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(54) **Electromagnetic sensors for biological tissue applications**

Elektromagnetische Sensoren für Anwendungen am biologischen Gewebe

Capteurs électromagnétiques destinés à des applications sur des tissus biologiques

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Description

TECHNICAL FIELD

[0001] The present disclosure relates in general to the detection of fluid and other materials in biological tissues and, more particularly, to electromagnetic sensors and methods of using those sensors for the detection of fluid and other materials in tissues. While the present invention is generally applicable to sensing of bodily or injected fluid levels or the presence of other foreign materials, such as tumors, in tissues, as well as microwave imaging and the like, it will be described herein primarily with reference to extravasation for which it is particularly applicable and initially being utilized.

BACKGROUND ART

[0002] Sensing changed, elevated or abnormal fluid levels in living tissues is often important to patient treatment. One example of abnormal fluid levels in tissue is edema, i.e., an abnormal accumulation of watery fluid in the intercellular spaces of connective tissue. Edematous tissues are swollen and, when punctured, secrete a thin incoagulable fluid. Edema is most frequently a symptom of disease rather than a disease in itself, and it may have a number of causes, most of which can be traced back to gross variations in the physiological mechanisms that normally maintain a constant water balance in the cells, tissues, and blood. Among the causes may be diseases of the kidneys, heart, veins, or lymphatic system; malnutrition; or allergic reactions. Abnormal fluid levels also arise in tissues due to hemorrhage or the discharge of blood from blood vessels with the collection and clotting of blood in tissues leading to hematomas. Hematomas normally are the result of injury.

[0003] In addition to the accumulation of body fluids, elevated fluid levels in tissues can arise as a result of introduction of a fluid into the body, for example, during an injection procedure. In that regard, in many medical diagnostic and therapeutic procedures, a physician or other person injects fluid into a patient's blood vessels. Moreover, in recent years, a number of injector-actuated syringes and powered injectors for pressurized injection of contrast medium in procedures such as angiography, computed tomography, ultrasound and nuclear magnetic resonance/magnetic resonance imaging (NMR/MRI) have been developed.

[0004] Extravasation or infiltration is the accidental infusion or leakage of an injection fluid, such as a contrast medium or a therapeutic agent, into tissue surrounding a blood vessel rather than into the blood vessel itself. Extravasation can be caused, for example, by rupture or dissection of fragile vasculature, valve disease, inappropriate needle placement, or patient movement resulting in the infusing needle being pulled from the intended vessel or causing the needle to be pushed through the wall of the vessel. High injection pressures and/or rates of some modem procedures can increase the risk of extravasation. In computed tomography, for example, contrast injection flow rates can be in the range of 0.1 to 10 ml/s.

[0005] Extravasation can cause serious injury to patients. In that regard, certain injection fluids such as contrast media or chemotherapy drugs can be toxic to tissue. It is, therefore, very important when performing fluid injections to detect extravasation as soon as possible and discontinue the injection upon detection.

[0006] Several extravasation detection techniques are known in the art. Two simple and very useful techniques for detecting extravasation are palpation of the patient in the vicinity of the injection site and simple visual observation of the vicinity of the injection site by a trained health care provider. In the palpation technique, the health care provider manually senses swelling of tissue near the injection resulting from extravasation. By visual observation, it is also sometimes possible to observe directly any swelling of the skin in the vicinity of an injection site resulting from extravasation.

[0007] In addition to palpation and observation, there are a number of automatic methods of detecting extravasation that include automatically triggering an alarm condition upon detection. For example, U.S. Pat. No. 4,647,281 discloses subcutaneous temperature sensing of extravasation to trigger such an alarm. In this method of extravasation detection, an antenna and a microwave radiometer instantaneously measure the temperature of the subcutaneous tissue at the site where fluid is injected. An algorithm periodically determines the temperature difference between tissue and injected fluid, and compares the difference to a fixed threshold. An alarm processor uses the comparison to determine an alarm condition.

[0008] U.S. Pat. No. 5,334,141 discloses a microwave extravasation detection system employing a reusable microwave antenna and a disposable attachment element for releasably securing the microwave antenna to a patient's skin over an injection site. The attachment element holds the antenna in intimate contact with the patient's skin to optimize microwave transfer therebetween, while shielding the antenna from environmental noise signals. U.S. Patent No. 5,954,668 also discloses use of a microwave antenna to sense temperature of tissue to detect extravasation.

[0009] In addition to microwave radiometry for the detection of extravasation as described above, radiometry has also been proposed for the detection of pulmonary edema as described in U.S. Patent No. 4,488,559. U.S. Patent No. 4,240,445 discloses detection of pulmonary edema via transmitting electromagnetic energy through a transmission line coupled to tissue. U.S. Patent No. 4,690,149 discloses detection of brain edema via impedance changes detected by a sensor. A proposed method of detection of brain edema is also disclosed in U.S. Patent No. 6,233,479, in which a measured signal from a microwave antenna is compared to stored characteristic hematoma signals from hematomas of different thick-

nesses and a predetermined threshold value which can be used for judging whether or not a hematoma signal from an actual patient represents a real blood pool or not.

[0010] Microwave energy has also been used for the detection of tumors in living tissue as described in U.S. Patent No. 6,061,589. Unlike the passive measurements in microwave radiometry, U.S. Patent No. 6,061,589 disclosed transmission of electromagnetic energy into the body (breast tissue) using a microwave antenna with collection and measurement of a resultant signal. In that regard, U.S. Patent No. 6,061,589 describes a microwave antenna to detect incipient tumors in accordance with differences in relative dielectric characteristics. Electromagnetic energy in the microwave frequency range is applied to a discrete volume in the tissue and scattered signal returns are collected. The irradiated location is shifted or changed in a predetermined scanning pattern. The returned signals are processed to detect anomalies indicative of the present of a tumor.

[0011] Likewise, microwave energy has been proposed for use in water content mapping in human tissue as described in U.S. Patent No. 5,995,863. Microwave energy has also been used in non-invasive tomographic spectroscopy imaging. See U.S. Patent Nos. 6,332,087 and 6,026,173.

[0012] Microwave energy has also further been used to measure the fat content in nonliving organic tissue. For example, M. Kent, "Hand Held Fat/Water Determination", (1993), available at www.distell.com/products/papers/paper2.htm, discloses a microstrip transmission line type sensor for such a determination. In general, the fat content of pelagic and other fatty species of fish is proportion to water content. The dielectric properties of the fish depend on the water content. In the device of Kent, changes in the transmission properties of the microstrip transmission line held against the fish were calibrated against water content. Through simulations it was found that the present invention is significantly more sensitive to changes within biological tissue due to the fact that it relies on the tissue as the transmission path rather than a transmission line. In an open transmission line type sensor, a significant fraction of the transmitted energy travels through the transmission line itself and is significantly less impacted by changes in the underlying tissue. In the present invention, a large fraction of the energy travels through the tissue and therefore changes in the tissue path will impact the signal more drastically.

[0013] It is very desirable to develop improved sensors and methods for their use in detecting elevated or otherwise abnormal levels of fluids in living tissue, for example, as the result of edema, hematoma or extravasation. Such sensors and methods would also be desirable for detecting the presence of other materials, such as tumors, in living tissue as well as for microwave imaging and other like applications.

DISCLOSURE OF INVENTION

[0014] The present invention is defined by claim 1. Its attendant advantages will be further understood by reference to the following detailed description and the accompanying drawings. Preferred embodiments are defined by the dependent claims. Further embodiments disclosed herein are for exemplary purpose only.

BRIEF DESCRIPTION OF DRAWINGS

[0015]

Fig. 1 illustrates a detection system in which the sensors and sensor elements of the invention of the present application can be used.

Fig. 2 illustrates the detection system of Fig. 1 in use to detect extravasation.

Fig. 3 illustrates a first antenna array positioned about an injection site for use in the detection of extravasation.

Fig. 4A illustrates a second embodiment of an antenna array including tapered-slot antennae.

Fig. 4B illustrates a side view of use of an antenna array as illustrated in Fig. 4A to pass electromagnetic energy across a surface to detect a change in, for example, the geometry, shape or morphology of the surface corresponding to a change in fluid level or material presence in underlying tissue.

Fig. 4C illustrates a side view of an antenna used to transmit electromagnetic energy to and measure reflected electromagnetic energy from a surface to detect a change in, for example, the geometry, shape or morphology of the surface corresponding to a change in fluid level in underlying tissue.

Fig. 5 illustrates a second antenna array positioned about an injection site for use in the detection of extravasation.

Fig. 6 illustrates an embodiment of a transmitter and/or receiver including a coupling or superstrate layer suitable for coupling the transmitter/receiver to the skin.

Fig. 7A illustrates a side, cross-sectional view of an embodiment of an antenna including a sensor element of the present invention with a linearly tapered superstrate.

Fig. 7B illustrates a side, cross-sectional view of the antenna of Fig. 7A coupled to a patient's arm.

Fig. 7C illustrates a side, cross-sectional view of an antenna of the present application with a square superstrate coupled to a patient's arm.

Fig. 7D is a plan view of the antenna or Fig. 7A showing resonance sizing of a square patch antenna and a circular patch antenna, one of many alternate patch antenna geometries.

Fig. 7E is a broken-away, side, cross-sectional view of an alternate embodiment of an antenna of the present invention showing a curvilinear tapered superstrate.

Fig. 8A illustrates a bottom view of a "bowtie" sensor of the present invention including two antenna as illustrated in Figs. 7A and 7B.

Fig. 8B illustrates a side, cross-sectional view of the sensor of Fig. 8A.

Fig. 8C illustrates a perspective view of the sensor of Fig. 8A.

Fig. 8D illustrates a side view of the sensor of Fig. 8A coupled to a patient's arm.

Fig. 8E illustrates a side, cross-sectional view of an embodiment of an antenna of the present invention positioned within a base member having a tapered profile to assist in conforming to tissue.

Fig. 9A illustrates a bottom view of a U-shaped sensor of the present invention including two antenna as illustrated in Figs. 7A and 7B.

Fig. 9B illustrates a bottom view of a U-shaped sensor of the present invention including two linear arrays of four antennae as illustrated in Figs. 7A and 7B.

Fig. 10 illustrates a top view of an embodiment of a phantom used to model elevated or otherwise abnormal fluid levels in the human body.

Fig. 11 illustrates a side, cross-sectional view of the phantom of Fig. 7.

