporated into the

activation unit 86. The microphone 80 may be connected to the activation unit 86 or to the controller 96 via a wired or wireless signal-transmitting connection to convey acoustic emission data 104 to the controller 96. The data acquisition system 102 is capable of capturing both electrical performance data from the activation unit 86 and
5 acoustic signals from the microphone 80 at an appropriate resolution and data sampling rate.

In other embodiments, a microphone 80, hydrophone or other vibration or acoustic sensor may be positioned elsewhere, for example by being mounted, integrated with
10 or otherwise located on or near the distal tip of a supporting catheter 84. In that case, the microphone 80 is most conveniently connected to the activation unit 86 or to the controller 96 via a wired signal-transmitting connection extending along the catheter 84, although a wireless connection would also be possible in principle. The catheter 84 supporting the microphone 80 may house an active wire 82 or may be separate from
15 an active wire/catheter system.

The microphone 80 or other vibration or acoustic sensors may be designed to operate in the audible acoustic range, hence from 20Hz to 20kHz, and/or up to 250kHz or in any other suitable range of frequencies.

20 In an embodiment of a processing algorithm of the invention, exemplified in Figure 29, the acoustic emission data signal 104 acquired from the microphone 80 is converted by the data acquisition system 102 from the time domain to the frequency domain. Conversion from the time domain to the frequency domain may be effected by a fast
25 Fourier transform (FFT), power spectrum or other known method. The data acquisition system 102 also acquires electrical performance data 106 such as transducer voltage and current acquired from the transducer of the activation unit 86.

Frequency domain data at 108 and power spectrum data at 110 are evaluated to
30 determine characterising features such as peaks in the frequency or power spectrum at 112 and powers in frequency band ranges at 114. Once determined, those features are compared with threshold parameters evaluated through extensive testing to

determine interaction between the active element and the patient's tissue, which may include occlusions in vessels or cavities in the patient's body.

Peaks detected at 112, powers in a range of frequency bands at 114 and the electrical
5 performance data 106 are combined to form a feature dataset at 116. The features in
the dataset 116 can then be interpreted by a pre-trained machine learning decision
algorithm at 118 for classification. Specifically, such an algorithm 118 is trained
previously on a supervised dataset derived from extensive test runs and data with
classification labels. The feature dataset can expand over time as new information-
10 bearing features are discovered and added.

Characterising features of the processed data are not limited to frequency peaks 112
and bands 114. For example, a full frequency spectrum can serve as a characterising
feature in itself. In this respect, a full frequency spectrum may contain information that
15 is not human-observable and requires a machine learning algorithm to extract. For
example, sequenced images of spectrograms sampled at regular intervals could be
subjected to a deep learning neural net or similar image processing technique to
identify and classify images and hence, for example, to identify and characterise
stages in a wire crossing process.

20 The system described adopts a sensor fusion approach by combining electrical and
acoustic sensor data while driving the transducer of the activation unit 86 in a 'normal'
mode in which the wire 82 will excavate an opening 90 in the obstruction 92.
Combining data from two different sources in this way provides a richer dataset 116,
25 with multiple features that may be extracted simultaneously. This allows for more
sophisticated analysis, while also improving confidence in the measurement results.

In 'normal' mode excitation, the system merges electrical feedback data with acoustic
emission data with the goal of analysing and determining device performance and
30 inferring interactions between wire 82 or other active element and the tissue. This is
done by interrogating extracted features such as peaks and maxima/minima values in
the measurand. Such interactions may include, but are not limited to, wire-tissue
contact, characterising tissue composition, wire emergence distal to the obstruction 92,
and the resulting profile of the opening 90 after crossing through the obstruction 92.

Figure 30 shows an FFT plot of an acoustic emission signal 104 of an activated wire 82 captured via an external microphone 80. The peaks detected are related to the driving frequency, while other harmonics are indicative of the wire configuration and the locations and amplitudes of peaks, indicated by arrows, change in response to changing wire configuration. For example, as a greater length of wire 82 emerges from the distal end of the catheter 84, peak locations will change in response as shown by the arrows in Figure 30.

Figure 31 shows how wire tissue contact events, also indicated here by arrows, can be detected by monitoring power in a range of power or frequency bands.

Figure 32 shows another example in which the acoustic emission data 104 from a microphone 80 is converted to the frequency domain. Here, the power in a particular band (in this case, from 600Hz to 800Hz) is extracted, and the total power is plotted over time as the system crosses a 3mm lesion.

The example shown in Figure 32 reflects experimental work that demonstrates how it is possible to assess the diameter of an aperture or opening 90 produced in an obstruction 92 and the composition or 'tone' of the surrounding vessel 94. This is done by advancing the wire 82 a certain distance distally beyond the obstruction 92 which, for a given wire profile, establishes lateral displacement of the wire 82 as illustrated in Figures 6 to 8. Then, interrogation of variations in the power in characteristic power band response or frequency spectra enables the diameter of the opening 90 to be estimated. Real-time monitoring and processing of fluctuations or variations of the primary electrical and acoustic signals by digital signal processing or image processing using various mathematical treatments can also be used to determine the diameter and mechanical tone of the vessel 94.

More specifically, advancing the distal tip of the wire 82 to distances beyond the obstruction 92 allows for the expression of lateral modes of displacement of the wire 82 at characteristic subharmonics. This lateral, hypotrochoidal, displacement set up in the wire 82, determined by its geometry, opens up an aperture or opening 90,

producing a tunnel of a specific diameter extending longitudinally through the obstruction 92.

5 The power and slope of the electrical and acoustic response in the system is characteristic of how the wire 82 interacts with the materials or structures with which it comes into contact, and thus of the nature of those materials and structures. Mathematical treatment of the data allows characterisation of the geometry and composition of the obstruction 92 and of the vessel 94 through which the wire 82 is passed.

10

Line 120 in Figure 32 shows the wire 82 in a simple active mode, with ultrasonic energy producing largely axial vibration of the distal tip but not yet in contact with or therefore ablating any material of the obstruction 92. Conversely, line 122 in Figure 32 shows ablation of the obstruction 92 with radial vibration of the distal tip after contact
15 with the obstruction 92.

Line 124 in Figure 32 shows the slope of decay in power as the material of the obstruction 92 is ablated by the wire 82 and the opening 90 in the obstruction 92 widens out. Line 126 in Figure 32 corresponds to line 124 but shows a situation in
20 which the wire 82 has been advanced distally to a greater extent than in line 124 ('y' mm being greater than 'x' mm) and excavates a tunnel-like opening 90 of greater diameter through the obstruction 92.

Various other characterising features that can be observed in this example are
25 annotated in Figure 32, namely:

- a general increase in broadband noise when the ultrasonic generator starts to apply power to the transducer of the activation unit 86;
- 30 a significant increase in the band power when the wire 82 makes contact with an obstruction 92 or other tissue;

a significant decrease in the band power when the wire 82 crosses through the obstruction 92; and

5 a gradual decay in the band power as the lateral motion of the wire 82 continues to widen the opening 90 or lumen through the obstruction 92.

The noise floor in Figure 32 is due to background noise from the environment. The background noise can be measured while the ultrasonic generator is off, and later subtracted from all subsequent measurements.

10

The example shown in Figure 32 uses only one extracted characterising feature. In other examples, features extracted from other frequency ranges could be used independently or combined with a range of identified features such as locations of frequency peaks, amplitudes of peaks or powers in a range of bands, or how any of
15 these features change over time or relative to some baseline value.

Another aspect of the system is the ability to multiplex or switch between 'normal' and 'probe' modes. In this respect, the goal of characterising tissue composition is achieved by a system identification approach in which statistical methods build
20 mathematical models of dynamic systems from measured data. More specifically, an input-output system identification approach can be adopted because it is possible to control the stimulus to the system of the invention. In other words, extraction of characterising features can be eased by selecting a particular type of stimulus that is designed to create a particular type of response.

25

During activation, a vibrating active element such as an endovascular wire 82 interacts with fluids and tissues in and around the vasculature nearby. The vibrating wire 82 is, itself, the source of acoustic energy as its movement within the body 88 results in the generation of acoustic emissions and reflections. During operation, the dynamics of
30 the transducer-wire system also determine the exact nature of the electrical feedback signals.

In the 'probe' mode, deliberate manipulation of the input stimulus allows for the creation of more explicit features that can be extracted and exported for use in characterising or classifying the structures or materials with which the wire 82 is interacting. One example of this approach has already been described above with
5 reference to Figure 12, namely measurement of the Q factor, which may be influenced by the nature of an obstruction 92 with which the wire 82 is in contact. It will be recalled that when an input voltage signal ceases, the system continues to resonate for a length of time proportional to Q. By curve-fitting an exponential decay function, the controller 96 may derive a value for Q to determine the damping effect of the
10 obstruction 92 and hence to characterise the nature of the obstruction 92 itself.

The controller 96 can alternate between the 'normal' and 'probe' modes periodically without significantly affecting the primary function of the device, in particular to cross an obstruction 92. This ability to multiplex different modes and to search for different
15 characterising features allows for a richer set of data to characterise the materials or structures in contact with or around the active wire 82.

It is possible deliberately to change the nature of the stimulus signal applied to the transducer of the activation unit 86. In the general case (and as shown in Figures 21 to
20 26), the stimulus applied is a continuous sine wave of one frequency. However, the use of other waveforms, such as pulsed, multi-tone, chirp or noise waveforms, allows different characteristics to be extracted from the corresponding response signals. This exploits the ability of the controller 96 to correlate the input stimulus with the output responses.

25

Figure 33 shows, by way of example, a spectrogram of an electrical current signal as the amplitude of the driving current is varied. This is taken from a paper "*Self-Sensing Ultrasound Transducer for Cavitation Detection*" by Bornmann *et al.* delivered at the 2014 IEEE International Ultrasonics Symposium Proceedings. Broadband changes
30 and/or changes in distinct frequencies can indicate different features of the system, such as the onset of cavitation.

Figure 34 shows another example in which complex impedance of the transducer of the activation unit 86 is plotted against frequency. This response can be measured using various different stimuli, including a frequency sweep of a single tone, a chirp signal, or broadband noise. In this example, the parasitic resonance just below 43kHz
5 is an indication of an extra vibration mode in the system, in this case caused by a short length of unsupported wire 82 extending distally beyond the support catheter 84.

Combining these examples with the example shown in Figure 32, it will be apparent that the combination of electrical and acoustic data allows for more precise
10 characterisation of the opening 90 in an obstruction 92. This information could be used in various ways, for example to inform the user of the diameter of the opening 90 or to recommend that the support catheter 84 is retracted or advanced to modify the activity of the distally-protruding wire 82 so as to create the opening 90 that is required.

15 As the feature dataset 116 grows, the correlation between tissue characteristics and data features becomes more complex. This classification problem is apt for the application of machine learning techniques including feature learning techniques. Thus, another aspect of the system is to allow for the data to be processed in any type of machine learning model, including artificial neural networks.

20

A machine learning model can be trained in advance using a standard set of training data, and the algorithms of the model can be programmed accordingly. However, the system also allows the training data to be updated over time. For example, if a particular device is used successfully to cross an obstruction 92, the user has the
25 ability to upload relevant data to a server. The user also has the option of manually entering and uploading metadata about the procedure, for example to confirm tissue classification and so on.

Following independent validation, this uploaded data and metadata may then be
30 incorporated into the training data, allowing for unsupervised learning using unlabelled data, supervised learning using labelled data, or semi-supervised learning using a mix of labelled and unlabelled data. The updated training data allows for the identification of previously unrecognised features, and the creation of new algorithms for their

extraction. The new algorithms may then be downloaded to any device of the invention at any time.

Machine learning models of the invention may execute on any available hardware as the performance requirements demand. For example, the controller 96 can run a machine learning model locally on the device operating on a standalone basis. Alternatively, the device can transmit data to a networked local server, which provides more processing power but is located on the same computer network. Real-time feedback is still possible in this example, as is the potential to aggregate data across multiple laboratories and users within a hospital, or indeed any health facility or organisation connected by a private network. Another option is for the device to transmit data to a cloud-based service, which provides for elastic scalable performance and the potential to aggregate data across multiple hospitals, laboratories and locations. Again, real-time feedback remains possible in a cloud-based solution.

Turning finally to Figures 35 to 37, these drawings illustrate the possibility of integrating inertial sensing into a handheld activation unit 2 of the invention. The availability of inertial data representing orientation and acceleration of the activation unit 2 adds another source of non-acoustic operational feedback that can usefully enrich an operational dataset.

Figure 35 shows X, Y and Z axes about which the activation unit 2 can be turned and along which the activation unit 2 can experience accelerations when manipulated by a physician in use. Specifically, where the Y axis coincides with the longitudinal axis of the activation unit 2 held horizontally, the activation unit 2 may pitch about the horizontal X axis, roll about the horizontal Y axis and yaw about the vertical Z axis.

Figure 36 corresponds generally to Figure 13 and includes like numerals for like features but also shows an inertial measurement unit comprising inertial sensors 128 within the housing of the activation unit 2. By sensing orientation and acceleration of the activation unit 2, the inertial sensors 128 can, in real time, generate information about the precise hand movements of the physician holding the activation unit 2. For this purpose, the inertial measurement unit is apt to employ MEMS

(microelectromechanical systems) technology and can comprise inertial sensors 128 being a three-axis accelerometer for measuring linear acceleration and a three-axis gyroscope for measuring angular velocity.

5 Figure 37 corresponds generally to Figures 10 and 11 and also includes like numerals for like features but also comprises the inertial sensors 128 of the inertial measurement unit shown in Figure 36. Thus, briefly to recap, the system 130 shown in Figure 37 comprises a controller 36, which may be in the housing of the activation unit 2. The controller 36 controls an ultrasonic generator 38 to generate a signal that is
10 converted to ultrasonic energy by a transducer 40. The ultrasonic energy is fed via a coupling 42 to the active wire 4 that navigates the vasculature and crosses a blockage such as a CTO. Figure 37 also shows a catheter 26 that may surround the wire 4. The catheter 26 could be passive or could also be activated with ultrasonic energy by the activation unit 2.

15 Acoustic feedback from the active wire 4 is received by one or more acoustic sensors 44. In this example, acoustic sensors 44 are shown located in or on the activation unit 2, on or adjacent to the catheter 26 and/or the wire 4, and elsewhere, for example at a location distal to the activation unit 2 and inside, outside or against the patient's body
20 close to the active distal portion of the wire 4. In practice, acoustic sensors 44 can be positioned at any, some or all of those locations.

Acoustic feedback from the or each acoustic sensor 44 is amplified at 46, filtered at 48, converted to digital feedback data at 50 and sent to a processor 52. The controller 36
25 controls a communications system 54 to receive data from the processor 52 and to communicate that data to local storage 56 and/or to the cloud 58. As before, Figure 37 also shows a means for providing feedback to a user, such as the aforementioned display 60 and/or a haptic feedback system.

30 In the system 130 shown in Figure 37, non-acoustic feedback is obtained from one or more additional sources, namely an electrical feedback receiver 64 and/or inertial sensors 128 that may be located in or on the activation unit 2. Signals from the electrical feedback receiver 64 and/or the inertial sensors 128 are amplified at 46 and

filtered at 48 before undergoing analog-to-digital conversion at 50. This generates additional, auxiliary feedback data that is streamed to the processor 52, typically via a serial peripheral interface.

- 5 In this way, the processor 52 can correlate changes in other sensor signals such as electrical impedance or acoustic emissions with the motion of the activation unit 2 and hence with the motion of the active wire 4. In one example, this would facilitate identification by an algorithm of contact and break-through events as the active wire 4 encounters and crosses through a lesion. Those events would cause significant
- 10 changes in electrical or acoustic response signals that can be correlated with forward movements of the active wire 4 represented by simultaneous changes in the output of the inertial sensors 128.

- In another example, significant changes in electrical or acoustic response signals
- 15 when the active wire 4 is moved slightly backwards or proximally would indicate that the distal tip of the active wire 4 has contacted a hard material such as a calcific lesion. Conversely, if the electrical or acoustic response signals do not change significantly when the active wire 4 is moved slightly backwards or proximally, this would indicate that the distal tip of the active wire 4 is in a homogeneous fluid-filled section of a
- 20 vessel.

- Information concerning orientation and acceleration derived from the inertial sensors 128 could also be used to monitor the rate of crossing of a lesion. This information may be used to provide feedback to a physician on how well the system is operating,
- 25 and potentially to recommend to the physician that the active wire 4 should be advanced more quickly or more slowly as appropriate.

- In other potential uses, the inertial sensors 128 can be used to record all motion of the activation unit 2 and hence of the active wire 4 during a procedure. This would allow
- 30 playback subsequently in conjunction with a time-correlated sequence of events involving the active wire 4. This could be used for various purposes such as to provide feedback to a physician to improve their technique, to fine-tune machine learning

models and/or to facilitate clinical review, for example to investigate a professional negligence claim.

By detecting tactile control inputs such as single or double taps on a housing or control
5 element of the activation unit 2, accelerometers among the inertial sensors 128 could be used to control the activation unit 2. In principle, a change in orientation of the activation unit 2 could also be used as a control input to the system 130.

Many other variations are possible within the inventive concept. For example, one or
10 more acoustic sensors 44 could be disposed on a distal tube like those disclosed in our previous patent application published as WO 2021/224357. Such tubes extend distally from the activation unit 2 to protect and guide the wire 4 within, to provide strain relief and/or to apply damping force to the wire 4. They may also serve as a connector to a structure disposed distally of the activation unit 2, such as a luer fitting
15 or other entry port.

To maximise the sensitivity of the system when analysing response signals from the electrical feedback receiver 64, inertial sensors 128 and/or acoustic sensors 44, it is possible to create a 'baseline' response signal that may be subtracted later from the
20 changing response signals. The baseline is most usefully obtained when the distal tip of the wire 4 is close to a lesion 30 but not touching it. In this way, the baseline response signals encapsulate all of the underlying characteristics of the system, including the tortuosity of the vasculature through which the wire 4 extends to the lesion 30. Alternatively, the baseline may be obtained automatically, on a continuous
25 basis, and the system itself can decide when to apply a subtraction algorithm.

In an example of a workflow to acquire a baseline response signal or signals using tactile control inputs detected by inertial sensors 128 as shown in Figures 36 and 37, a user firstly positions the distal tip of the wire 4 in the vicinity of a lesion. Next, the user
30 selects an active mode on a controller of the activation unit 2 to activate the wire 4 with ultrasonic energy. That action may require the user to look away momentarily and to move the activation unit 2 slightly. The user then fine-tunes the exact positioning of the distal tip of the active wire 4 before double-tapping the housing of the activation unit 2

with one finger, while holding the activation unit 2 steady. This triggers the processor 52 to acquire the baseline response signal or signals.

Claims

1. Endovascular apparatus for determining the condition of a vessel, cavity or structure in a body, the apparatus comprising:

5

an elongate waveguide element;

10

an activation unit comprising a source of ultrasonic energy and a coupling for coupling the source to the waveguide element to activate the waveguide element, thereby transmitting ultrasonic energy from the source along the waveguide element to an active distal section of the waveguide element; and

15

a signal acquisition system that is configured to acquire feedback signals from the apparatus for interpreting the condition of the vessel, cavity or structure;

wherein the signal acquisition system comprises:

20

at least one acoustic sensor for acquiring acoustic feedback signals generated by the apparatus when the waveguide element is activated; and/or

at least one inertial sensor for acquiring information representing orientation and/or acceleration of the activation unit.

25

2. The apparatus of Claim 1, wherein the at least one acoustic sensor is mounted in or on the activation unit.

30

3. The apparatus of Claim 2, wherein the at least one acoustic sensor is mounted in longitudinal alignment with, or proximally relative to, the coupling of the activation unit.

4. The apparatus of any preceding claim, wherein the at least one acoustic sensor is mounted distally relative to the activation unit.

5. The apparatus of any preceding claim, wherein the at least one acoustic sensor is mounted on or parallel with the waveguide element.
6. The apparatus of Claim 5, wherein the at least one acoustic sensor is mounted
5 proximally or distally relative to the length of the waveguide element.
7. The apparatus of Claim 5 or Claim 6, wherein the waveguide element is, or comprises, or is surrounded by, a catheter and at least one acoustic sensor is mounted on the catheter.
- 10
8. The apparatus of Claim 5 or Claim 6, wherein the waveguide element is, or comprises, a wire and at least one acoustic sensor is mounted on the wire.
9. The apparatus of any preceding claim, wherein a strain gauge is fixed to the
15 waveguide element to acquire operational feedback signals from the wire.
10. The apparatus of Claim 9 when dependent on Claim 8, wherein the waveguide element is, or comprises, a wire and the strain gauge serves as the at least one acoustic sensor.
- 20
11. The apparatus of any preceding claim, wherein the at least one acoustic sensor is an extra-corporeal sensor arranged to lie against a part of the body.
12. The apparatus of any preceding claim, wherein the at least one acoustic sensor is
25 an intra-corporeal sensor arranged to be inserted into the body.
13. The apparatus of any preceding claim, wherein the signal acquisition system comprises at least two acoustic sensors longitudinally spaced from each other.
- 30
14. The apparatus of any preceding claim, configured to be controlled by sensing orientation and/or acceleration of the activation unit using the at least one inertial sensor of the signal acquisition system.

15. The apparatus of any preceding claim, further comprising a recorder for recording orientation and/or acceleration of the activation unit sensed by the at least one inertial sensor of the signal acquisition system during a surgical procedure.
- 5 16. The apparatus of any preceding claim, wherein the signal acquisition system further comprises at least one electronic sensor that is configured to acquire operational feedback signals representing operational parameters of the source of ultrasonic energy.
- 10 17. The apparatus of Claim 16, wherein the operational parameters are frequency and/or amplitude and/or phase of current drawn by, or voltage dropped across, the source of ultrasonic energy.
18. The apparatus of Claim 16 or Claim 17, wherein the signal acquisition system is
15 configured to monitor variations in frequency or amplitude of vibration of the waveguide element via the coupling.
19. The apparatus of any preceding claim, further comprising a signal processing system for processing feedback signals acquired by the signal acquisition system.
- 20 20. The apparatus of Claim 19, wherein the signal processing system is configured to employ numerical algorithms selected for specific types of the waveguide element.
21. The apparatus of Claim 19 or Claim 20, wherein the signal processing system is
25 configured to determine characteristics of an obstruction from the acquired feedback signals.
22. The apparatus of any of Claims 19 to 21, wherein the signal processing system is
30 configured to compare relative contributions of losses from anatomical tortuosity in navigating the active distal section to an obstruction versus losses arising from the passage of the active distal section through the obstruction.

23. The apparatus of any of Claims 19 to 22, wherein the signal processing system is configured to compare the acquired feedback signals with stored data that characterises known obstructions, and to characterise an obstruction with reference to that comparison.

5

24. The apparatus of any of Claims 19 to 23, wherein the signal processing system further comprises an output to a user interface and/or to an external data acquisition system.

10 25. The apparatus of any of Claims 19 to 24, wherein the signal processing system further comprises an input from a user interface and/or from an external data network.

26. The apparatus of any of Claims 19 to 25, wherein the signal processing system is configured to convert the acoustic feedback signals from the time domain to the
15 frequency domain.

27. The apparatus of any of Claims 19 to 26, wherein the signal processing system is configured to evaluate frequency domain data and/or power spectrum data.

20 28. The apparatus of Claim 27, wherein the signal processing system is configured to determine characterising features from peaks in the frequency domain data and/or power spectrum data.

29. The apparatus of Claim 27 or Claim 2289, wherein the signal processing system is
25 configured to determine characterising features from powers in frequency band ranges.

30. The apparatus of any of Claims 19 to 29, wherein the signal processing system is configured to determine characterising features of a full frequency spectrum of the
30 acoustic feedback signals.

31. The apparatus of Claim 30, wherein the signal processing system is configured to sample and process sequenced images of spectrograms.

32. The apparatus of any of Claims 28 to 31, wherein the signal processing system is configured to compare the characterising features with threshold parameters evaluated through prior testing.

5

33. The apparatus of any of Claims 28 to 32, wherein the signal processing system is configured to form a feature dataset by combining the characterising features with electrical performance data relating to the source of ultrasonic energy.

10 34. The apparatus of Claim 33, wherein the signal processing system is configured to subject the feature dataset to classification by a machine learning algorithm.

35. The apparatus of any of Claims 28 to 34, wherein the signal processing system is configured to assess and compare two or more of said characterising features.

15

36. The apparatus of any of Claims 19 to 35, wherein the signal processing system is configured to detect and monitor harmonics in the acoustic feedback signals indicative of configuration of the waveguide element.

20 37. The apparatus of any of Claims 19 to 36, wherein the signal processing system is configured to detect and monitor power in two or more frequency bands of the acoustic feedback signals.

25 38. The apparatus of any of Claims 19 to 37, wherein the signal processing system is configured to subtract background noise from the acoustic feedback signals.

39. The apparatus of any of Claims 19 to 38, further comprising a controller that is responsive to the signal processing system.

30 40. The apparatus of Claim 39, wherein the controller is configured to modulate excitation voltage applied to, or excitation current supplied to, the source of ultrasonic energy.

41. The apparatus of Claim 40, wherein the controller is configured to control the source of ultrasonic energy by varying frequency and/or amplitude of the excitation voltage applied to the source of ultrasonic energy.
- 5 42. The apparatus of Claim 40 or Claim 41, wherein the controller is configured to drive the frequency of the excitation voltage by employing a phase difference between the excitation voltage and the excitation current in conjunction with amplitude of the excitation voltage.
- 10 43. The apparatus of any of Claims 39 to 42, wherein the controller comprises an amplitude feedback controller and is configured to use a resonant frequency as an operating point of control.
44. The apparatus of any of Claims 39 to 43, wherein the controller is configured to
15 pulse or vary a drive signal to the source of ultrasonic energy.
45. The apparatus of any of Claims 39 to 44, wherein the controller is configured:
- 20 to monitor modulation of transmitted signals and to control the source of ultrasonic energy automatically to compensate for background energy loss encountered in the waveguide element as the active distal section approaches an obstruction; and
- 25 to distinguish the background energy loss from additional energy loss as the active distal section passes through the obstruction and to compensate for the background energy loss to sustain displacement at the active distal section.
46. The apparatus of any of Claims 39 to 45, wherein the controller is configured to
30 modify or change a control algorithm in response to variation in operational parameters of the source of ultrasonic energy arising from interaction of the active distal section with an obstruction in use.

47. The apparatus of any of Claims 39 to 46, wherein the controller is configured to multiplex or switch between operational modes, in at least one of which modes the source of ultrasonic energy is driven to optimise diagnosis of a lesion or condition.

- 5 48. The apparatus of Claim 47, wherein the controller is configured to alternate between the operational modes, in at least one of which modes the source of ultrasonic energy is driven to optimise treatment of a lesion or condition.

49. A communication system comprising the apparatus of any preceding claim in data
10 communication with a computer system that is arranged to receive data from the apparatus, to optimise and update control algorithms accordingly and to output the optimised, updated control algorithms to the apparatus.

50. The communication system of Claim 49, wherein two or more such apparatuses
15 are in data communication with the computer system, which is arranged to optimise control algorithms in accordance with data received from multiple procedures performed using the apparatuses and to output the optimised, updated control algorithms to the apparatuses.

- 20 51. A method for determining the condition of a vessel, cavity or structure in a body, the method comprising:

navigating a distal section of an elongate waveguide element to a site in the
vessel, cavity or structure;

25

activating the waveguide element by transmitting ultrasonic energy to the distal
section;

30

acquiring feedback signals being acoustic signals generated when the
waveguide element is activated and/or inertial signals representing orientation
and/or acceleration of an activation unit that activates the waveguide element;
and

interpreting the feedback signals to characterise the condition of the vessel, cavity or structure.

52. The method of Claim 51, comprising engaging the distal section of the activated
5 waveguide element with a lesion in the vessel, cavity or structure, and interpreting consequential changes in the acoustic feedback signals to characterise the lesion.

53. The method of Claim 52, comprising disrupting the lesion with the distal section of the activated waveguide element.

10

54. The method of Claim 52 or Claim 53, further comprising comparing sensed data representing the response of the activated waveguide element to the lesion with stored data representing the response of a corresponding activated waveguide element to interaction with a known lesion.

15

55. The method of any of Claims 51 to 54, comprising acquiring the acoustic feedback signals in an extra-corporeal activation unit disposed proximally of the waveguide element.

20 56. The method of any of Claims 51 to 55, comprising acquiring the acoustic feedback signals at one or more locations along the waveguide element.

57. The method of Claim 56, comprising acquiring the acoustic feedback signals at an intra-corporeal distal location along the waveguide element.

25

58. The method of any of Claims 51 to 57, comprising acquiring the acoustic feedback signals at one or more locations outside the vessel or cavity.

59. The method of any of Claims 51 to 58, comprising acquiring the acoustic feedback
30 signals at two or more locations longitudinally spaced from each other.