Fig. 12 illustrates an experimental setup in which a single antenna was used as both the transmitter and receiver.

Fig. 13 the effect of increasing fluid level on the received signal in the setup of Fig. 9.

Fig. 14 illustrates an experimental setup in which one antenna was used as a transmitter and another antenna was used as a receiver.

Fig. 15 illustrates a comparison of the resonance frequencies of the two antennae of Fig. 14.

Fig. 16 the effect of increasing fluid level on the received signal in the setup of Fig. 14.

Fig. 17 illustrates the sensor of Fig. 8A in connection with a chicken phantom.

Fig. 18 illustrates signal data resulting from extravasation studies on a single-skinned chicken phantom.

Fig. 19A illustrates "complex distance" as a function of injected volume and frequency in the upper graph and maximum "complex distance" over all frequencies as a function of injected volume in a lower graph for an extravasation study on a double-skinned chicken phantom.

Fig. 19B illustrates "complex distance" as a function of injected volume and frequency in the upper graph and maximum "complex distance" over all frequencies as a function of injected volume in a lower graph for another extravasation study on a double-skinned chicken phantom.

Fig. 19C illustrates "complex distance" as a function of injected volume and frequency in the upper graph and maximum "complex distance" over all frequencies as a function of injected volume in a lower graph for an extravasation study on a single-skinned chicken phantom.

Fig. 20 illustrates a graphical representation of "complex distance".

Fig. 21A illustrates signal data resulting from studies using the sensor of Fig. 8A on a human subject on areas of varying fat layer thickness.

Fig. 21B illustrates signal data resulting from studies using the sensor of Figs. 8A on another human subject on areas of varying fat layer thickness.

Fig. 22A illustrates signal data resulting from studies using the sensor of Fig. 8A on a human subject's arm at various arm positions.

Fig. 22B illustrates signal data resulting from studies using the sensor of Fig. 8A on a human subject's arm at various arm positions wherein sensor cables were maintained in separation.

Figs. 23 and 24 illustrate an alternate embodiment of a sensor with opposing directional planar antennae.

BEST MODE FOR CARRYING OUT THE INVENTION

[0016] While the sensors and methods of the present disclosure are generally applicable to the sensing of bodily or injected fluid levels or other foreign materials of the levels of such foreign materials in tissues, they will be described herein primarily with reference to extravasation for which it is particularly applicable and initially being utilized. Complex permittivity and permeability govern how an electromagnetic wave will propagate through a substance. Complex permittivity typically has the greatest effect since it varies significantly between tissue types and fluids of interest. The complex permeability of various tissues and many fluids of interest is approximately that of a vacuum, reducing the effect of this parameter. However, some fluids such as MRI contrast agents may have an appreciable complex permeability difference from tissue. Although blood contains small amounts of iron, the permeability value for any significant volume of blood is typically insignificant. Complex permittivity is generally expressed as

$$\varepsilon^* = \varepsilon' - j\varepsilon''$$

wherein ε' is the real component of the complex value and is known as the dielectric constant or sometimes simply referred to as the "permittivity." The term ε'' is the imaginary component of the complex value and is often referred to as the "loss factor." The ratio of $(\varepsilon''/\varepsilon')$ is known as the "loss tangent." The complex permittivity (and sometimes permeability) of certain substances differ from the body tissue at certain frequencies. Such differences in permittivity and/or permeability are used for the detection and level monitoring of certain fluids and substances in biological tissue.

[0017] The studies leading to the present invention have shown that electromagnetic energy having, for example, a frequency in the range of approximately 300MHz to approximately 30GHz (and, more preferably, in the range of approximately 1 GHz to approximately 10GHz, and, even more preferably, in the range of approximately 3GHz to approximately 5GHz) provides good penetration into tissue. In general, such electromagnetic energy is launched into the subcutaneous tissue and a resultant signal is measured. Electromagnetic energy in the frequency range set forth above has been found to transmit through the skin and to transmit or propagate well within, for example, fat. Good transmission through the fat layer is beneficial for detection of extravasation as many extravasations occur in the fat layer. The sensitivity to extravasation of the systems and methods utilizing the present invention is thus increased as compared, for example, to impedance plethysmography wherein the majority of the electrical current passes through highly conductive layers such as skin and muscle where extravasation is much less likely to occur.

[0018] Using the detection system configuration illustrated in Fig. 1, the presence or level of a foreign material, liquid, body fluid, or substance in the subcutaneous tissue can be determined. One or more electromagnetic sources 10, typically antennae, transmit electromagnetic waves into the tissue in an area of interest, for example, a portion of an arm 100 of a human patient as shown in Fig. 1. The scattered and/or reflected electromagnetic waves are then received by the launching antenna(e), represented by the dashed line in Fig. 1, and/or by one or more receiving antenna(e) 20. A signal can be transmitted and received with a single antenna which acts as both the source and the sensing element. However, using multiple receiving antennae can be advantageous as noise, motion artifacts, and other anomalies can sometimes be more readily discerned from changes due to abnormal levels of fluid/substance of interest.

[0019] A signal is supplied to the active antenna(e) 10 from one or more signal sources 30. The signal source(s) 30 is preferably in communicative control with a data processing and the control unit 40, for example, a computer. The control unit 40 can be in communication with a user interface 50, for example, a keyboard, a monitor etc., and an alarm 60. The data processing and control unit 40 is also preferably in communication with a signal processor 70 which receives signals from the antenna 10 and/or the antenna 20.

[0020] In general, the detection system illustrated in the present application is well suited for the detection of abnormal and/or changing levels of a variety of fluids in the human body, including both body fluid and foreign substances. In several embodiments of the detection system, one or more antennae as described above can be used to determine if an extravasation has occurred during an injection procedure. Several antenna(e) designs, configurations and/or placements are described below in the context of detection or determination of extravasation.

[0021] For example, Fig. 2 illustrates the use of the detection system of Fig. 1 in the detection of an extravasation 120 during an injection procedure. The transmitting antenna 10 and the receiving antenna 20 are positioned on opposing sides of an injection site wherein a catheter 160 is positioned within, for example, a vein 110. The catheter 160 can, for example, be in operative connection with a source of pressurized injection fluid such as a syringe 170 in connection with a powered injector 180 as known in the art.

[0022] The detection system uses electromagnetic waves in the RF and microwave region, well below the optical frequency range. Applicators/antennae to transmit and/or receive electromagnetic energy for use in the present invention are, for example, resonant structures and may take on several forms including, but not limited to, the following: microstrip antenna(e), waveguide(s), hom(s); helical antenna(e) and dipole antenna(e) as known in the art. As used herein, the term "microstrip antenna" refers generally to a thin, low-profile antenna

of a wide variety of patterns including, but not limited to, linear, square, circular, annular ring, triangular, rectangular, dipole, tapered slot, planar spiral and others.

[0023] In the RF and microwave frequency electromagnetic energy ranges of detection system, resonant structures or other energy transmitting antennae interact with the tissue of interest via nearfield interactions and propagated waves. Energy is exchanged with the tissue in the nearfield and waves are propagated into the tissue. Reflections and scattering occurs at boundaries when permittivity and/or permeability variations and differences occur.

[0024] In the detection system, a measured signal is compared to a reference signal or signals to determine if an abnormal (for example, elevated) level of fluid is present in the area of tissue being monitored. A reference signal can, for example, be a baseline signal that is measured when the fluid/substance level of interest is known or in a known state. Following the baseline determination, a search mode is entered where changes in reflected or scattered waves are detected by measuring the received signal(s) and comparing them to the reference signal(s). If, for example, the measured signal deviates from the reference signal by a predetermined amount or in a predetermined manner, the alarm 60 can be activated. In an injection procedure, the injection can be stopped upon activation of the alarm 60. For example, the control unit 40 can be in communication with the powered injector 180 to stop an injection procedure upon detection of extravasation.

[0025] Measurements and signal processing can be made in the time domain and/or the frequency domain as known in the art. In the frequency domain, the signal source is generally a sinusoidal wave source in which the frequency is swept or stepped through a desired frequency range. At each frequency of interest, the magnitude and/or phase of the measured signal can be compared to the magnitude and/or phase of the reference signal to detect changes of, for example, a pre-determined amount. Alternatively, in the time domain, the signal source can be a substantially narrow impulse or sharp step that excites the resonant modes of the sending antenna(e) which in turn launch electromagnetic waves into the tissue of interest. Fluid or substance presence or level changes alter the received signal(s) such that they differ from the reference signal in terms of delay, frequency content, and/or overall shape.

[0026] The detection system also embodies other types of measurements and signal processing. When using the same antenna(e) to send and receive energy, such measurement modes can include, for example, antenna impedance or resonant mode frequency shift detection. Furthermore, more sophisticated signal processing techniques of the reference and/or received signals can be employed. For example, the signals may be mathematically manipulated, such as averaged, integrated, median filtered, band pass filtered, low pass filtered, or high pass filtered in the time or frequency domain to emphasize subtle patterns in the data that may not be as readily apparent when simple reference subtraction/comparison is performed.

[0027] In general, to compare or to make a comparison refers to making a decision or judgment based upon a relationship between two or more measurements, sets of measurements, or functions of measurements. The relationship is generally expressed as a mathematical relationship, algorithm or heuristic. For example, a comparison of magnitude or "complex distance" from a reference or baseline measurement, as further described below, can be made. It is also possible to compare the slopes or rate of change of the received and reference signals. An algorithm similar to that applied in statistical process control can, for example, be applied whereby an abnormality is judged to occur if more than a predetermined number of successive measurements, for example four successive measurements, are on one side of the reference signal, or if one measurement is outside of a standard band, or if there is a trend of a predetermined number of measurements, for example seven measurements, moving in a consistent direction. As known to those skilled in the art there, are many other comparisons that can be made.

[0028] In a first antenna array positioned about an injection site illustrated in Fig. 3, two generally linear arrays of antennae are used. In this embodiment, one array of antennae is an active, launching/transmitting, array 200 and an opposing array of antennae on the other side of the injection site is a passive, receiving, array 220. The signal source of the system excites or drives the active array 200 via, for example, amplifiers by using sinusoidal or impulse waveforms. The signal source(s) create an electromagnetic wave which is launched generally normally (perpendicularly) to the skin surface and into the subcutaneous tissue. The wave then scatters and propagates through the subcutaneous tissue (for example, through adipose/fat tissue). Tissue layers that are more conductive than fat, such as muscle and skin, tend to reflect and guide the electromagnetic energy. The antennae of the passive antennae array 220 then receive the signals which are, in turn, processed by the signal and data processing subsystems. The received or measured signals are then compared to the reference, for example baseline, signals that were collected during the baseline procedure. As discussed above, baseline measurements can be repeated or updated to create a running baseline. As known by those skilled in the art, a wide variety of microstrip antenna designs are suitable for use in the present invention including: line, square, circular, annular ring, triangular, rectangular, dipole, tapered slot, planar spiral and others. In general, any design that yields sufficient energy coupling in the preferred frequency ranges set forth above are suitable for use in detection system.