60. The method of any of Claims 51 to 59, comprising acquiring the acoustic feedback signals at one or more locations that are distal with respect to an activation unit that activates the waveguide element.

5 61. The method of any of Claims 51 to 60, comprising acquiring the acoustic feedback signals at one or more locations on or beside the waveguide element, or on a tube or catheter that surrounds the waveguide element.

62. The method of any of Claims 51 to 61, comprising acquiring the acoustic feedback
10 signals at one or more locations in the body.

63. The method of Claim 62, wherein the or each of said locations in the body is outside the vessel, cavity or structure.

15 64. The method of any of Claims 51 to 63, comprising acquiring the acoustic feedback signals at one or more extra-corporeal locations against the body.

65. The method of any of Claims 51 to 64, comprising controlling the activation unit by responding to the inertial feedback signals representing orientation and/or acceleration
20 of the activation unit.

66. The method of any of Claims 51 to 65, comprising recording orientation and/or acceleration of the activation unit during a procedure involving the method.

25 67. The method of Claim 65 or Claim 66, comprising correlating the inertial feedback signals with the acoustic feedback signals.

68. The method of any of Claims 51 to 67, further comprising acquiring electrical feedback signals representing operational parameters of a source of ultrasonic energy
30 coupled with the waveguide element.

69. The method of Claim 68, comprising determining from the operational parameters how the source responds to the waveguide element encountering the vessel, cavity or structure and any lesion in the vessel, cavity or structure.

- 5 70. The method of Claim 68 or Claim 69, wherein the non-acoustic feedback signals represent variations of frequency and/or amplitude and/or phase of current drawn by, or voltage dropped across, the source of ultrasonic energy.

71. The method of Claim 70, comprising determining damping of the waveguide
10 element by monitoring decay of a current signal over time.

72. The method of any of Claims 68 to 71, comprising monitoring variations in frequency or amplitude of vibration of the waveguide element.

- 15 73. The method of any of Claims 68 to 72, comprising generating data sets from the acoustic and non-acoustic feedback signals and using combinations of, or comparisons between, the respective data sets to characterise the condition of the vessel, cavity or structure.

- 20 74. The method of any of Claims 68 to 73, further comprising, in response to the non-acoustic feedback signals, adjusting amplitude or frequency of the ultrasonic energy transmitted to the distal section along the waveguide element.

75. The method of any of Claims 68 to 74, further comprising, in response to the non-
25 acoustic feedback signals, controlling the source to maintain a resonant frequency in the waveguide element.

76. The method of any of Claims 68 to 75, comprising correlating the electrical
feedback signals with the inertial feedback signals and/or the acoustic feedback
30 signals.

77. The method of any of Claims 68 to 76, comprising generating data sets from the inertial feedback signals, the acoustic feedback signals and/or the electrical feedback

signals and using combinations of, or comparisons between, the respective data sets to characterise the condition of the vessel, cavity or structure.

78. The method of any of Claims 51 to 77, comprising: outputting data to an external data network; receiving data from the network in response; and, on receiving data from the network, modifying or changing a control algorithm accordingly.

79. The method of any of Claims 51 to 78, comprising: outputting data to an external computer system; in the external computer system, optimising and updating a control algorithm in accordance with that data; outputting the optimised, updated control algorithm from the external computer system; and using the optimised, updated control algorithm to control activation of the waveguide element.

80. The method of Claim 79, wherein the computer system optimises the control algorithm in accordance with data received from multiple procedures.

81. The method of any of Claims 51 to 80, comprising assessing a decay in amplitude of, or a shift of frequency of, displacement of the waveguide element caused by losses resulting from contact with a wall of the vessel or with material in the vessel.

82. The method of any of Claims 51 to 81, comprising applying two or more different waveforms sequentially to a source of the ultrasonic energy, those waveforms being selected from sinusoidal, pulsed, multi-tone, chirp or noise waveforms.

83. The method of any of Claims 51 to 82, comprising:

advancing the distal section of the activated waveguide element close to a lesion in the vessel;

acquiring baseline feedback signals;

advancing the distal section of the activated waveguide element into engagement with the lesion;

acquiring operational feedback signals; and

5 subtracting the baseline feedback signals from the operational feedback signals.

84. The method of any of Claims 51 to 83, comprising converting the acoustic feedback signals from the time domain to the frequency domain.

10 85. The method of any of Claims 51 to 84, comprising evaluating frequency domain data and/or power spectrum data.

86. The method of Claim 85, comprising determining characterising features from peaks in the frequency domain data and/or power spectrum data.

15

87. The method of Claim 85 or Claim 86, comprising determining characterising features from powers in frequency band ranges.

20 88. The method of any of Claims 51 to 87, comprising determining characterising features of a full frequency spectrum of the acoustic feedback signals.

89. The method of Claim 88, comprising sampling and processing sequenced images of spectrograms.

25 90. The method of any of Claims 86 to 89, comprising comparing the characterising features with threshold parameters evaluated through prior testing.

30 91. The method of any of Claims 86 to 90, comprising forming a feature dataset by combining the characterising features with electrical performance data relating to a source of the ultrasonic energy.

92. The method of Claim 91, comprising subjecting the feature dataset to classification by a machine learning algorithm.

93. The method of any of Claims 86 to 92, comprising assessing and comparing two or more of said characterising features.

- 5 94. The method of any of Claims 51 to 93, comprising detecting and monitoring harmonics in the acoustic feedback signals indicative of configuration of the waveguide element.

- 10 95. The method of any of Claims 51 to 94, comprising detecting and monitoring power in two or more frequency bands of the acoustic feedback signals.

96. The method of any of Claims 51 to 95, comprising subtracting background noise from the acoustic feedback signals.

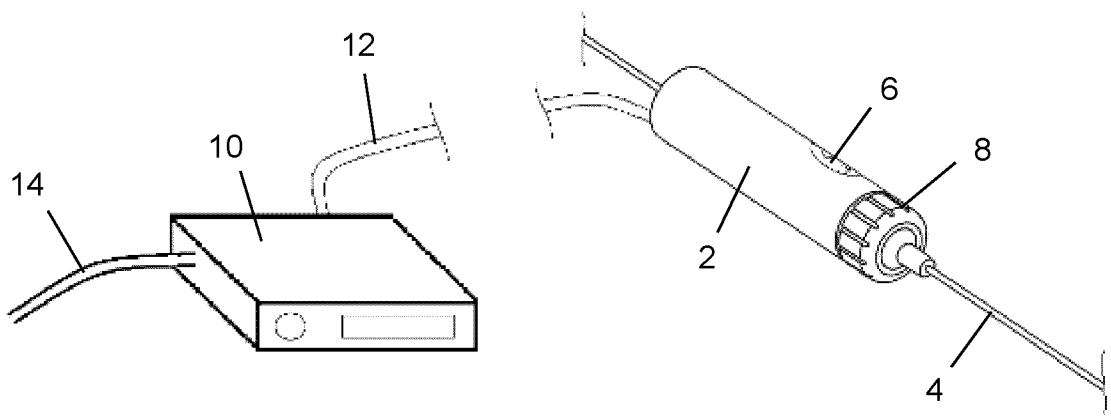


Figure 1

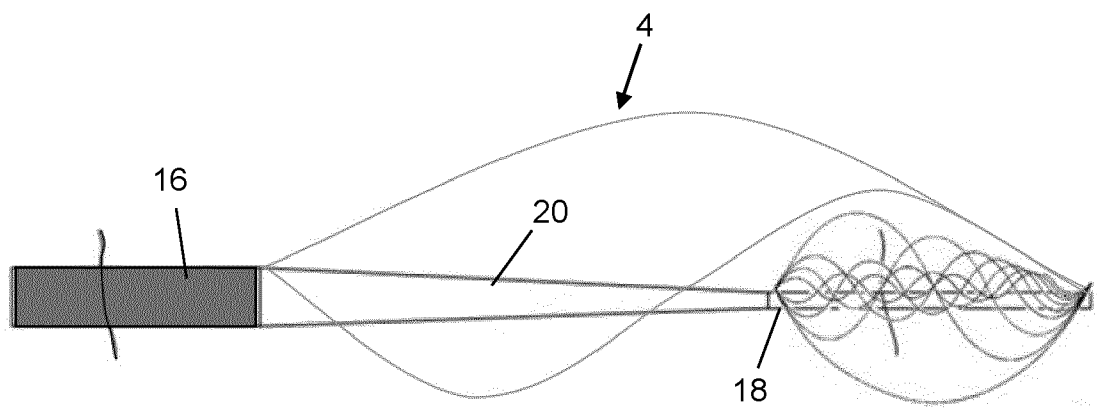


Figure 2

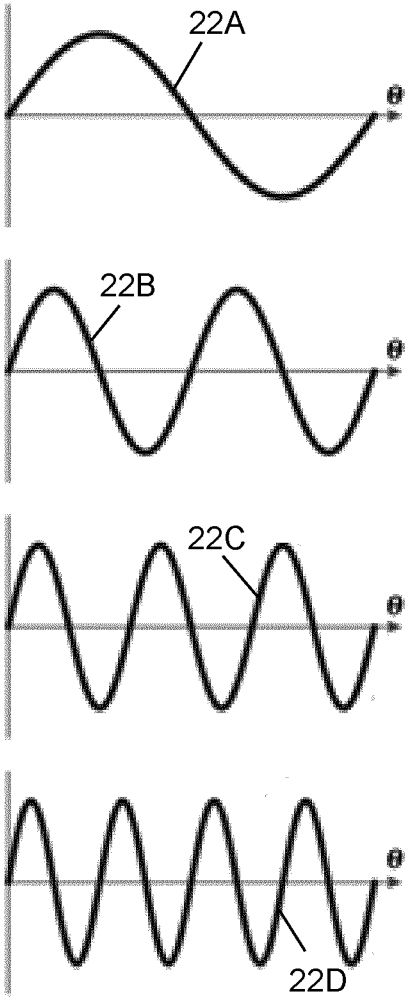


Figure 3a

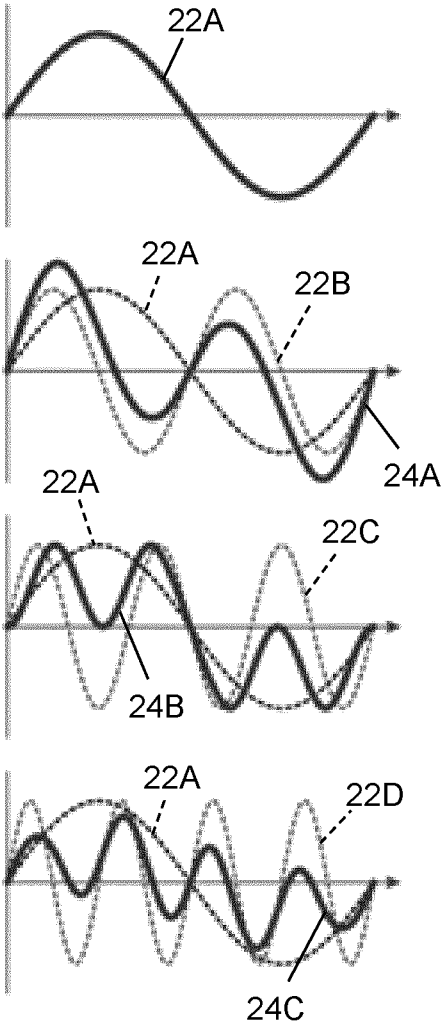


Figure 3b

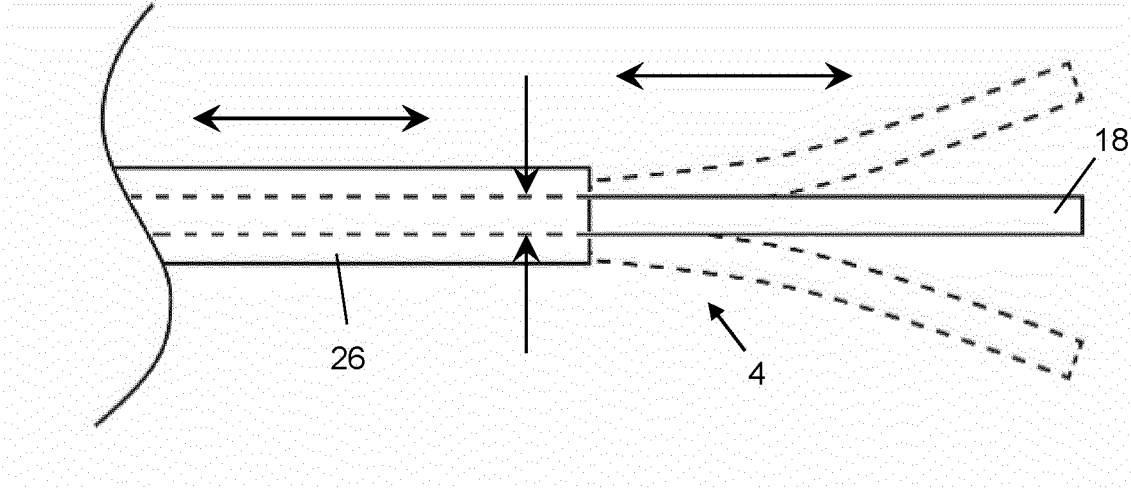


Figure 4

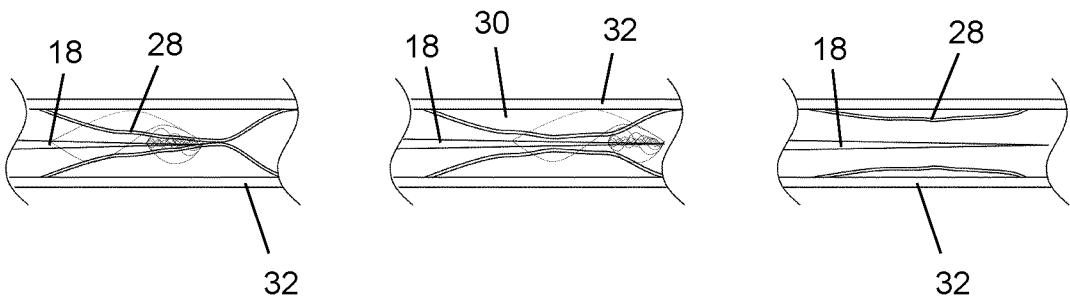


Figure 5

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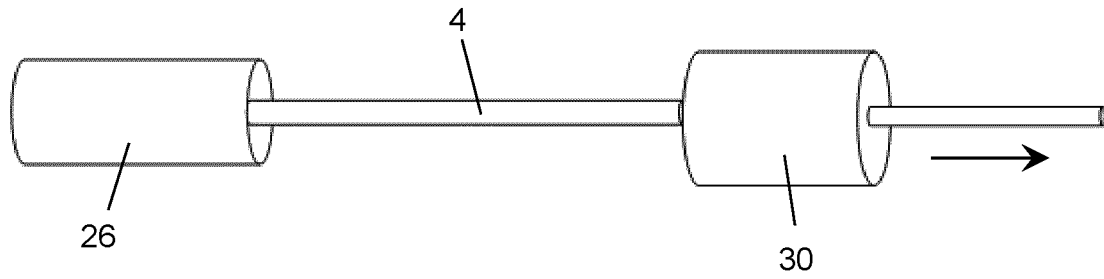