[0029] In Fig. 4A, a generally linear array 240 of transmitting microstrip antennae with a tapered-slot design are illustrated. The tapered-slot design yields improved directionality and increased bandwidth. The antennae or

array 240 are angled toward the skin of arm 100 so that the waves can be launched into the tissue, yet in the general direction toward a passive/receiving antennae 260. Use of such tapered-slot antennae can improve signal coupling and overall sensitivity.

[0030] In another embodiment of the detection system, electromagnetic waves are propagated in the vicinity of the surface of the skin or other body surface using antennae, for example arrays of antennae as illustrated in Fig. 4A, above or close to the surface. The propagated waves interact with the surface in a manner that is affected by the surface shape, geometry or morphology. This method can be useful, for example, when the tissue of interest has a thin fat layer. In this embodiment of the present invention, surface/skin deformation caused by the fluid/substance of interest can be detected by monitoring signals reflected and/or scattered by the surface. Tapered-slot antennae in a configuration similar to that shown in Fig. 4A can, for example, be used to propagate surface waves across moderately conductive skin. For example, Fig. 4B illustrates transmission of electromagnetic waves across the surface of the arm 100 by a pair of transmitting/receiving antennae 250a and 250b. Surface deformation caused by changed, elevated or abnormal fluid levels (for example, extravasation) induce a change in the signal measured by the antenna(e) 250a and 250b. Fig. 4C illustrates another embodiment in which a transmitting/receiving antenna 260 transmits electromagnetic energy generally normal to the surface of the arm 100 and receives a reflected signal. Once again, surface deformation induces a change in the measured signal. In the embodiment of Fig. 4C, separate transmitting and receiving antennae can be used as described above as either a single antenna pair or as an array of multiple transmitting/receiving antennae.

[0031] Another embodiment of a multiple antenna configuration or antenna array is shown in Fig. 5 wherein a plurality of individual antennae 310 are arranged to surround the area to be monitored. The web array of antennae 310 in Fig. 5 enables a phasing approach to concentrate the wave energy at a particular location 320. The phased drive signals to each antenna can then be altered such that the focal point 320 is moved in a scanning pattern. This phasing approach can increase the overall sensitivity of the system. Furthermore, directional couplers can be employed, as known in the art, to allow the transmitting antennae in the web array to also perform as receiving antennae simultaneously. Directional couplers are used in equipment such as network analyzers to allow the analyzer to send energy to a device, like an antenna, while simultaneously receiving reflected energy from the device/antenna. Therefore you can transmit and receive on an antenna simultaneously.

[0032] The detection system illustrated in the present application is not limited to the antenna configurations or arrays set forth above. A wide variety of antenna configurations are suitable for use in the present invention. In general, any antenna configuration positioned near the anticipated location of the liquid or substance to be detected or monitored is suitable.

[0033] For example, extravasation typically occurs in the immediate vicinity of the injection site, near the position of the catheter tip. Extravasation may sometimes occur, however, at a site remote from the injection site. In the detection system of the present application, extravasation can be detected at the injection site and at site(s) remote from an injection site (generally along a path of potential extravasation) using, for example, antennae positioned as an array along a path of potential extravasation.

[0034] Because certain body surfaces such as skin are somewhat reflective to electromagnetic waves in the frequency ranges used in the present invention, coupling the waves into the surface and tissue can improve system performance. Coupling can, for example, be improved by providing a layer of material in contact with the skin/other surface of interest (for example, the surface of an internal organ) that couples with the surface by having an intrinsic impedance similar to the surface. Such material may comprise, for example a relatively high permittivity, low-loss material, such as magnesium calcium titanium dioxide, MgCaTiO2. A disposable de-ionized water pouch can also be used. Preferably, deformation of such a water pouch or container during use thereof is limited as deformation can impact the received or measured signal. In that regard, a thin-walled, rigid water container can be used or a pressurized water pouch that limits deformation can be used. Fig. 6 illustrates a sensor 350 in accordance with the present invention wherein an intermediate, spacing or superstrate layer 360 of a coupling material as described above is in direct contact with the skin of the arm 100, while an antenna, for example, a resonant structure 370, is spaced from the skin by the intermediate or superstrate layer 360. In the embodiment of Fig. 6, resonant structure 370 is positioned within a substrate 380 and the sensor is shielded up to the transmitting/receiving face 362 of the sensor. A microstrip antenna 350' used in several studies that led to the invention of the present application was structured substantially the same as the sensor 350 but without the shielding.

[0035] Figs. 7A and 7B illustrate an embodiment of a microstrip antenna 400 in accordance with the present invention. Like the antenna 350, the antenna 400 includes a superstrate layer 410 fabricated from a coupling material and having an outer surface extending away from the substrate 430 which contacts the skin of the arm 100, see Fig. 7B. An antenna or resonant structure 420 is positioned on a substrate 430. In general, the antennae or resonant structures of the present invention are fabricated from a conductive material such as copper, silver, gold or other appropriate material as known in the art.

[0036] Preferably, the substrate material is a moderate to high permittivity, low-loss material, such as MgCaTiO2, and is often the same as the superstrate to prevent discontinuities between the substrate and the superstrate. However, prototypes with differing materials

for the superstrate layer and substrate layer have been fabricated and successfully operated. In general, any material with moderate to high permittivity values (for example, in the range of approximately 10 to approximately 100 and, more preferably, in the range of approximately 50 to approximately 80) and low-loss characteristics such that its intrinsic impedance is reasonably close to the surface of the tissue to be interrogated will be suitable. Furthermore, materials with low moisture absorption characteristics and low permittivity to temperature correlation are also desirable.

[0037] In some of the microstrip antennae used in the studies leading to the present invention, the antennae were fabricated from a ceramic laminate material coated with thin layers of copper on the front and back thereof. In particular, a product sold under the name RT/duroid® 6010LM by Rogers Corporation of Chandler, Arizona, was used. Such microwave laminates are ceramic-PTFE (polytetrafluoroethylene) composites designed for electronic and microwave circuit applications requiring a relatively high dielectric constant or permittivity. RT/duroid 6010LM laminate has a dielectric constant of 10.2 ± 0.25. The laminates used to fabricate the microstrip antennae were approximately 2.5 mm thick for the substrate and 1.25 mm for the superstrate and were supplied with both sides thereof clad with 1/2 oz./ft^2 electrodeposited copper foil (cladding thickness of approximately 16 μm - 1/4 to 2 oz./ft^2 electrodeposited copper foil available with cladding thicknesses of 8μm to 70 μm).

[0038] In fabricating the sensor elements/sensors of the present invention, some of the copper material was etched from the top of the laminate to form a generally planar microstrip antenna element or resonant structure 420, thereby forming a margin between the outer edge of the resonant structure 420 and the outer edge of the substrate 430. In that regard, a margin d (see Fig. 7A) was created between the resonant structure 420 and the periphery of the substrate 430. The copper on the bottom side of the laminate forms a ground plane 440 for the antenna 400. Side shielding 450 of a conductive material can be provided to, for example, improve tissue coupling and reduce the leakage of stray energy. In certain embodiments, stray surface waves can, for example, increase motion and other artifacts. However, such "stray" or side energy can also be used to monitor surface geometry changes as discussed above in connection with Figs. 4A through 4C. Silver side shielding was used in several antennae of studies leading to the present invention.

[0039] Side shielding 450 and ground plane 440 form an electrically conductive cavity C. Preferably, the resonant structure 420 and the cavity C resonate together in the frequency range of interest. Such resonance improves efficiency by increasing power output relative to power input for transmission, and power received relative to power available for reception for receipt. In general, margin size impacts resonance of a patch or resonant structure with a cavity. It was found by the present inventor that when the diagonal dimension 420d (see Fig. 7D) of a square resonant structure 420 is generally equal to the non-diagonal distance or side width 400w across the cavity C (total antenna width), resonant structure 42 and the cavity C resonate together in the frequency range of interest. It is believed that the first mode of the resonant structure or patch 420 resonates with the second resonant mode of the cavity C. In this embodiment, the matching of the diagonal dimension 420d with the non-diagonal distance or side width 400w, determines the size of margin d.

[0040] Although square resonant structures 410 were used in the studies resulting in the present invention, it is clear to one skilled in the art that many alternative antenna element or resonant structure geometries, including for example circular or rectangular, can be used in the sensor elements and sensors of the present invention. Circular resonant structures can, for example, provide increase bandwidth as compared to square resonant structures in certain embodiments.

[0041] Energy is supplied to the resonant structure 420 via, for example, a microcoaxial cable 460 as known in the art. Energy can be supplied to an inner corner of the resonant structure 420 to induce circular polarization which can improve coupling between antennae by decreasing the sensitivity of such coupling to the relative orientations of the antennae. In the fabrication of the antennae or sensor elements/sensors of the present invention, a base of the superstrate layer 410 was secured to the substrate 430 using an appropriate adhesive, such as a cyanoacrylate or "superglue." In that construction, potential air pockets adjacent the resonant structure 420 are filled with the superglue to substantially avoid any negative effect on transmission of the microwaves. However, an indentation corresponding to and receiving the resonant structure 420 can be formed on the underside of the superstrate layer 410. Such an indentation can also or alternately accommodate a solder bump SB formed by connection of the center conductor of the microcoaxial cable 460.