Figure 6

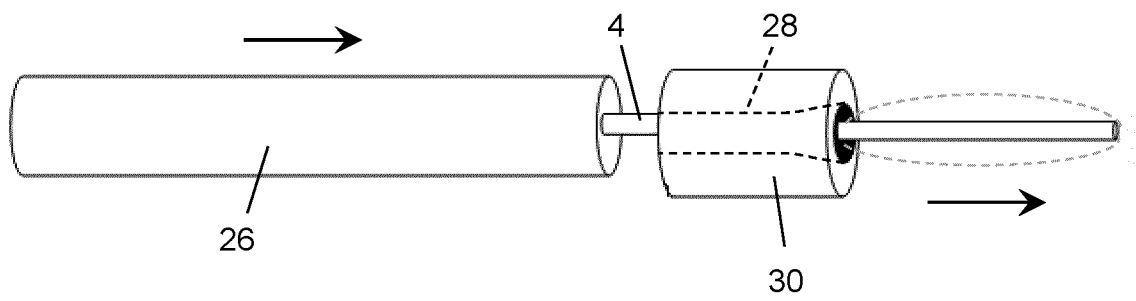


Figure 7

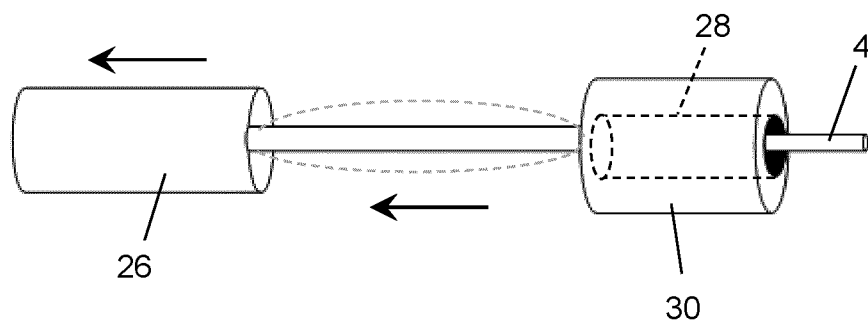


Figure 8

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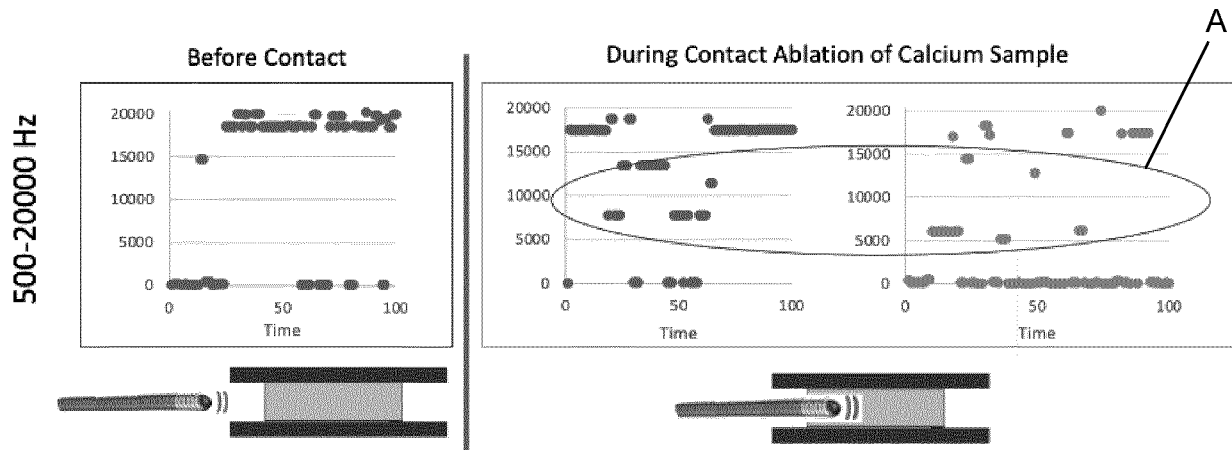


Figure 9

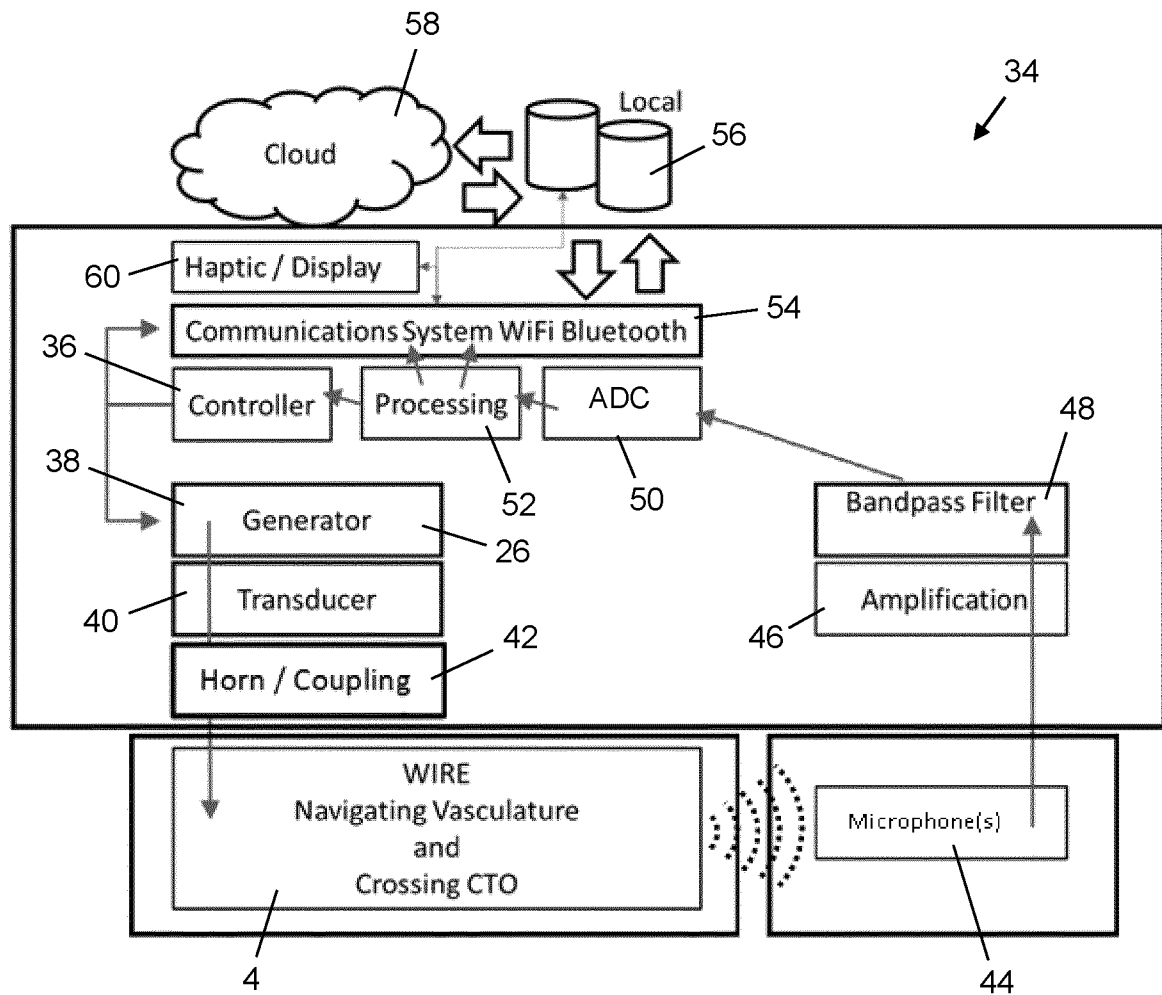


Figure 10

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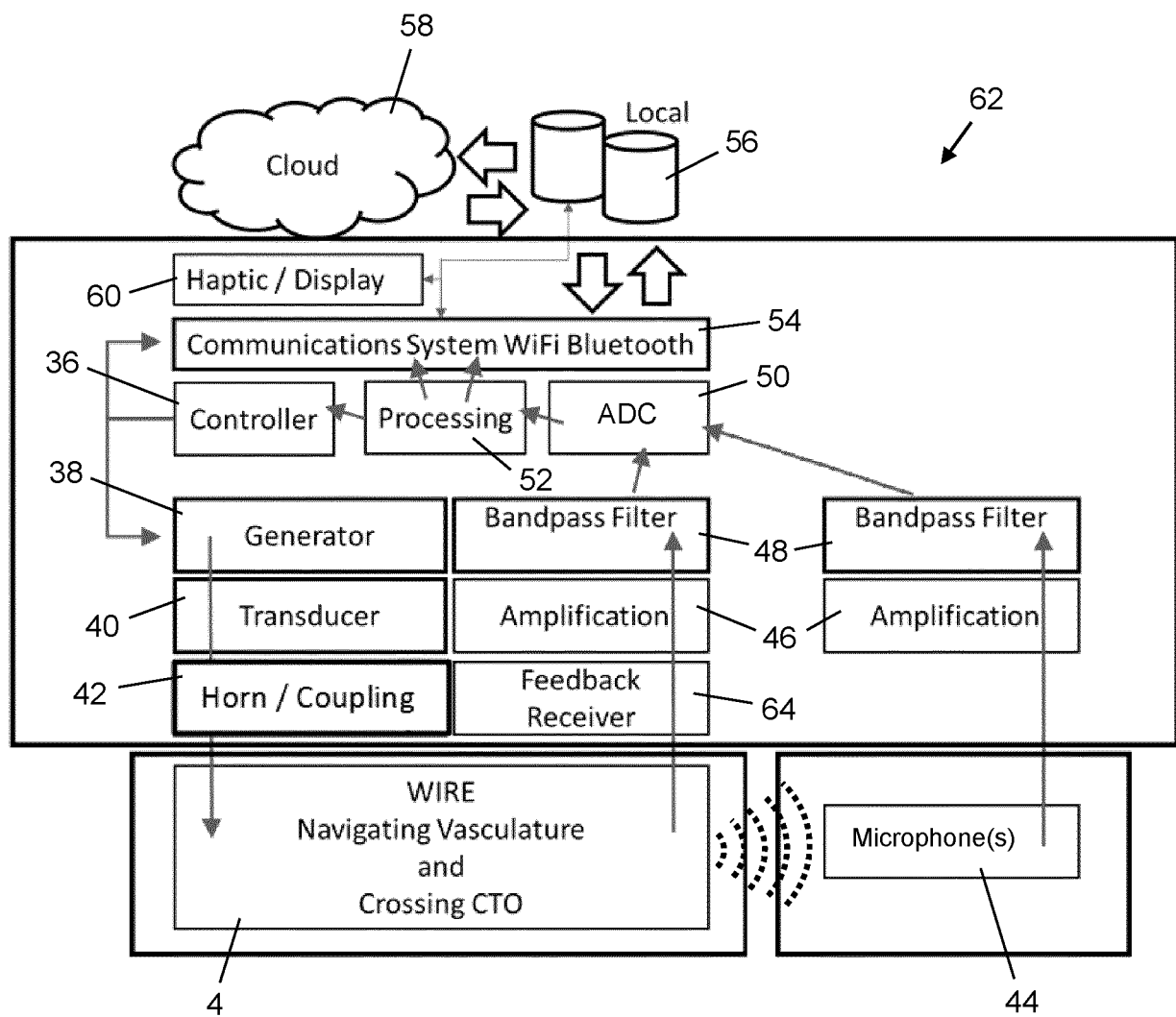


Figure 11

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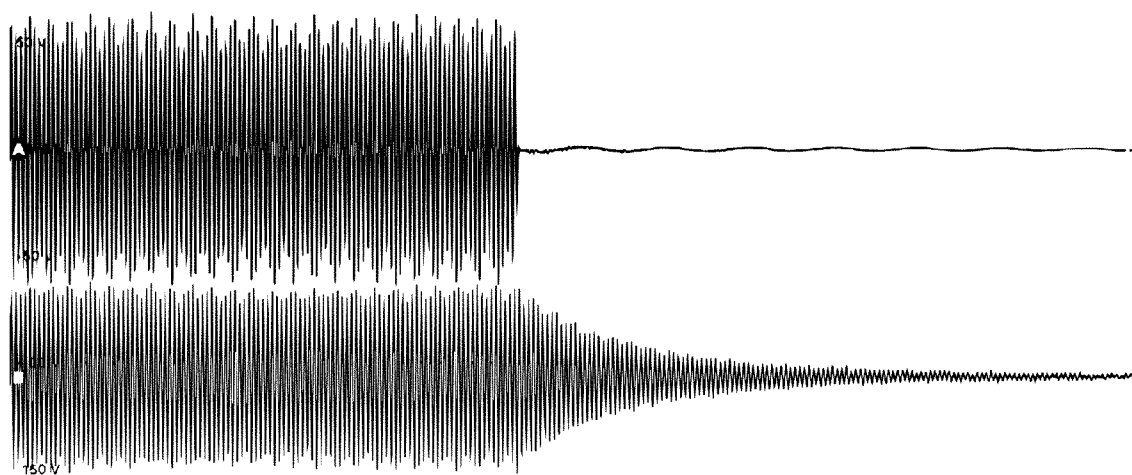