[0042] In some of the microstrip antennae used in the studies leading to the present invention, the antennae superstrate layer was fabricated from a ceramic filled PTFE laminate material reinforced with woven fiberglass available from Rogers Corporation of Chandler, Arizona under product number RO3210. That material has a dielectric constant of 10.2 ± 0.5. It was discovered that beveling the edges of the superstrate layer 410 to form a transitional periphery 421 interconnecting a base B of the superstrate layer 410 to an outer surface plateau 423 extending over at least a central portion of the superstrate layer 410 improved skin conformance and reduced motion artifacts in a measurement signal resulting from patient movement, see Fig. 7A. As illustrated, for example, in Figs. 7A and 7B, the outer edges of the superstrate layer 410 are beveled at an angle θ which is greater than 0° and less than 90°. Preferably, θ is between approximately 20° and 50°. In several of the antennae or sensor

elements/sensors studied in the Experimental Example set forth below, θ was approximately 30°. In addition to improving skin conformance/coupling, the superstrate layer 410 can have only a portion tapered so that it can also direct energy in the direction of the tapered portion, for example toward a receiving antenna in the manner of a "microwave lens" to improve transmission between antennae. Rather than a linear taper as shown in Figs. 7, 8 and 9, giving the upper surface of the superstrate layer 410 an appearance of a truncated pyramid, the taper can be a smooth curvilinear surface CS, as shown in Fig. 7E, to improve the conformance of the superstrate 410 to a patient's skin.

[0043] Fig. 7C illustrates an antenna 400' which is substantially identical to the antenna 400 except that the superstrate 410' of the antenna 400' is square, rather than being beveled or curvilinear. In comparing Figs. 7B and 7E to 7C, it is seen that the skin tissue of the arm 100 does not conform as well to the contour of the antenna 400' as it does to the contour of the antenna 400, resulting in the formation of air pockets p on the periphery of the antenna 400'. Such air pockets can, for example, scatter the microwave energy, negatively affect coupling and cause increased artifacts as a result of subject/patient motion.

[0044] Antennae of the sensor elements/sensors of the present invention can be made to have somewhat directional transmission and/or reception of microwaves by having only a portion of the transitional periphery of the outer surface of the superstrate have a generally smooth transition from the base of the superstrate to the surface plateau of the superstrate in the desired directional transmission and/or reception. For example, the antenna 400' as shown in Fig. 7C can be made to be provide directional transmission and/or receipt of microwaves by making only a portion, such as one side of the transitional periphery 411', have a generally smooth transition so that transmission and/or reception is improved in that direction, to the right side of Fig. 7C. For such antenna construction, the shield 450' should be extended as shown by the dotted lines. Thus, one or more pairs of antennae can be mated to favor transmission by one antenna and receipt by its mate.

[0045] Whether the sensors of the present invention comprise a single antenna, a pair of antennae or an array of more than two antennae, the injection site preferably remains open or available for visualization and/or palpation. The sensors and methods of the present invention readily afford such availability. As illustrated, for example, in Figs. 2, 3, 4A and 5, a plurality of antennae can be placed on the subject/patient in a disconnected state. However, it is often desirable to generally maintain a predetermined distance between antennae.

[0046] Figs. 8A through 8D illustrate a sensor 500 including a sensor support, housing or base member 505 that is shaped like a "bowtie" having first and second expanded portions or base sections 510a, 510b interconnected by a more narrow portion or flexible bridge 520. The flexible bridge 520 allows some bending and/or twisting of the first base section 510a and the second base section 510b relative to each other to conform to, for example, a patient's arm or other region of interest. The base sections 510a, 510b each receive or house an antenna 400 with the bridge 520 generally or approximately maintaining a predetermined distance or range of distances between the antennae 400, while providing the needed flexibility to conform to a patient's tissue, see, for example, Fig. 8D, and allowing access to the vicinity of the detection area, for example, an injection site in an extravasation detection.

[0047] For a number of applications, the sensor base 505 is thus preferably fabricated from a durable, flexible/resilient material having a relatively low dielectric constant. Many polymeric materials, such as, for example, polyurethane, are suitable for fabrication of the sensor base 505. In several embodiments of the sensor of the present invention, the sensor base 505 was molded from an integral piece of polyurethane. It is also contemplated that the sensor base 505 can be fabricated of more rigid materials for given applications.

[0048] It is further contemplated that the linear taper or smooth curvilinear surface, described above relative to the superstrate 410, can be formed on the sensor support, housing or base member 510a", see Fig. 8E, rather than on the superstrate 410" to assist in conforming to tissue. The superstrate 410" in such an embodiment can be made generally flat or planar over its outward transmitting/receiving surface 412". If a support, housing or base member defines the taper, linear or curvilinear, or is generally flush with the face of an antenna, such as antenna 400", the shielding 450" for antenna 400" can be extended to the transmitting/receiving face 412" of superstrate 410" as illustrated in Fig. 8E. Also see Fig. 6.

[0049] The bridge 520 maintains a separation between the first base section 510a and the second base section 510b and the respective antennae 400 to ensure suitable coupling and to provide visual and tactile access to the injection site as defined, for example, by a catheter tip.

[0050] Figs. 9A and 9B illustrate alternative embodiments of sensors 600, 700 of the present invention that provide flexibility to conform to the patient's tissue and allow access to the vicinity of the detection area, for example, an injection site in an extravasation detection application. The sensor 600 of Fig. 9A is a generally U-shaped sensor including a sensor support, housing or base member 605 having a first base section 610a and a second base section 610b connected by a bridge 620. As described above for the sensor 500, the sensor base 605 is preferably fabricated from a resilient material such as a polyurethane; however, other more rigid materials are contemplated for use in the present invention. Each of the first base section 610a and the second base section 610b supports an antenna 400 as described above.

[0051] The sensor 700 of Fig. 9B is also a U-shaped sensor including a sensor support, housing or base 705 having a first base section 710a and a second base sec-

tion 710b connected by a flexible bridge 720. The sensor base 705 is also preferably fabricated from a resilient material such as a polyurethane; however, other flexible materials and more rigid materials can be used. Each of the first base section 710a and the second base section 710b supports a linear array of antennae 400. While each of the antennae 400 are shown as being the same size, the sizes of the antennae can vary to provide various resonance frequencies of interest for the sensor or to generally increase the bandwidth of the sensor and therefore frequency range over which it is sensitive.

[0052] Each of the antennae 400 of the sensor 700 of Fig. 9B can be connected to a power source/measurement device via individual wires or connective paths. Alternatively, integrated power/signal splitters, as known in the art, can be used. In that regard, as known in the RF communications arts, power splitters can be integrated into microstrip (planar) antenna designs, such that an array of antennae located on one layer can be fed through apertures located on another layer which are in turn fed by a power splitter and feeds on a third layer. This structure allows the simultaneous feeding of multiple transmitting antennae with one input signal or connection 730. Such a splitting method is also an effective method of combining signals from multiple receiving antennae into one signal or connection 740 to be processed. Adjustments in phasing for the antennae that make up the transmitting/receiving arrays can be done during the design phase, but will be fixed once the device is fabricated. This method can offer advantages in sensors of the present invention by, for example, improving directionality and therefore signal-to-noise ratio (SNR) for the sensor.

[0053] Fig. 23 illustrates another embodiment of a sensor 750 of the present invention with sensor elements comprising opposing directional planar antennae 752. The directional planar antennae are structured similar to the antennae used in the other sensors of the present application with an antenna element 754 mounted between first and second substrates 756, 758 with shielding 759 surrounding the antennae except for the electromagnetic emitting/receiving faces adjacent to tissue 761 being sensed. However, the directional planar antennae 752 are structured to emit microwaves from the ends or edges 760 of the antennae 752 rather than from the planar faces of the antennae. Such antennae, referred to as "edge-firing" types, are well known in the art and include Yagi, Quasi-Yagi, Tapered Slot, Vivaldi and others. Fig. 24 illustrates an experimental mounting arrangement wherein the angular orientations of the antennae 752 relative to each other can be varied. Currently, an angular orientation θ' of approximately 30° to a surface of a body to be sensed, i.e., an angle θ" of approximately 120° relative to each other, is believed to be preferred; however, the specific angular orientations can be any reasonable value required for a given application and it is contemplated that different angular orientations can be used for each of the antennae.

Experimental Examples

1. Inorganic phantom experiments.

[0054] Several experiments demonstrating the use of the sensors of the present invention were carried out using single and dual microstrip patch antenna configurations and an inorganic phantom to represent human tissue. Such inorganic phantoms provide the opportunity to accurately control both the position and amount of a simulated extravasation in an environment of generally known and simple dielectric properties as compared to human tissue.

[0055] Below approximately 1 GHz, the wavelength becomes too large to provide adequate sensitivity to changes of interest in the tissue and approaching and, beyond 10GHz, the penetration of the waves into the tissue becomes too small to provide adequate sensing depth. Thus, the antennae of the present invention that were used for this experiment were designed to resonate at an intermediate frequency of approximately 4 Ghz.

[0056] The microstrip antennae used in the studies leading to the present invention were designed using Finite Difference Time Domain (FDTD), a well known modeling technique. Standard equations, generally available for well-understood geometries, were used to determine approximate dimensions required for the resonant structures of the various antennae in the studies resulting in the present invention. Following that, substrate thickness was chosen to be a fraction of the wavelength corresponding to the primary resonant mode of the resonant structure. Finally, FDTD simulation techniques were used to refine dimensions and determine the best location for the feed connection. A FDTD software package available from Remcom Inc. of State College, Pennsylvania was used for the design of the antennae which were then etched and fabricated using well known laboratory techniques. As known in the art, moving a feed point outward towards the edge of a square resonant patch will (to, for example, induce circular polarization) increases the impedance of the antenna. Ultimately an impedance similar to the driving circuitry is desired to maximize power transfer.

[0057] The microstrip antennae included a ceramic material coated with thin layers of copper for the resonant structure and ground plane as described above in connection with Figs. 6 and 7A-7E. As known to those skilled in the art, other materials, such as gold or silver, can be used for the resonant structure. The phantom 800 included emulated skin 810, comprising carbon-loaded foam, an emulated fat layer 820, comprising glycerin, and a movable, emulated muscle bundle 830, comprising "Ultravist 370" contrast medium or contrast agent available from Schering AG of Berlin, Germany as illustrated in Figs. 10 and 11. The emulation materials were chosen to approximate the dielectric properties of the tissues to be emulated.

[0058] As illustrated in Figs. 12 and 13, single and dual

patch antenna configurations were arranged on the phantom 800. An HP8510C network analyzer 900 was used to generate a source signal and to determine the response of the antenna(e) 350' (see Fig. 6 and description above). Extravasation was emulated by filling a balloon 850 with Ultravist 370 contrast medium. The balloon 850 was filled via tubing 860 in fluid connection with a source of contrast medium (not shown). The thickness of the emulated fat layer 820 in the configuration shown in Figs. 10 and 11 was approximately 8mm. The balloon 850 was filled with the contrast agent Ultravist 370 and placed between the muscle bundle 830 and the skin layer 810.