Figure 12

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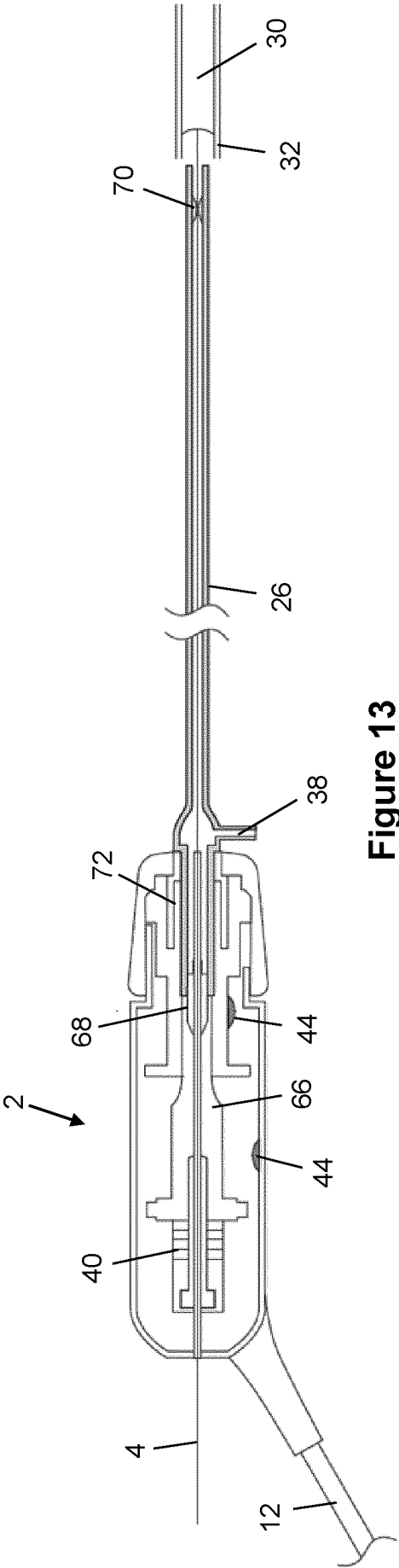


Figure 13

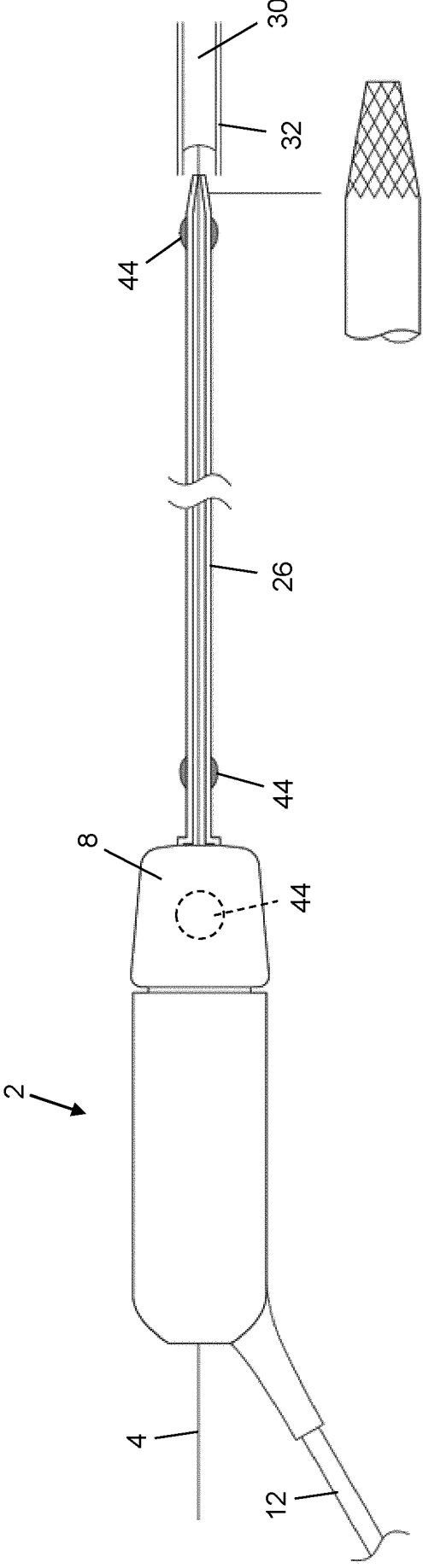


Figure 14

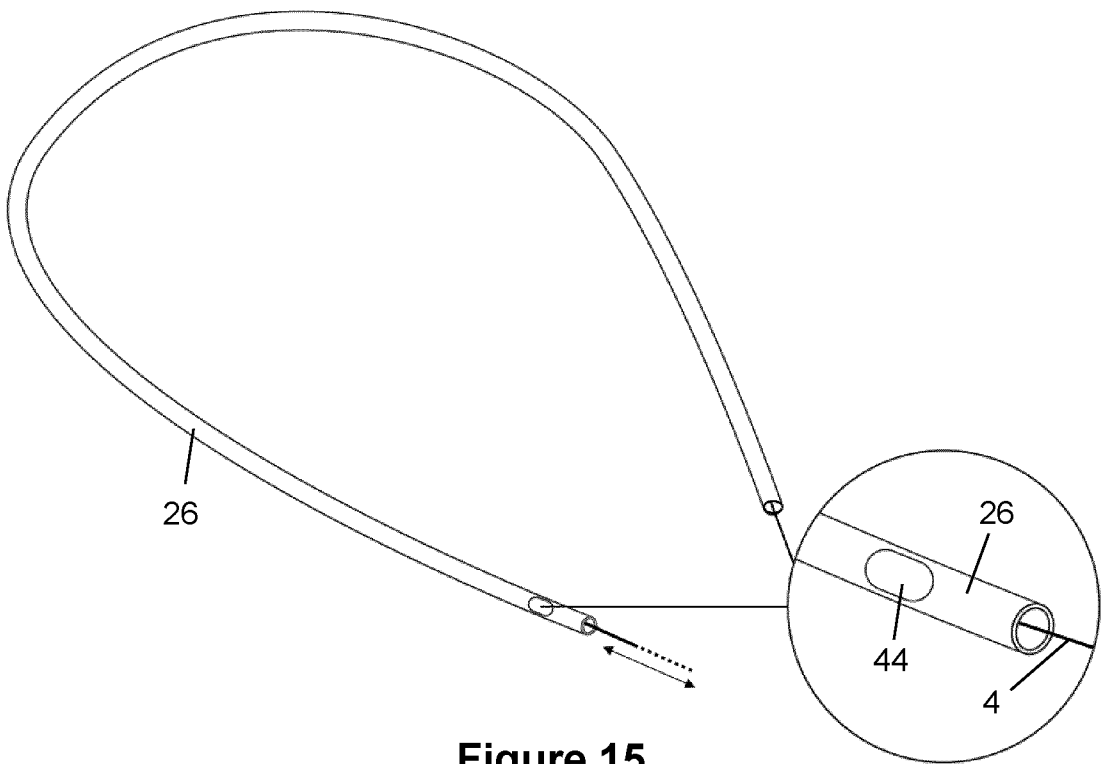


Figure 15

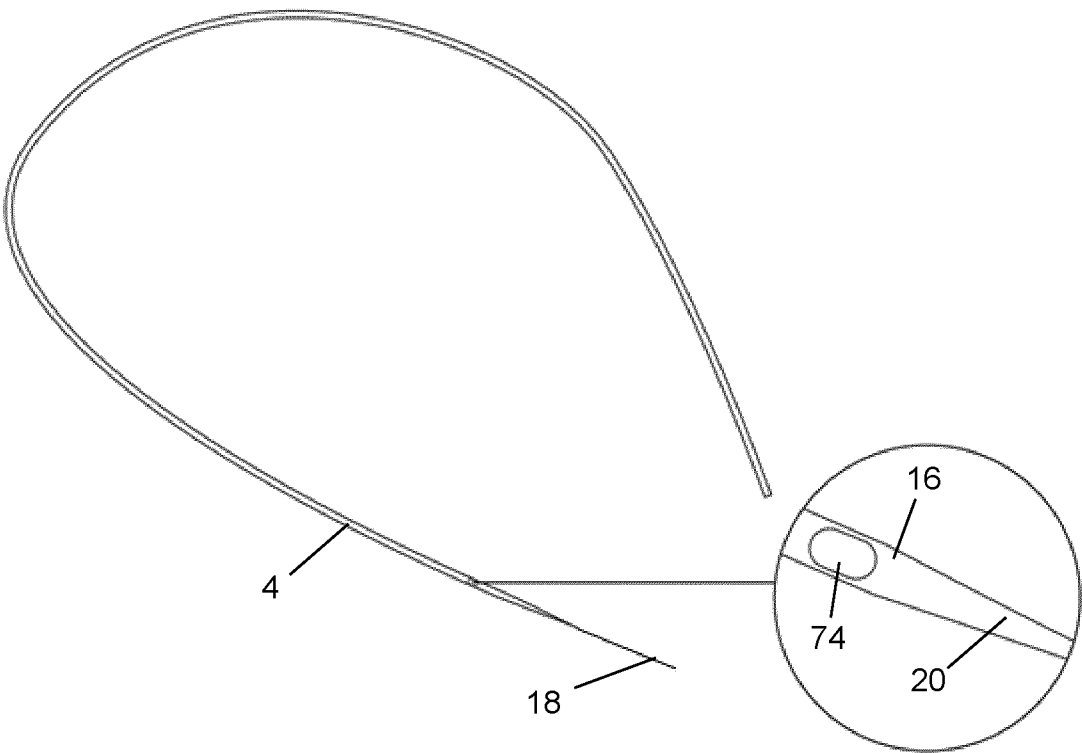


Figure 16

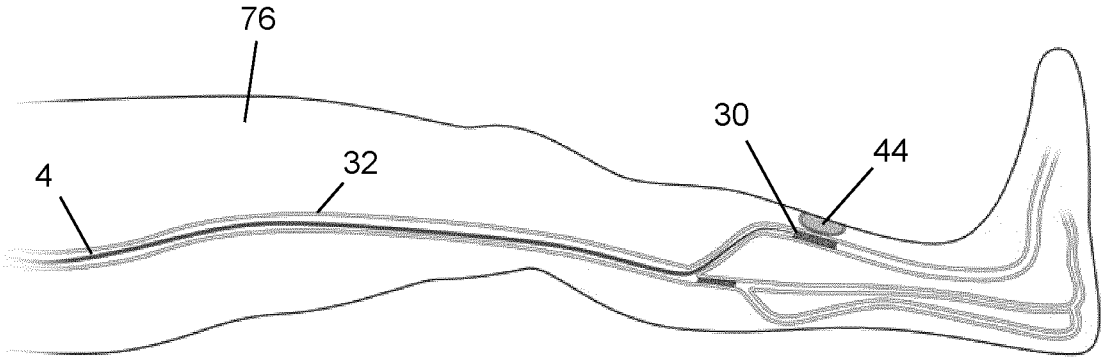


Figure 17

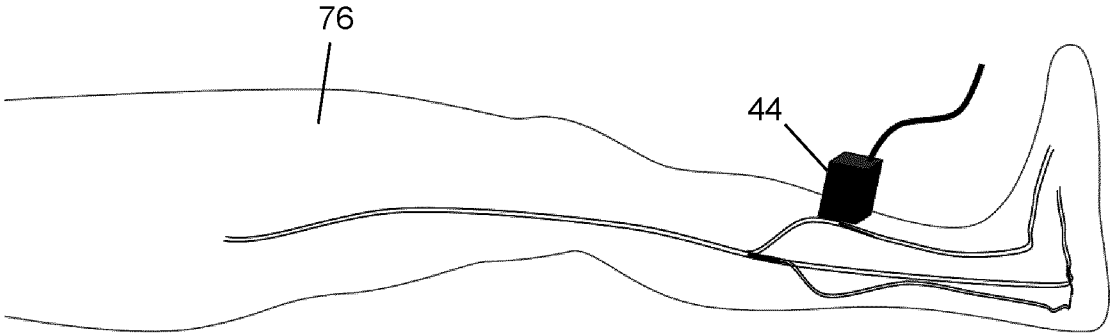


Figure 18

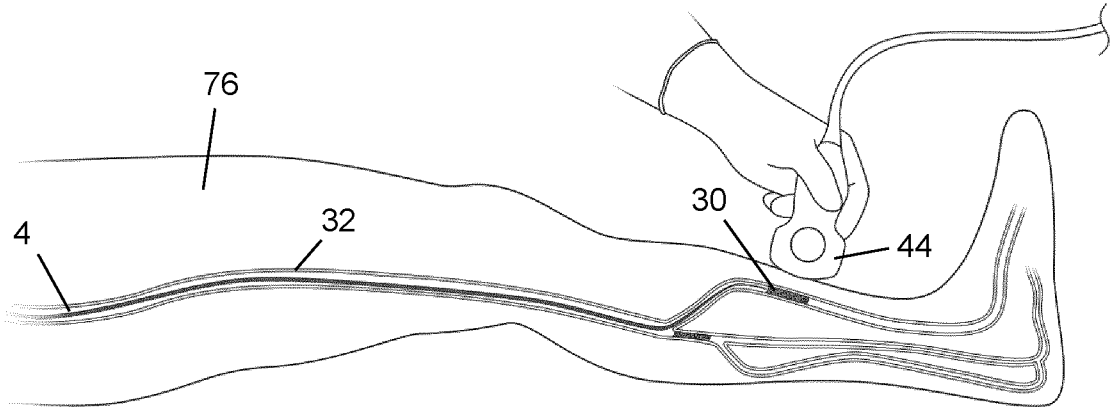


Figure 19

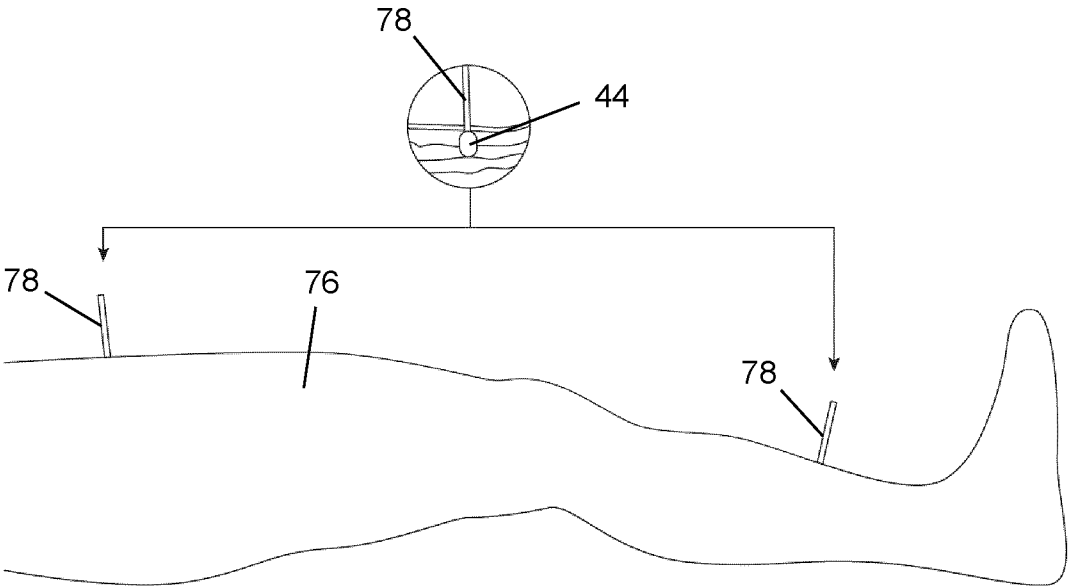


Figure 20

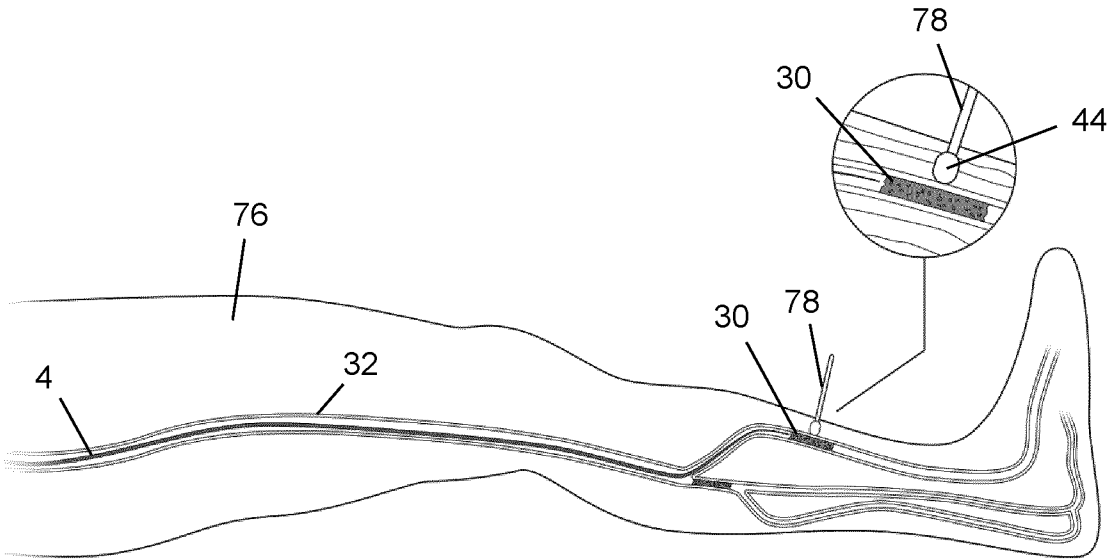


Figure 21

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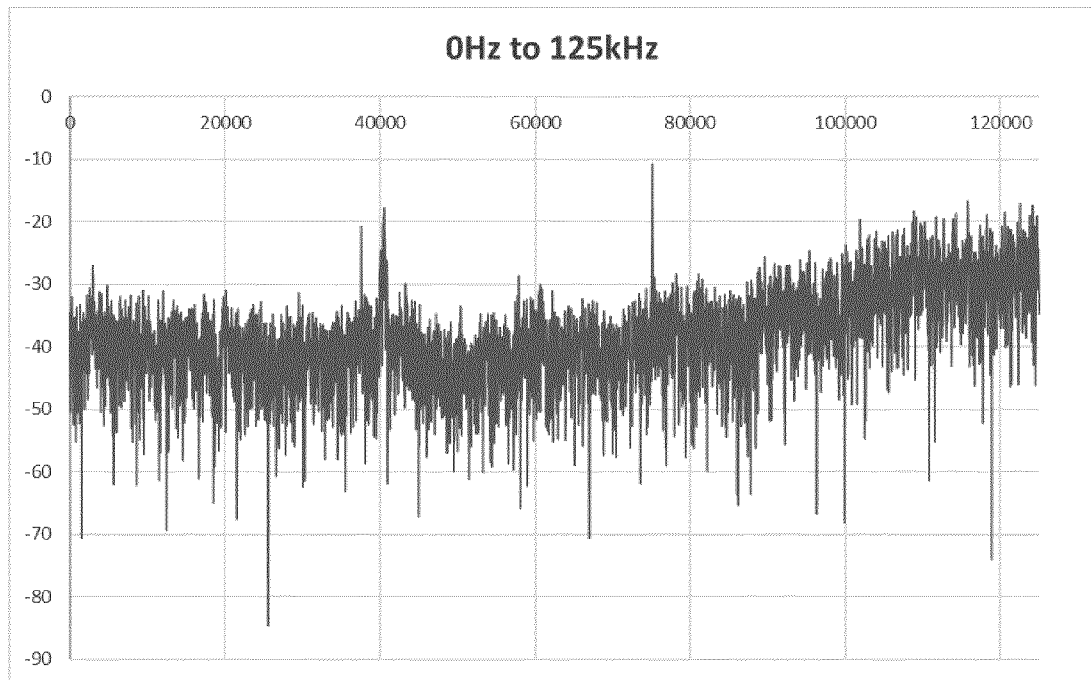


Figure 22

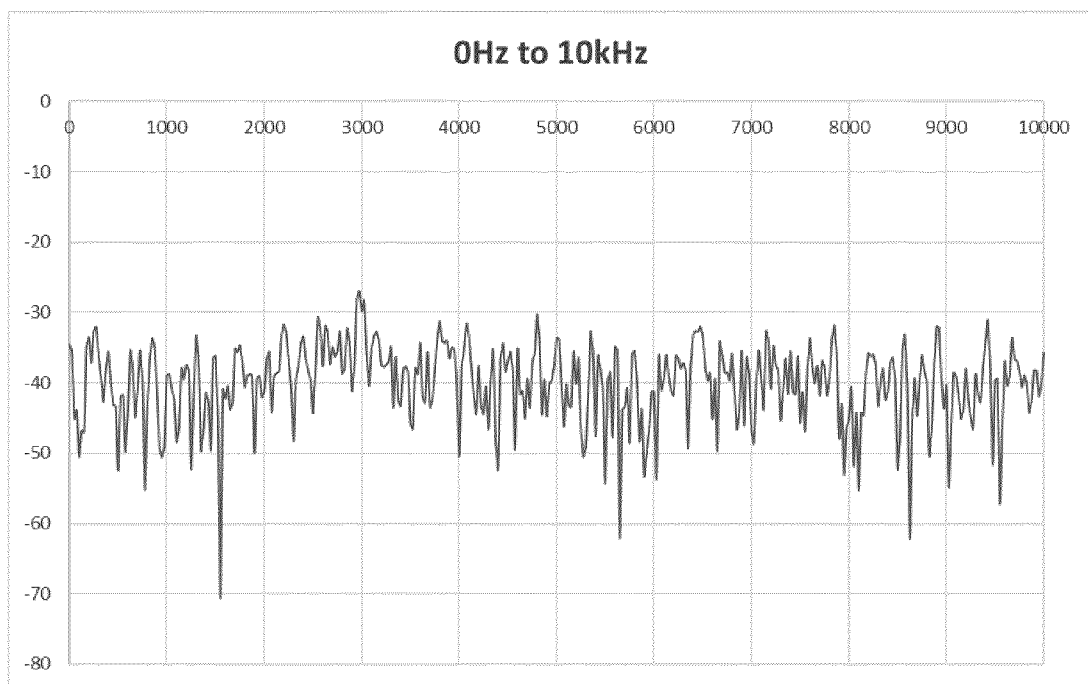


Figure 23

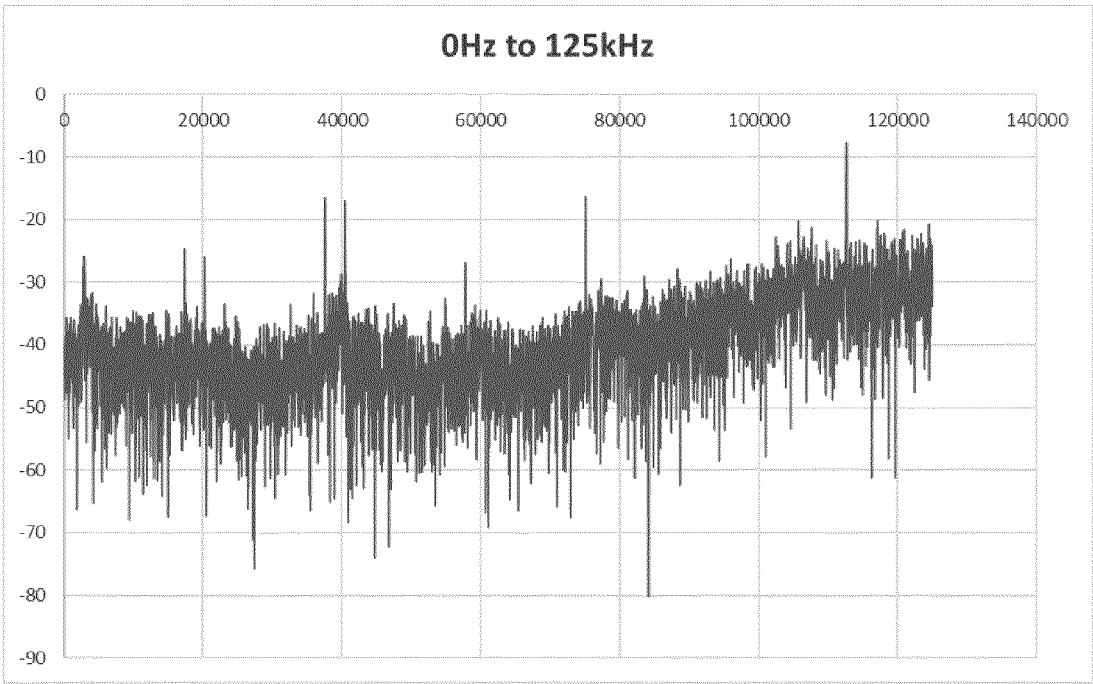


Figure 24

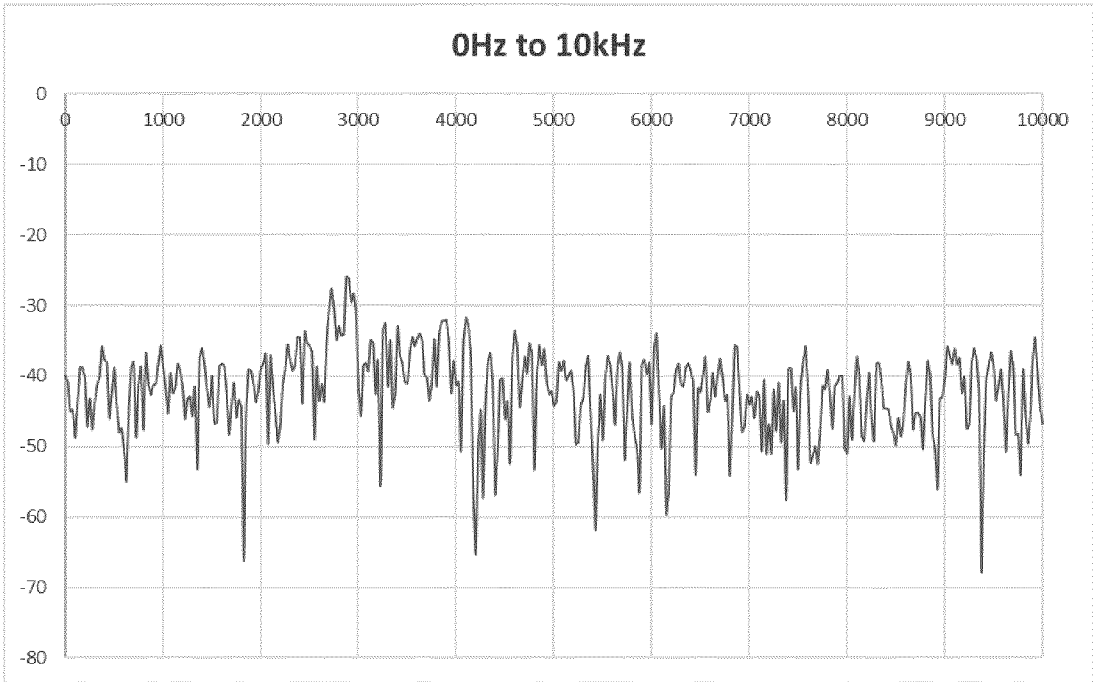


Figure 25

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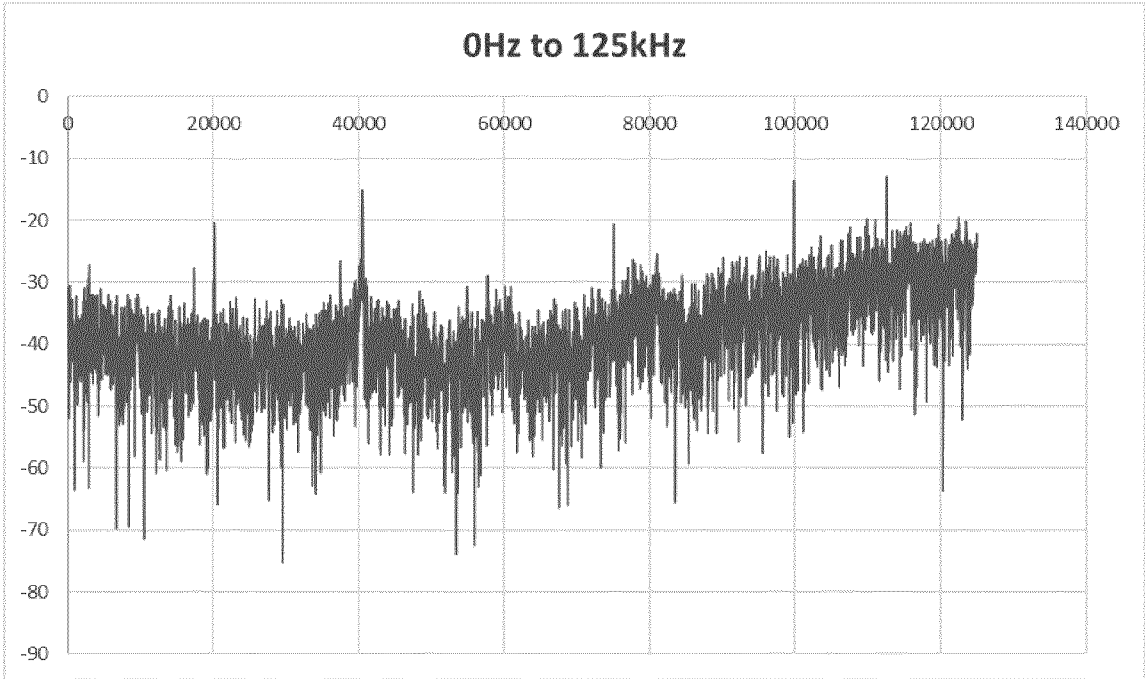