[0059] The microstrip patch antennae 350', 350 were designed to couple efficiently into tissue as described in connection with Fig. 6. By spacing the resonating patch element 370 from the skin layer 810 as illustrated in Fig. 6, one can reduce near-field loading. Furthermore, by using high-permittivity ceramic material in the superstrate 360 to provide this non-conductive spacing and intrinsic impedance matching, energy coupling into tissue can be increased. In these experiments of the sensors of the present invention, the substrate thickness was approximately 2.5 mm and the superstrate thickness was approximately 1.5 mm. The relative permittivity values at 5GHz for each of the substrate 380 and the superstrate 360 were 10.2 and 20, respectively.

1A. Single Patch Antenna Experiments

[0060] In these experiments, a single antenna 350' was applied to phantom 800 generally directly over the extravasation site, i.e., the balloon 850. The configuration is shown in Fig. 12. The emulated skin 810 and the muscle bundle 830 were both in place during these experiments. S_{11} measurements, i.e., microwaves transmitted on a first antenna, port 1, and received on the same antenna, port 1, were made using network analyzer 900 to detect changes in the reflected energy created by the antenna 300. The results from these experiments are shown in Fig. 13. The baseline in the experiments corresponded to having the balloon 850 filled with approximately 1-2cc of Ultravist 370.

1B. Dual Patch Antenna Experiments

[0061] The setup for the dual patch antenna configuration is shown in Fig. 14. First, S_{11} measurements were made with each of the patch antennae 350' to determine if the antennae 350' resonated at similar frequencies and, therefore, coupled effectively. The results of these measurements are shown in Fig. 15. There was overlap in primary resonance modes for each antenna and sufficient S_{21} coupling, i.e., microwaves transmitted on a first antenna, port 1, and received on a second antenna, port 2, occurred, although the match was not optimized and can be readily improved to further increase coupling.

[0062] The separation between the substrates 380 of the antennae in the dual patch antenna configuration of Fig. 14 was approximately 1.0 cm, and the separation between active resonant elements 370 was approximately 2.5 cm. As clear to one skilled in the art, the substrate size can be changed, and separation distance can be changed. Parameters such as directionality, tissue coupling, data processing and signal processing were not optimized in these experiments. The results for the dual antenna configuration are shown in Fig. 16. The baseline in this experiment corresponded to having the balloon 850 filled with approximately 1-2cc of Ultravist 370.

[0063] The results of each of the single antenna experiments and the dual antenna experiments indicate that elevated fluid levels are readily detectible using the sensors of the present invention in the detection system of the present application by comparison of a measured signal to a reference signal.

2. Organic phantom experiments.

[0064] Although the inorganic phantom experiments described above indicate the sensitivity of the sensors of the present invention to even slightly elevated fluid levels, emulation of the "lossy" dielectric nature of human skin using synthetic, inorganic materials is difficult. Thus, further experiments were conducted on organic phantoms to confirm the sensitivity of the sensors of the present invention to elevated or changing fluid levels in organic tissue. In these experiments, chicken skin/tissue was chosen as a model for human skin/tissue on the basis of similarity in permittivity between chicken tissue and human tissue. In general, human skin varies in thickness from approximately 0.6 to 1.0 mm whereas chicken skin is approximately 0.4 mm thick. Experiments were thus performed with chicken phantoms having a single skin layer and a double skin layer, to better emulate human skin.

[0065] In several experiments on chicken skin/tissue phantoms, the bowtie sensors 500 were used to measure change during simulated extravasation using Ultravist 370 contrast medium. In several sensors 500 used in the studies leading to the present invention, the spacing between the antennae 400 was approximately 1.5 cm. Inner corner feeds were used to induce circular polarization. The substrate thickness was approximately 2.5 mm. The superstrate thickness, the distance between the resonant patch 410 and the outer surface plateau of the superstrate 420, was approximately 1.25 mm. The resonant structure 410 was square with a side length and width of approximately 8mm. Margin widths d were approximate 2mm. Taper angle θ of the superstrate 420 was approximately 30°.

[0066] Fig. 17 illustrates attachment of the sensor 500 to a chicken phantom 1000. The chicken phantom 1100 was wrapped tightly in plastic wrap 1100 for purposes of sanitation and to assist in maintaining the shape of the phantom. The sensor 500 was positioned on top of the

plastic wrap 1100. Double sided adhesive tape 475, see Fig. 7B, available from 3M under product number/name 1512, was applied to the bottom of the sensor 500 before being coupling to chicken phantom 1000. In some studies, superglue was also placed between the double-sided tape 475 and the plastic wrap 1100. Adhesive tape 575, see Fig. 8D, was placed over the sensor 500 to secure the sensor 500 to the chicken phantom 1000. Ultravist 370 contrast medium was injected/extravasated into chicken phantom 1000 via a catheter 1200 connected to a VISTORON CT® injector 1300 available from Medrad, Inc. of Indianola, Pennsylvania via flexible tubing 1210.

[0067] Use of the injector 1300 enabled accurate control of flow rate and volume of injected contrast medium. Contrast medium was injected at a flow rate of 2.5 cc/sec up to a volume of 10 cc. Fig. 18 illustrates data in several forms taken over a frequency range of 1 to 9 Ghz from a single-skin chicken phantom using the sensor 500 as described above. In that regard, Fig. 18 sets forth S_{11} and S_{22} data, i.e., microwaves transmitted on a second antenna, port 2, and received on the second antenna, port 2, S_{21} magnitude data, "complex distance" data, S_{21} delta magnitude data and delta phase from baseline data.

[0068] Of the above manners of expressing measured signal data, "complex distance" is believed to provide a direct relationship between extravasated volume and output. Other calculations that exhibit relationships to extravasation or fluid level change include, but are not limited to, changes from the reference (baseline) in S_{21} magnitude and S_{21} phase. Figs. 19A-19C illustrate "complex distance" as a function of frequency and volume injected in the upper graphs. The lower graphs of Figs. 19A-19C set forth the maximum "complex distance" over the measured range frequencies as a function of volume.

[0069] Fig. 20 provides a graphic illustration of a "complex distance" algorithm used in the studies leading to the present invention for a single frequency. The algorithm utilizes magnitude and phase information and enhances signal processing in frequency regions where signal coupling is strong. In one embodiment of the algorithm, a reference or baseline signal (corresponding to 0 cc of injected contrast medium, for example) is first measured at each frequency or band of frequencies to be investigated. The magnitude and phase data are converted to complex form, i.e., x + yi, and processed as illustrated by Fig. 20, wherein the complex data points are plotted on a complex plane having its abscissa as the real (Re) part, x, and its ordinate as the imaginary (Im) part, y. The reference or baseline magnitude and phase measurements thus become points in the complex plane. The magnitude and phase for measured data points are similarly converted to complex form and also plotted on the complex plane to become measured data points. The scalar distance between each baseline point and each measured data point at the corresponding frequency is determined and each of these distances are referred to herein as a "complex distance," see Fig. 20.

[0070] An alarm threshold can be defined for each frequency so that a plurality of alarm thresholds corresponding to the frequencies of the range of frequencies of interest can be defined. Each given alarm threshold forms a circle around a baseline point having a radius of some pre-determined value that is above levels caused by random noise or normal motion disturbances corresponding to the alarm threshold, see the dashed circular line forming an alarm loci in Fig. 20. The reference or baseline points can be reestablished as necessary during use of a sensor.

[0071] Rather than compare each point of measured data to a baseline point, as suggested by Fig. 20, it is also possible to determine a complex baseline curve across a given range of frequencies and also a "complex distance" curve across the same given range of frequencies. The area under the "complex distance" curve can then be determined and compared to a pre-determined threshold value that is above levels caused by random noise or normal motion disturbances. More particularly, for this embodiment, the calculation of the area under the "complex distance" curve across a frequency range of interest yields one number that is compared to a reference or baseline number that can be found with the same technique, i.e., by calculating the area under a reference or baseline curve across the frequency range of interest.

[0072] In other words, the "complex distances" at the various frequencies are calculated. At that step, instead of comparing each "complex distance" to the threshold at that point, one integrates all of the "complex distances" in the frequency range of interest, providing the area under the curve. The resultant value is compared to a threshold number corresponding to the area under the reference or baseline curve across the frequency range of interest. Under the algorithm illustrated in Fig. 20, a single "complex distance" at some frequency crossing the threshold can trigger an alarm. In the case of comparison of integrated areas, however, a sufficiently strong single "complex distance" or a group of such "complex distances" are required to create a sum/integral that exceeds a threshold value. It is also possible, for example, to accumulate individual "complex distance" comparisons with their corresponding thresholds and determine that an alarm will be indicated only if a predetermined number of the "complex distances" have exceeded their thresholds.

[0073] It has been found that variations in the measurement signals occur among different humans and among different anatomical sites on the same human for the same level of extravasation. Thus, for a given volume of extravasation in, for example, two different tissue anatomies, the "complex distance" calculation may yield significantly different values. To correct for such differences, the baseline or reference S_{21} magnitude curves are normalized by multiplying every point in the reference S_{21} curve to force the peak value (or area under the curve) to equal one and then multiplying all subsequent measurement curves, curves created during actual operation

of the detection system, by the same factor. Such normalization has been found to make the "complex distance" values more consistent when similar subcutaneous tissue changes occur in two different human subjects or in two different anatomical sites on the same human.

[0074] Figs. 19A and 19B correspond to experiments with double skin chicken phantoms 1000, while Fig. 19C corresponds to an experiment with a single skin chicken phantom 1000. The data of Fig. 18 and Fig. 19C are taken from the same experiment.

[0075] In Fig. 19A a gradual signal increase is observed as the volume of injected contrast medium increases. In Fig. 19B, a signal plateau is reached at injection of approximately 2 cc of contrast medium, indicative of signal saturation in the field of the sensor. In Fig. 19C, the signal increases to a maximum at approximately 4 cc of injected contrast medium and then subsequently decreases as more contrast medium is injected. It is believed, that tissue rupture may have led to dissipation of contrast medium from the tissue in the field of the sensor 500 in the experiment of Figs. 18 and 19C. Figs. 19A through 19C indicate that the sensors of the present invention are sensitive to even small volumes of fluid in organic tissue. Moreover, it is possible that even information regarding the nature of, for example, an extravasated bolus of fluid can be provided by the sensors of the present invention. In that regard, the shape of the "complex distance" curve can, for example, indicate whether the fluid is pooled in the field of the sensor or dissipated therefrom.