Figure 26

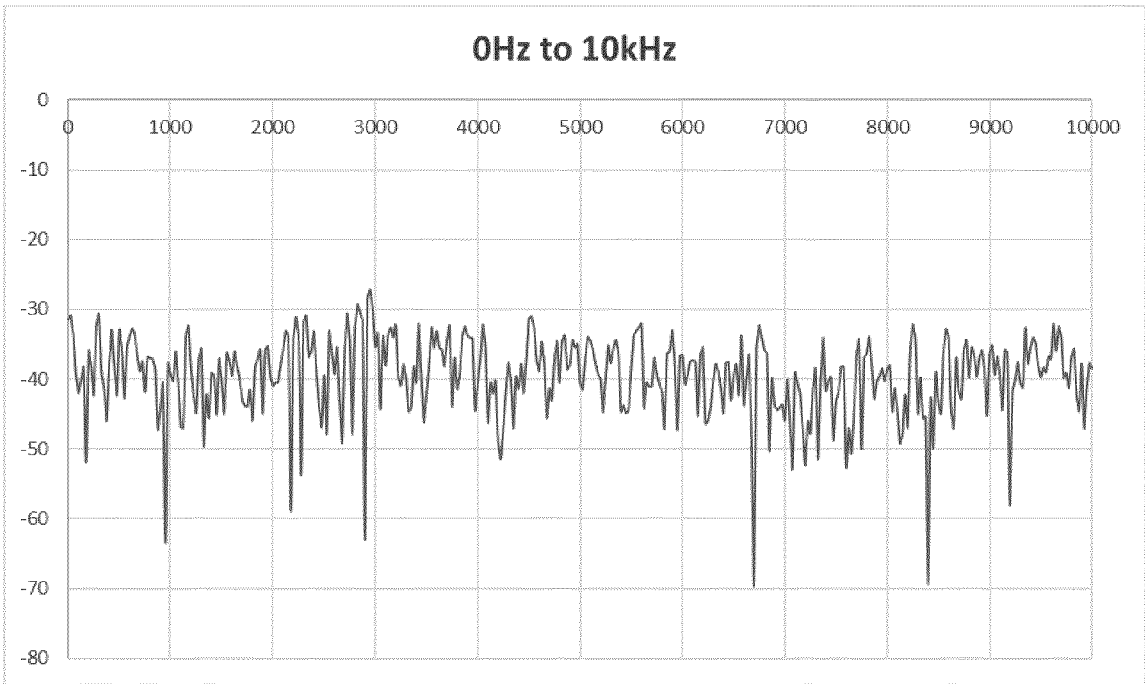


Figure 27

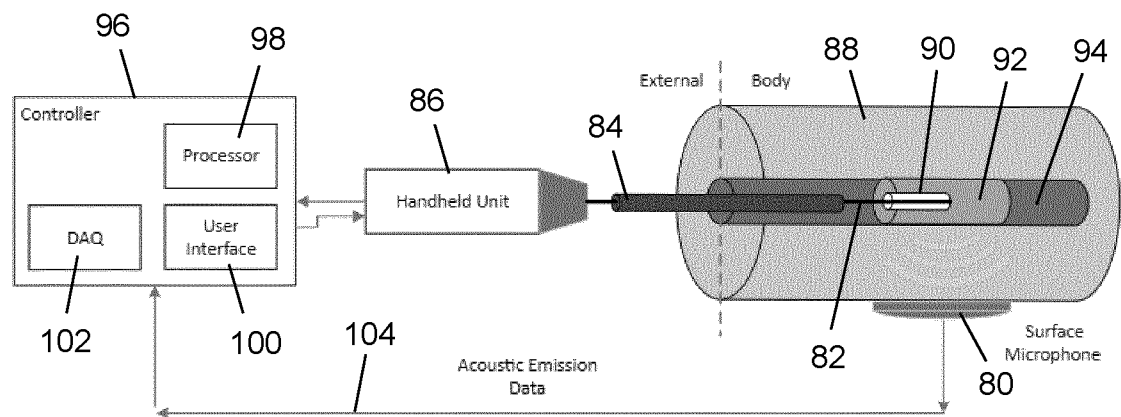


Figure 28

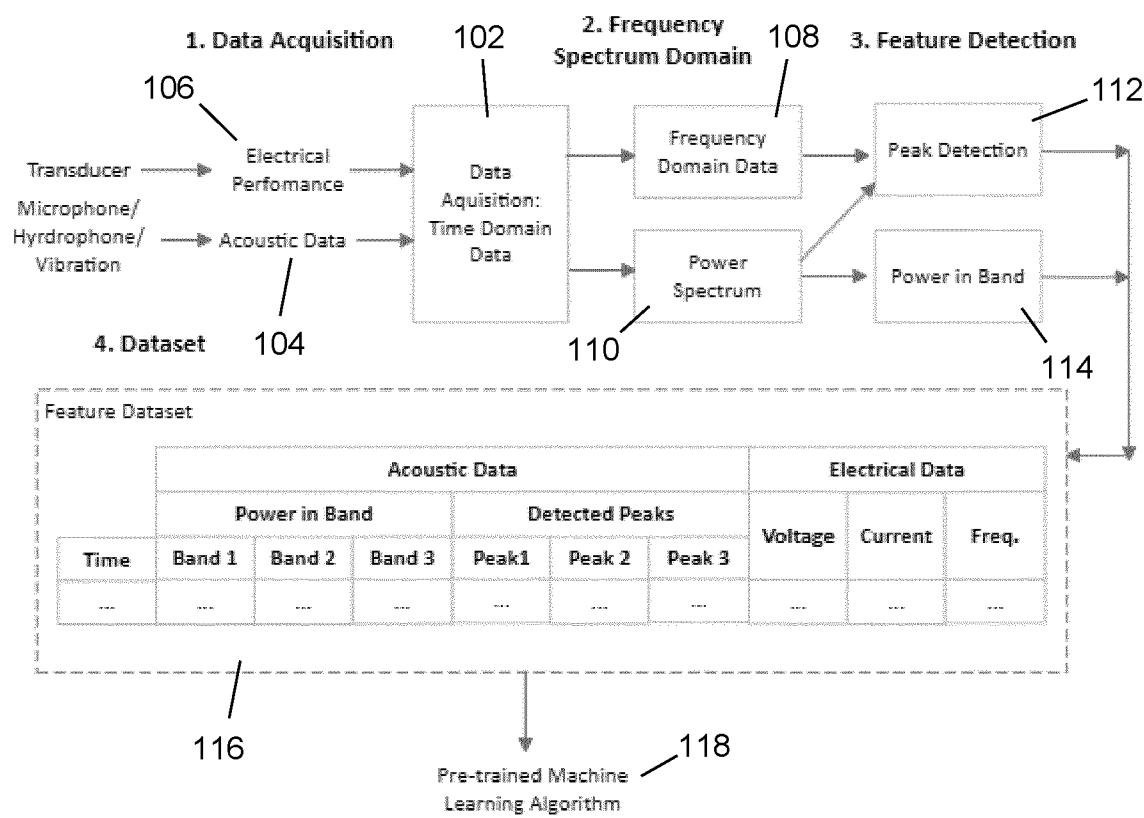


Figure 29

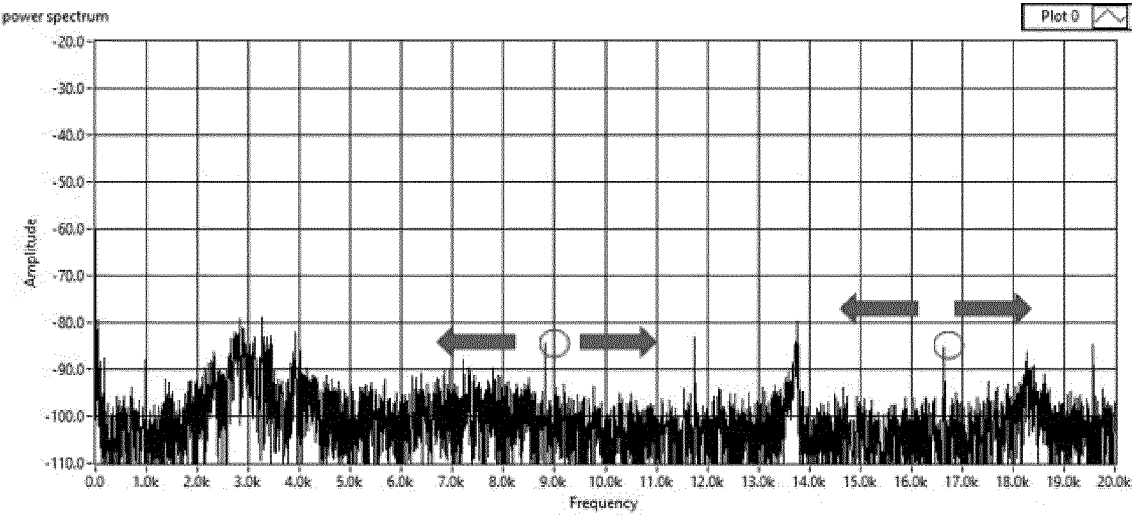


Figure 30

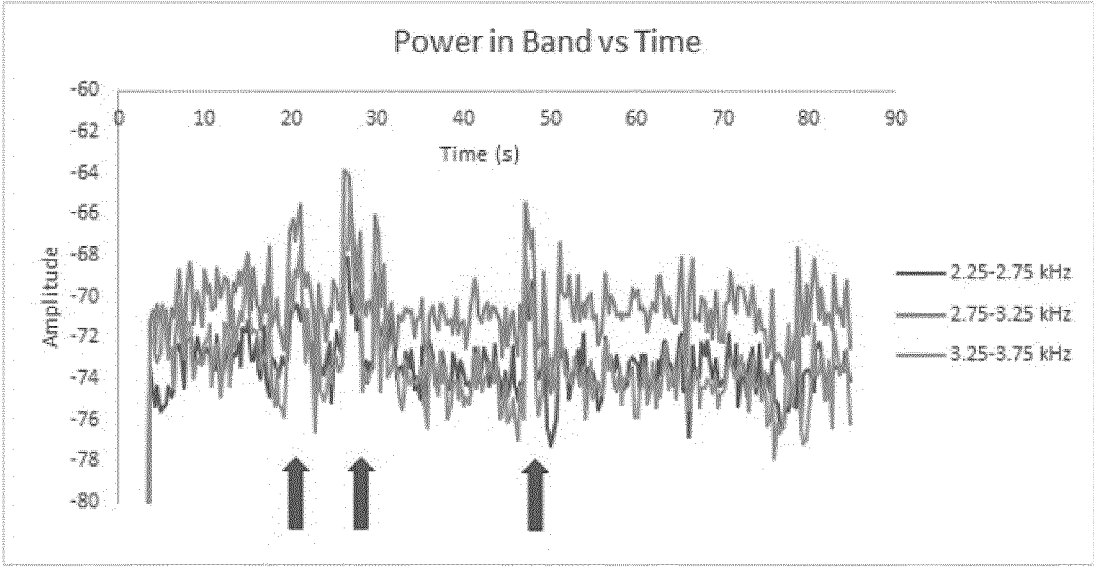


Figure 31

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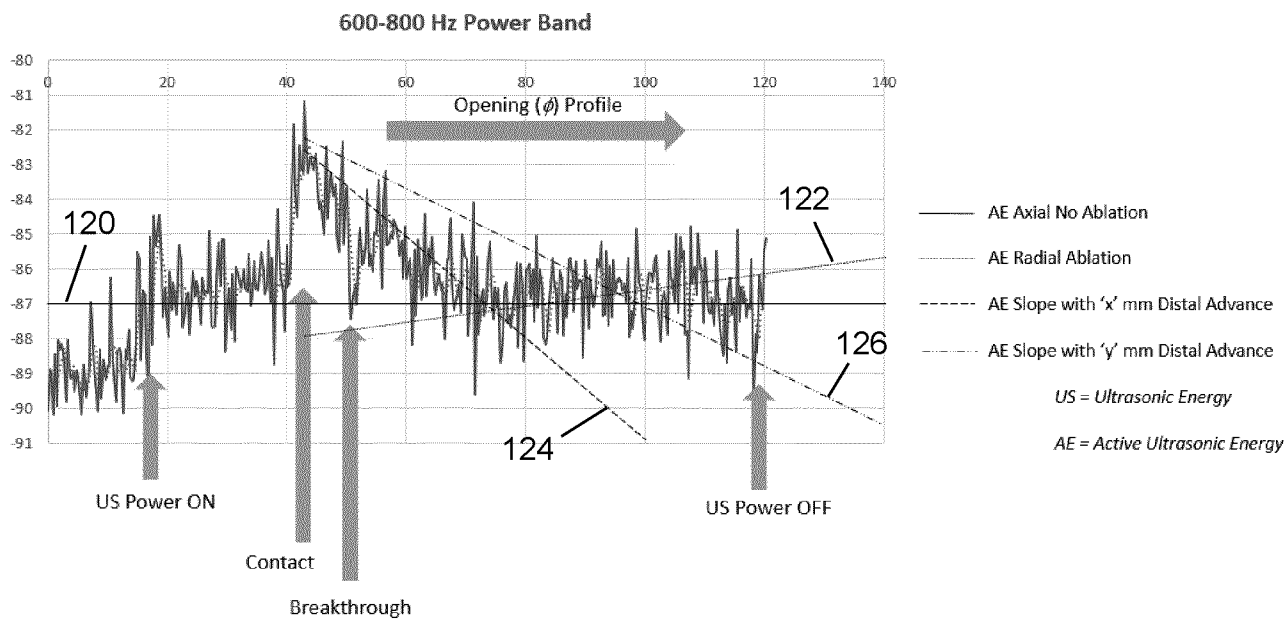