3. Human subject experiments.

[0076] The sensor 500 was also studied in several experiments with human subjects. In several such studies, signal output was measured at six different sites, for example side, abdominal, and upper forearm areas, having varying fat layer thicknesses as determined by skin fold measurements. Such measurements indicated fat layers of 2.5, 3.0, 4.0, 5.0, 8.0 and 12.0 mm.

[0077] Figs. 21A and 21B set forth S_{11} and S_{22} data, S_{21} magnitude data, "complex distance" data, S_{21} delta magnitude data and delta phase from baseline data for each of the fat layer thicknesses over a frequency range of approximately 1 to 9 GHZ in two studies. The data demonstrate good skin and fat penetration of the energy of the sensor 500 into human tissue at all the fat thicknesses studied.

[0078] The effect of patient motion on the output signal of the sensor 500 was also studied. In these experiments, the underside of the sensor 500, including the antennae 400, was covered with double-sided adhesive tape 475 as illustrated in connection with Fig. 7A. In several experiments, the double-sided tape was then placed in direct contact with the patients skin in the area of the antecubital fossa. Adhesive tape 575 was then placed over the sensor 500. The subject's arm was strapped in a jig to limit certain arm movements and the subject was led through six different arm position. In position 1 or the baseline position, the subject extended his or her arm to a straight position with the palm open and facing inward. In position 2, the subject clenched his or her fist. In position 3, the subject bent his or her elbow approximately 45° inward and opened his or her hand. In position 4, the subject maintained the elbow angle of position 3 and clenched his or her fist. In position 5, the subject maintained the elbow angle of positions 3 and 4 and supanated the wrist. In position 6, the arm was straightened and the wrist flexed.

[0079] Figs. 22A and 22B set forth S_{11} and S_{22} data, S_{21} magnitude data, "complex distance" data, S_{21} delta magnitude data and delta phase from baseline data for each of the above positions over a frequency range of approximately 1 to 9 GHZ in two studies. The data demonstrate that the effect of patient motion on the output signal or motion artifact is not large as compared to the signal effect of fluid introduction found in the phantom studies. Thus, motion artifacts will not present a substantial problem in, for example, detection of extravasation, and the effects of such artifacts can be further reduced via data manipulation such as averaging. In the studies of Fig. 22B, precaution was taken to prevent contact and excessive motion of the cable leads to the antennae 400. Such precautions were found to decrease motion artifacts as compared to the studies of Fig. 22A. It was determined that stray energy transfer traveling on the outside of the cables or crosstalk can cross from one cable to the other and back down to the opposite antenna(e). In this scenario, the motion of the cables will impact this stray energy and therefore its impact on the measurement signal. Furthermore, stray energy emitted by the transmitting antenna(e) can be reflected by nearby moving body parts such that the amount of stray energy scattered to the receiving antenna(e) can vary and impact the measured signal. Techniques such as proper shielding to minimize stray energy leakage and reception are therefore desirable. In addition to preventing contact and excessive motion of cable leads, it is also possible to user wireless transmission to reduce artifact.

[0080] Although the present invention has been described in detail in connection with the above embodiments and/or examples, it is to be understood that such detail is solely for that purpose and that variations can be made by those skilled in the art without departing from the invention. The scope of the invention is indicated by the following claims rather than by the foregoing description. All changes and variations which come within the meaning and range of equivalency of the claims are to be embraced within their scope.

Claims

1. A method of detecting a change in the level of fluid in tissue of a body comprising the steps of:

applying electromagnetic energy in the frequency range of approximately 300 MHz to approximately 30 GHz to a volume of the body over a period of time;
coupling at least one sensor element to skin of the body, wherein the at least one sensor element is a component of a detection system;
receiving, by a generally planar antenna element of the at least one sensor element of the detection system, a resultant signal from the body;
measuring the resultant signal; and
comparing the resultant signal to a reference signal to determine if fluid level in the tissue has changed during the period of time,
characterized in that
the sensor element comprises a housing with a substrate mounted within the housing, and a superstrate mounted to the substrate, wherein the generally planar antenna element is accommodated and mounted between the substrate and the superstrate; and **in that**
the at least one sensor element is secured to body tissue by adhesive that is included by the outer surface of the superstrate.

2. The method of Claim 1 wherein the reference signal is a baseline signal measured in the volume of the body.

3. The method of Claim 1 or 2 wherein the step of applying electromagnetic energy includes the step of coupling at least one transmitter with skin.

4. The method of Claim 3 wherein the at least one transmitter includes a generally planar antenna element.

5. The method of Claim 3 or 4 wherein the at least one transmitter includes a superstrate adjacent a resonant structure having an impedance suitable to couple with skin.

6. The method of Claim 5 wherein; the edges of the at least one transmitter are bevelled to conform to skin.

7. The method of Claim 6 wherein the at least one transmitter superstrate comprises a tapered portion.

8. The method of any of Claims 1 to 7 wherein the superstrate of the at least one sensor element is adjacent the resonant structure and has an impedance suitable to couple with skin.

9. The method of Claim 8 wherein the edges of the at least one sensor element superstrate are bevelled to conform to skin.

10. The method of Claim 9 wherein the at least one sensor element superstrate comprises a tapered portion.

11. The method of any one of Claims 3 to 10 wherein the at least one transmitter is an antenna including a first generally planar resonant structure and the at least one sensor element is an antenna including a second generally planar resonant structure, the at least one transmitter being connected to a first base member and the at least one sensor element being connected to a second base member, the first base member and the second base member being connected by a flexible bridge.

12. The method of any one of Claims 2 to 11 wherein the step of comparing the measured signal to the baseline signal includes the step of calculating a complex distance between the measured signal and the baseline signal.

13. The method of any one of Claims 1 to 12 further comprising calculating an area under a complex distance curve across a frequency range of interest, and comparing the calculated area to the area under a baseline curve over the frequency range of interest.

14. Method of use of an injection system;
the system comprising:

an injector suitable for injecting a fluid into a vascular structure in a body;
at least a first transmitter including an antenna to transmit electromagnetic energy to a volume of the body;
at least a first receiver to measure a returned signal; and
a signal processor in communication with the first receiver;
the method comprising the steps of detecting a change in the level of fluid in tissue according to claim 1;

wherein a reference signal is created by transmitting electromagnetic energy into the volume of the body prior to an injection and measuring a resultant signal; and
wherein the processor is configured to compare the returned signal to the reference signal to determine if the level of fluid in tissue outside the vascular structure has changed.

Patentansprüche

1. Verfahren zum Nachweisen einer Veränderung der Menge an Fluid in Gewebe eines Körpers, umfassend die Schritte:

Anlegen von elektromagnetischer Energie in dem Frequenzbereich von etwa 300 MHz bis etwa 30 GHz an ein Volumen des Körpers über einen Zeitraum;
Koppeln wenigstens eines Sensorelements an Haut des Körpers, wobei das wenigstens eine Sensorelement eine Komponente eines Nachweissystems ist;
durch ein im Wesentlichen ebenes Antennenelement des wenigstens einen Sensorelements des Nachweissystems Empfangen eines resultierenden Signals von dem Körper;
Messen des resultierenden Signals; und
Vergleichen des resultierenden Signals mit einem Referenzsignal, um zu bestimmen, ob sich die Menge an Fluid in dem Gewebe während des Zeitraums verändert hat,
dadurch gekennzeichnet, dass
das Sensorelement ein Gehäuse mit einem innerhalb des Gehäuses angebrachten Substrat und einem an dem Substrat angebrachten Superstrat umfasst, wobei das im Wesentlichen ebene Antennenelement zwischen dem Substrat und dem Superstrat angeordnet und angebracht ist; und dass das wenigstens eine Sensorelement durch Klebstoff, der an der Außenoberfläche des Superstrats enthalten ist, an Körpergewebe befestigt wird.

2. Verfahren gemäß Anspruch 1, wobei das Referenzsignal ein in dem Volumen des Körpers gemessenes Grundliniensignal ist.

3. Verfahren gemäß Anspruch 1 oder 2, wobei der Schritt des Anlegens von elektromagnetischer Energie den Schritt des Koppelns wenigstens eines Senders mit Haut umfasst.

4. Verfahren gemäß Anspruch 3, wobei der wenigstens eine Sender ein im Wesentlichen ebenes Antennenelement umfasst.

5. Verfahren gemäß Anspruch 3 oder 4, wobei der wenigstens eine Sender ein Superstrat benachbart zu einer Resonanzstruktur umfasst, das eine zum Koppeln mit Haut geeignete Impedanz aufweist.

6. Verfahren gemäß Anspruch 5, wobei die Ränder des wenigstens einen Sendersuperstrats abgeschrägt sind, um sich an Haut anzupassen.

7. Verfahren gemäß Anspruch 6, wobei das wenigstens eine Sendersuperstrat einen sich verjüngenden Teil umfasst.

8. Verfahren gemäß einem der Ansprüche 1 bis 7, wobei das Superstrat des wenigstens einen Sensorelements benachbart zu der Resonanzstruktur liegt und eine zum Koppeln mit Haut geeignete Impedanz aufweist.

9. Verfahren gemäß Anspruch 8, wobei die Ränder des wenigstens einen Sensorelement-Superstrats abgeschrägt sind, um sich an Haut anzupassen.

10. Verfahren gemäß Anspruch 9, wobei das wenigstens eine Sensorelement-Superstrat einen sich verjüngenden Teil umfasst.

11. Verfahren gemäß einem der Ansprüche 3 bis 10, wobei der wenigstens eine Sender eine Antenne ist, die eine erste im Wesentlichen ebene Resonanzstruktur enthält, und das wenigstens eine Sensorelement eine Antenne ist, die eine zweite im Wesentlichen ebene Resonanzstruktur enthält, wobei der wenigstens eine Sender mit einem ersten Basiselement verbunden ist und das wenigstens eine Sensorelement mit einem zweiten Basiselement verbunden ist, wobei das erste Basiselement und das zweite Basiselement durch eine flexible Brücke verbunden sind.

12. Verfahren gemäß einem der Ansprüche 2 bis 11, wobei der Schritt des Vergleichens des gemessenen Signals mit dem Grundliniensignal den Schritt des Berechnens eines komplexen Abstands zwischen dem gemessenen Signal und dem Grundliniensignal umfasst.

13. Verfahren gemäß einem der Ansprüche 1 bis 12, ferner umfassend Berechnen einer Fläche unter einer komplexer-Abstand-Kurve über einen Frequenzbereich von Interesse und Vergleichen der berechneten Fläche mit der Fläche unter einer Grundlinienkurve über den Frequenzbereich von Interesse.

14. Verfahren zum Verwenden eines Injektionssystems; wobei das System umfasst:

einen Injektor, der zum Injizieren eines Fluids in eine Gefäßstruktur eines Körpers geeignet ist;
wenigstens einen ersten Sender, der eine Antenne zum Senden von elektromagnetischer Energie an ein Volumen des Körpers enthält;
wenigstens einen ersten Empfänger zum Messen eines Antwortsignals;
und
einen Signalprozessor in Kommunikation mit dem Empfänger;
wobei das Verfahren die Schritte des Nachweisens einer Veränderung der Menge an Fluid in Gewebe gemäß Anspruch 1 umfasst;
wobei ein Referenzsignal durch Senden von elektromagnetischer Energie in das Volumen des Körpers vor einer Injektion und Messen ei-

nes resultierenden Signals erzeugt wird; und
wobei der Prozessor dafür gestaltet ist, das Antwortsignal mit dem Referenzsignal zu vergleichen, um zu bestimmen, ob sich die Menge an Fluid in Gewebe außerhalb der Gefäßstruktur verändert hat.

Revendications

1. Procédé de détection d'un changement du niveau de fluide dans un tissu d'un corps comprenant les étapes de :

couplage d'une énergie électromagnétique dans la plage de fréquences d'approximativement 300 MHz à approximativement 30 GHz à un volume du corps sur une période de temps ;
couplage d'au moins un élément de capteur à la peau du corps, dans lequel l'au moins un élément de capteur est un composant d'un système de détection ;
réception, par un élément d'antenne généralement plan de l'au moins un élément de capteur du système de détection, d'un signal résultant en provenance du corps ;
mesure du signal résultant ; et
comparaison du signal résultant à un signal de référence pour déterminer si un niveau de fluide dans le tissu a changé pendant la période de temps,
caractérisé en ce que
l'élément de capteur comprend un boîtier avec un substrat monté au sein du boîtier, et un superstrat monté sur le substrat, dans lequel l'élément d'antenne généralement plan est logé et monté entre le substrat et le superstrat ; et **en ce que** l'au moins un élément de capteur est arrimé à un tissu corporel par un adhésif qui est inclus par la surface externe du superstrat.

2. Procédé selon la revendication 1, dans lequel le signal de référence est un signal de ligne de base mesuré dans le volume du corps.

3. Procédé selon la revendication 1 ou 2, dans lequel l'étape d'application d'une énergie électromagnétique comporte l'étape de couplage d'au moins un émetteur avec la peau.

4. Procédé selon la revendication 3, dans lequel l'au moins un émetteur comporte un élément d'antenne généralement plan.

5. Procédé selon la revendication 3 ou 4, dans lequel l'au moins un émetteur comporte un superstrat adjacent à une structure résonante ayant une impédance appropriée pour se coupler à la peau.

6. Procédé selon la revendication 5, dans lequel les bords de l'au moins un superstrat d'émetteur sont biseautés pour se conformer à la peau.

7. Procédé selon la revendication 6, dans lequel l'au moins un superstrat d'émetteur comprend une portion effilée.

8. Procédé selon l'une quelconque des revendications 1 à 7, dans lequel le superstrat de l'au moins un élément de capteur est adjacent à la structure résonante et a une impédance appropriée pour se coupler à la peau.

9. Procédé selon la revendication 8, dans lequel les bords de l'au moins un superstrat d'élément de capteur sont biseautés pour se conformer à la peau.

10. Procédé selon la revendication 9, dans lequel l'au moins un superstrat d'élément de capteur comprend une portion effilée.

11. Procédé selon l'une quelconque des revendications 3 à 10, dans lequel l'au moins un émetteur est une antenne comportant une première structure résonante généralement plane et l'au moins un élément de capteur est une antenne comportant une seconde structure résonante généralement plane, l'au moins un émetteur étant raccordé à un premier organe de base et l'au moins un élément de capteur étant raccordé à un second organe de base, le premier organe de base et le second organe de base étant raccordés par un pont flexible.

12. Procédé selon l'une quelconque des revendications 2 à 11, dans lequel l'étape de comparaison du signal mesuré au signal de ligne de base comporte l'étape de calcul d'une distance complexe entre le signal mesuré et le signal de ligne de base.

13. Procédé selon l'une quelconque des revendications 1 à 12, comprenant en outre le calcul d'une aire sous une courbe de distance complexe à travers une plage de fréquences d'intérêt, et la comparaison de l'aire calculée à l'aire sous la courbe de ligne de base sur la plage de fréquences d'intérêt.

14. Procédé d'utilisation d'un système d'injection, le système comprenant :

un injecteur approprié pour injecter un fluide dans une structure vasculaire dans un corps ;
au moins un premier émetteur comportant une antenne pour transmettre une énergie électromagnétique à un volume du corps ;
au moins un premier récepteur pour mesurer un signal retourné ;
et

un processeur de signal en communication avec le premier récepteur ;
le procédé comprenant les étapes de détection d'un changement du niveau de fluide dans un tissu selon la revendication 1 ;
dans lequel un signal de référence est créé par transmission d'une énergie électromagnétique dans le volume du corps avant une injection et mesure d'un signal résultant ; et
dans lequel le processeur est configuré pour comparer le signal retourné au signal de référence pour déterminer si le niveau de fluide dans le tissu à l'extérieur de la structure vasculaire a changé.