Figure 32

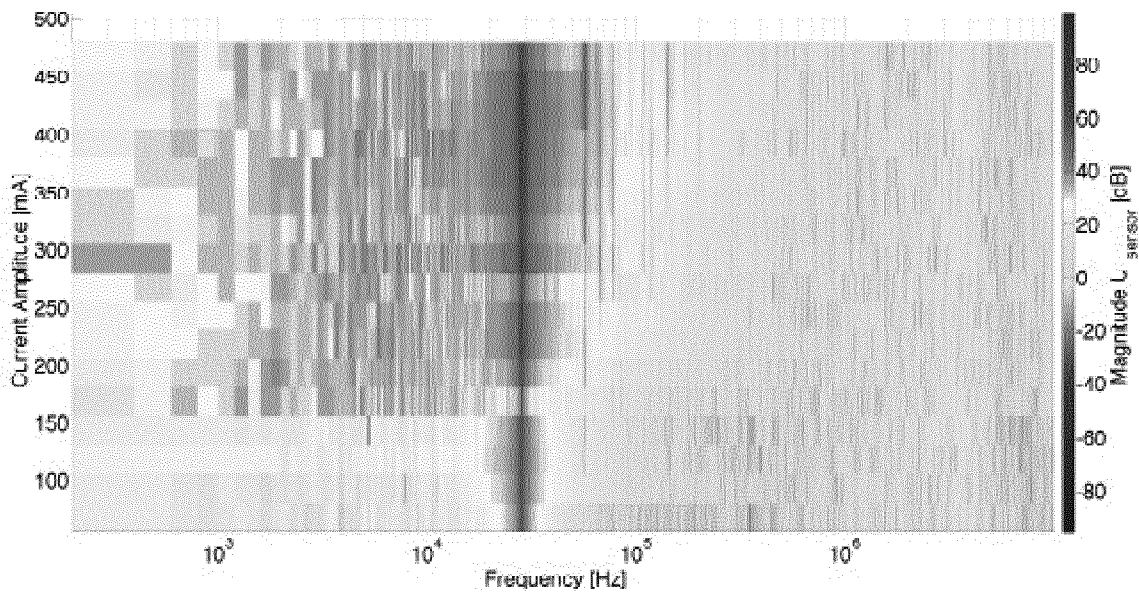


Figure 33

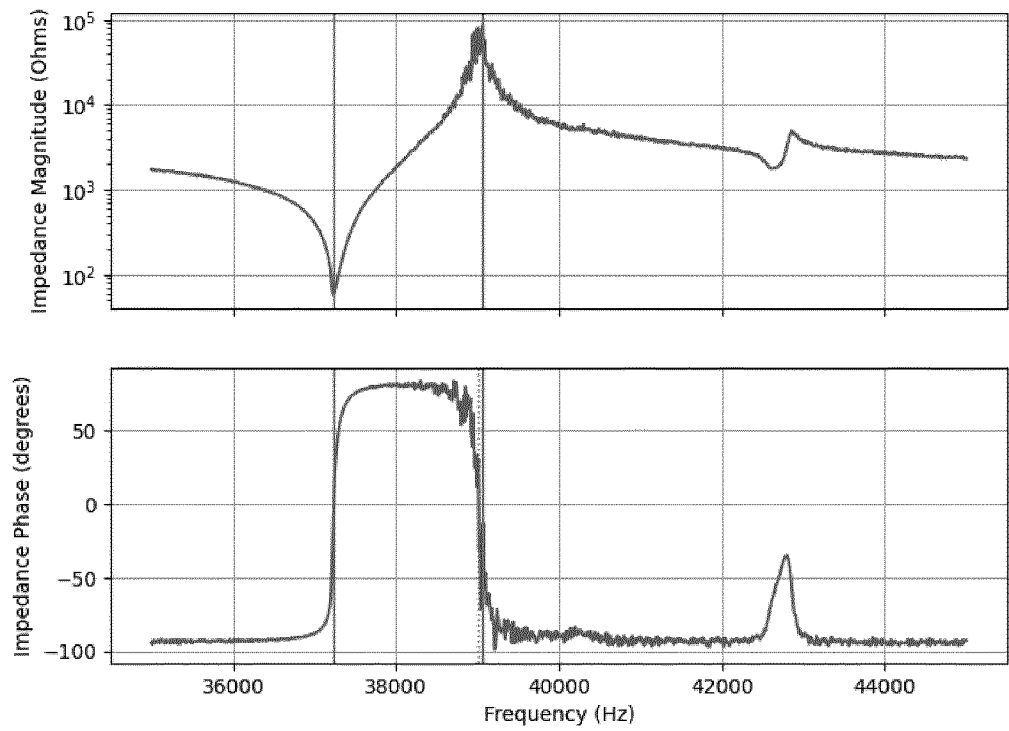


Figure 34

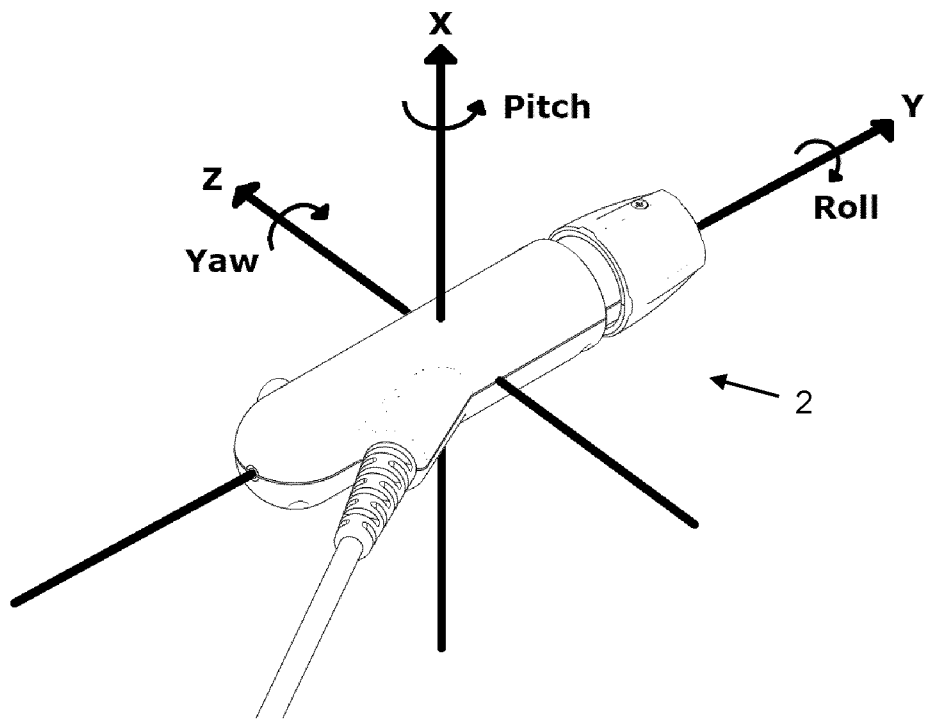


Figure 35

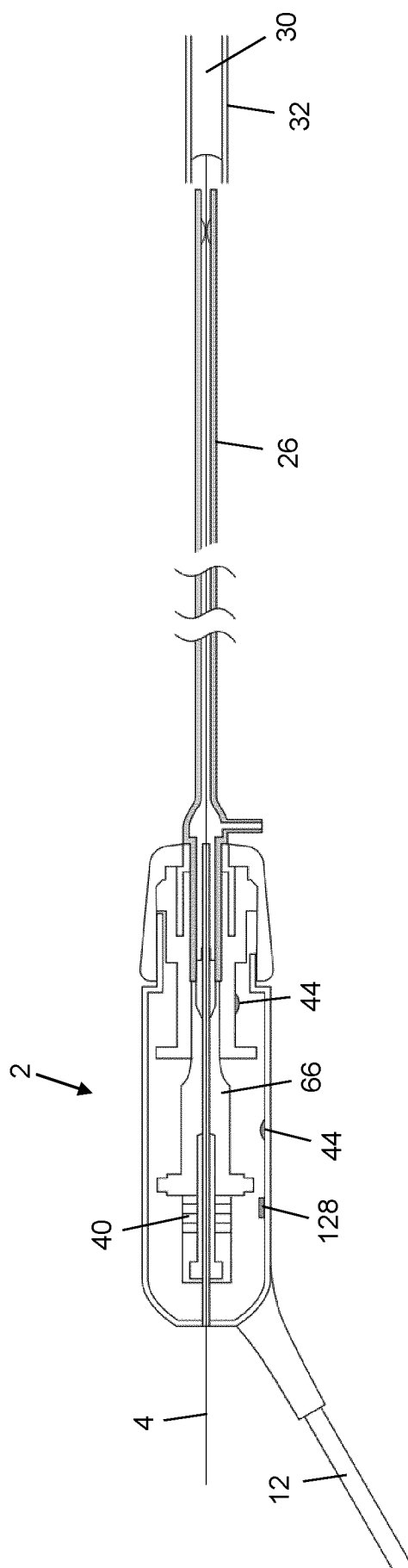


Figure 36

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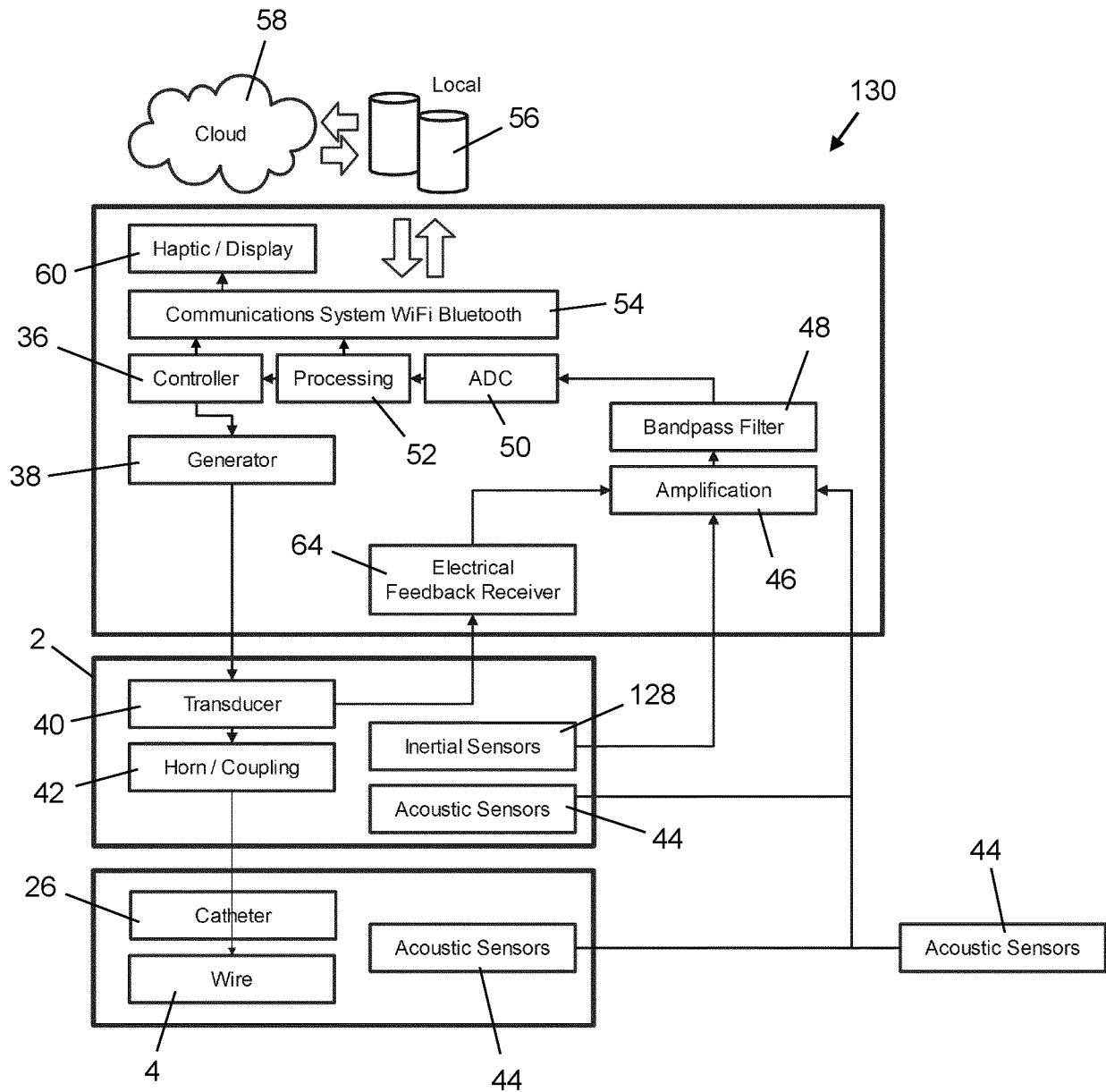


Figure 37

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP2022/086798

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: **51-96**
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims;; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

International application No
PCT/EP2022/086798

INV. A61B17/22
ADD. A61B8/12

B. FIELDS SEARCHED

EPO-Internal

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 2022/129623 A1 (VERSONO MEDICAL LTD [IE]) 23 June 2022 (2022-06-23)	1-6, 8, 12, 16, 17, 19, 21-23, 26, 27, 38, 40-44
A,P	page 12, line 23 - page 14, line 4; claims 1-6, 8, 12, 14, 15, 17, 19-21, 24, 25, 26, 27, 28, 29	7, 9-11, 13-15, 18, 20, 24, 25, 28-37, 39, 45-50
	----- -/--	

X See patent family annex.

"&" document member of the same patent family

16/03/2023

van Poelgeest, A

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2022/086798

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2019/152898 A1 (CAZE TECH [US]) 8 August 2019 (2019-08-08)	1, 16-29, 32-35, 39-46
Y	paragraphs [0012], [0015] - [0017], [0052], [0053], [0064], [0076] - [0077], [0079] - [0080], [0083], [0093] - [0100]; figures 1, 4a-b, 13, 20	2, 3, 14, 15, 30, 31, 36-38, 47-50
A	-----	4-13
Y	US 2017/215837 A1 (RAMAKRISHNA VENKATESH HOSMANE [IN] ET AL) 3 August 2017 (2017-08-03) paragraphs [0002], [0017]; figure 1	2, 3, 30, 31, 36-38
Y	US 2019/125302 A1 (CLARK DAVID WESLEY [US]) 2 May 2019 (2019-05-02)	14, 15
A	paragraph [0005]; figure 2	1
Y	US 2004/127791 A1 (MAST T DOUGLAS [US] ET AL) 1 July 2004 (2004-07-01) paragraph [0003]; figure 3	47, 48
Y	US 2004/260180 A1 (KANAI HIROSHI [JP] ET AL) 23 December 2004 (2004-12-23)	49, 50
A	figure 1	11

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2022/086798

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2022129623 A1	23-06-2022	NONE	
WO 2019152898 A1	08-08-2019	EP 3745969 A1 US 2021007760 A1 WO 2019152898 A1	09-12-2020 14-01-2021 08-08-2019
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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box II.1

Claims Nos.: 51-96

Pursuant to Article 17(2)(a)(i) and Rule 39.1 (iv) PCT, the subject-matter of claims 51-96 has not been searched, since it is directed to a method surgery. The method of independent claim 51, and therefore its dependent claims 52-96, requires parts of the system to be inserted into the patient and includes the surgical step of "navigating a distal section of an elongate waveguide element to a site in the vessel, cavity or structure". Hence this is considered a method of surgery.