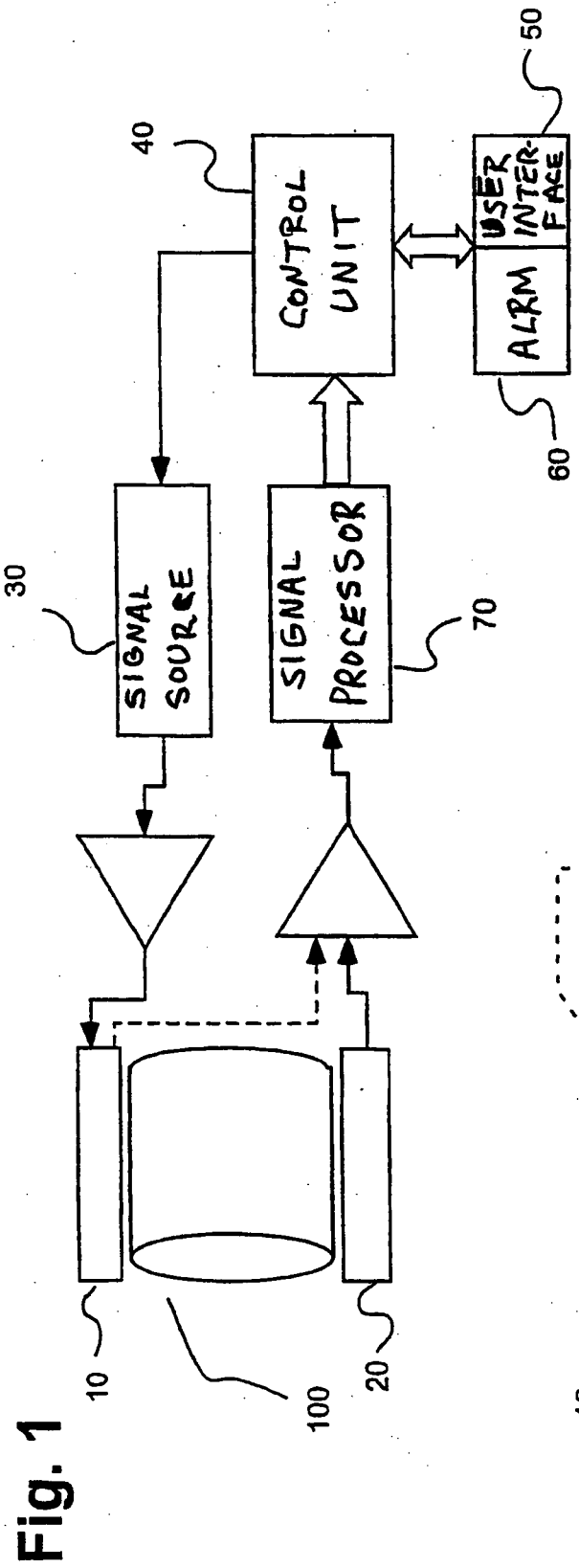

CONTROL UNIT
USER INTER-FACE
ALRM
SIGNAL SOURCE
SIGNAL PROCESSOR
40
50
60
30
70
10
100
20

Fig. 1

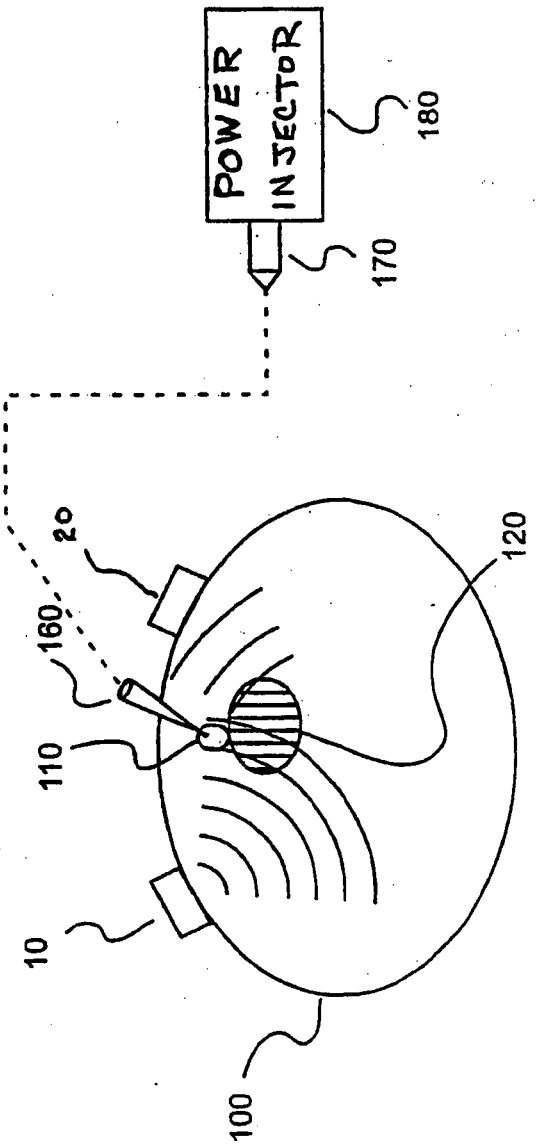

POWER INJECTOR
180
170
20
160
110
120
10
100

Fig. 2

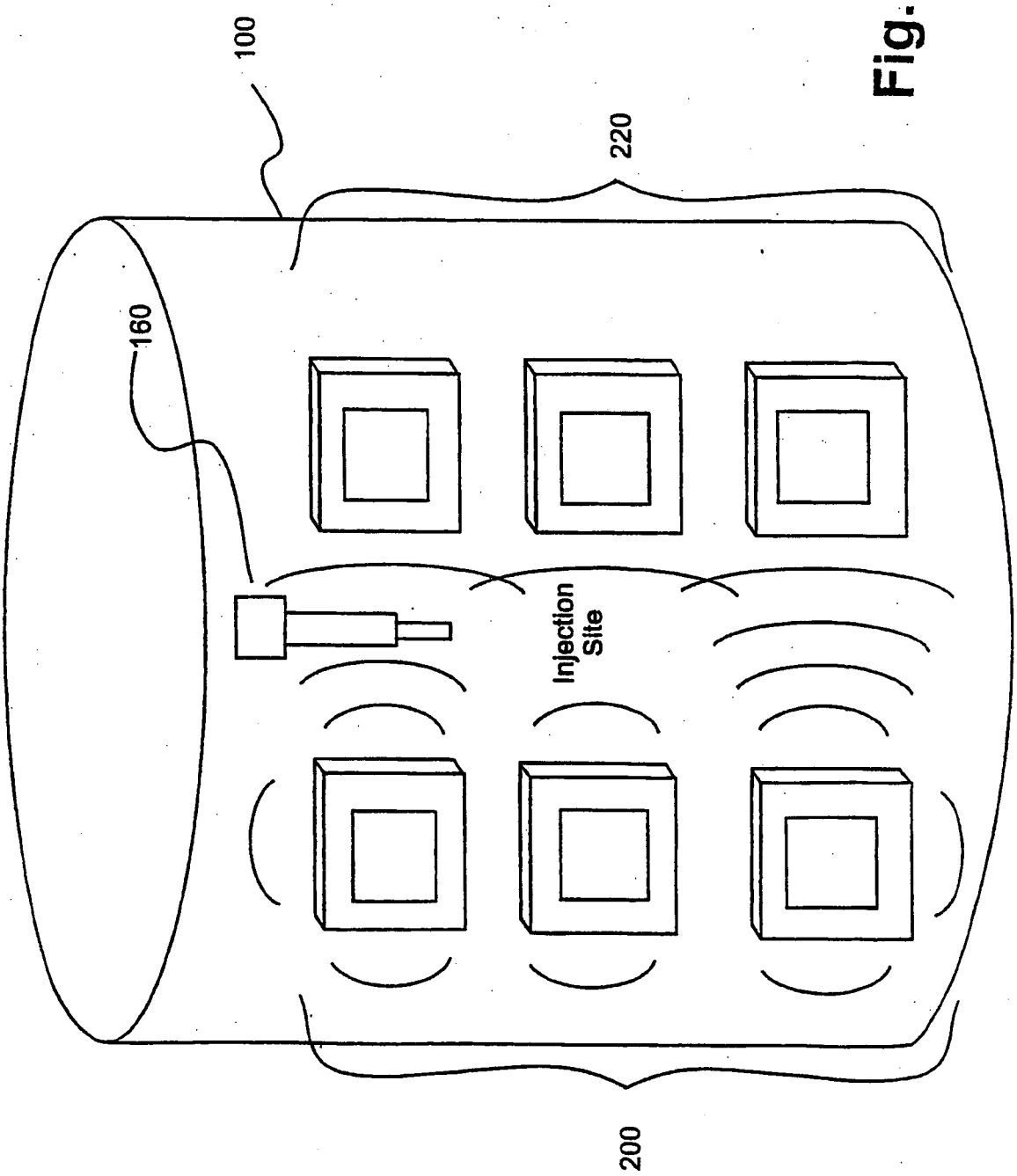


Fig. 3

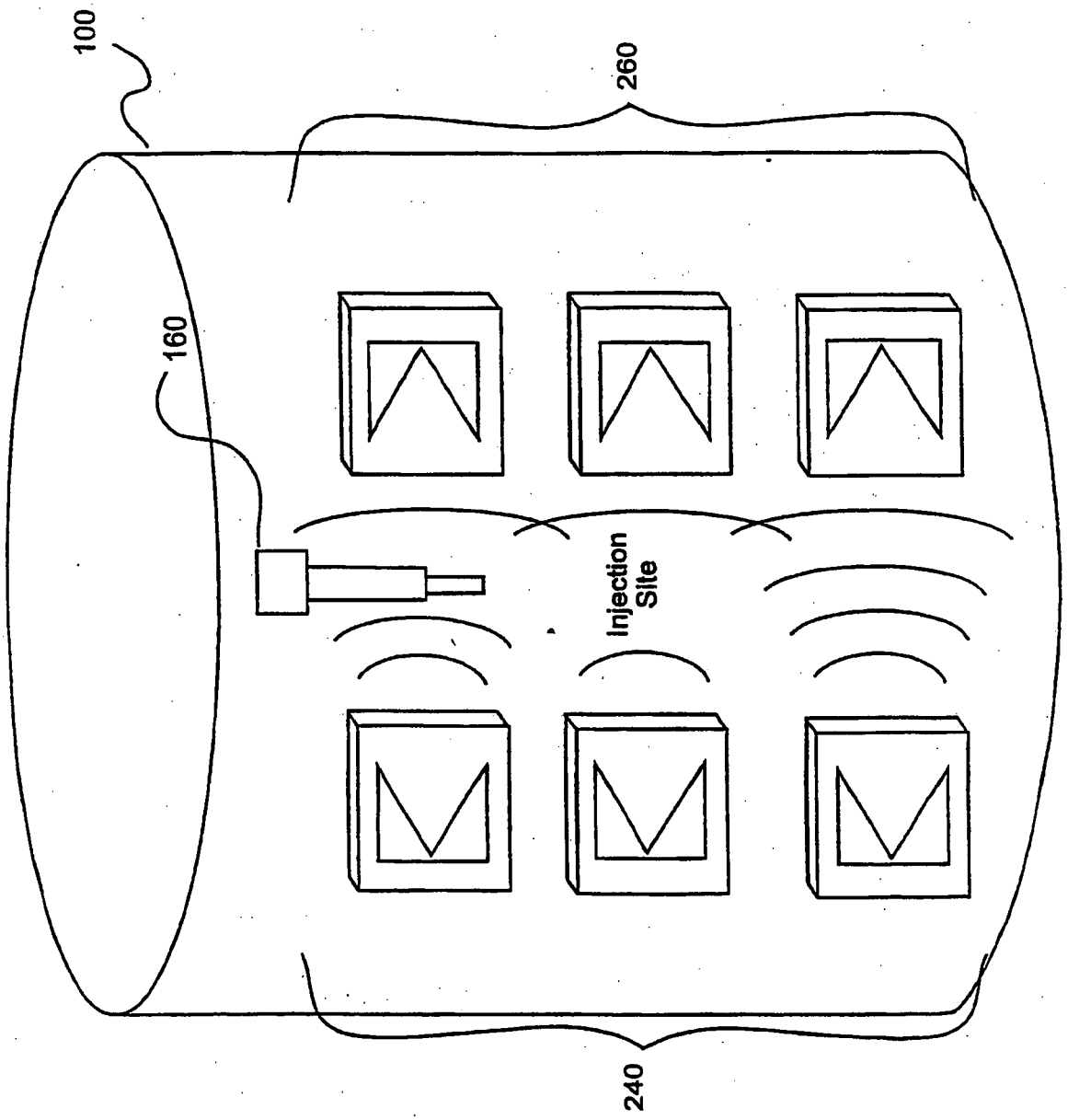


Fig. 4A

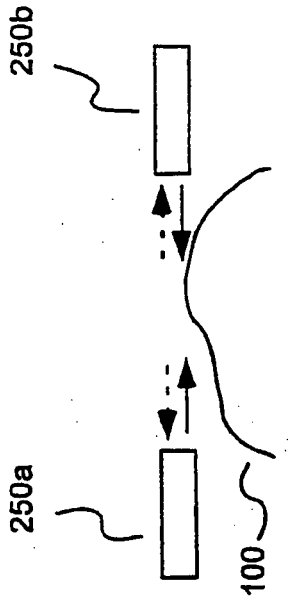


Fig. 4B

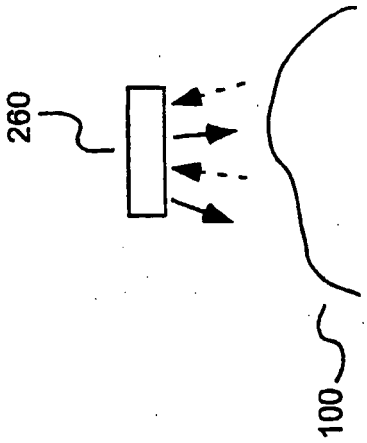
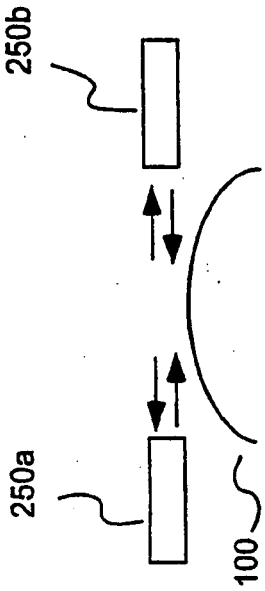
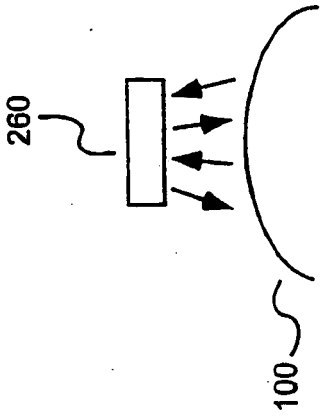


Fig. 4C





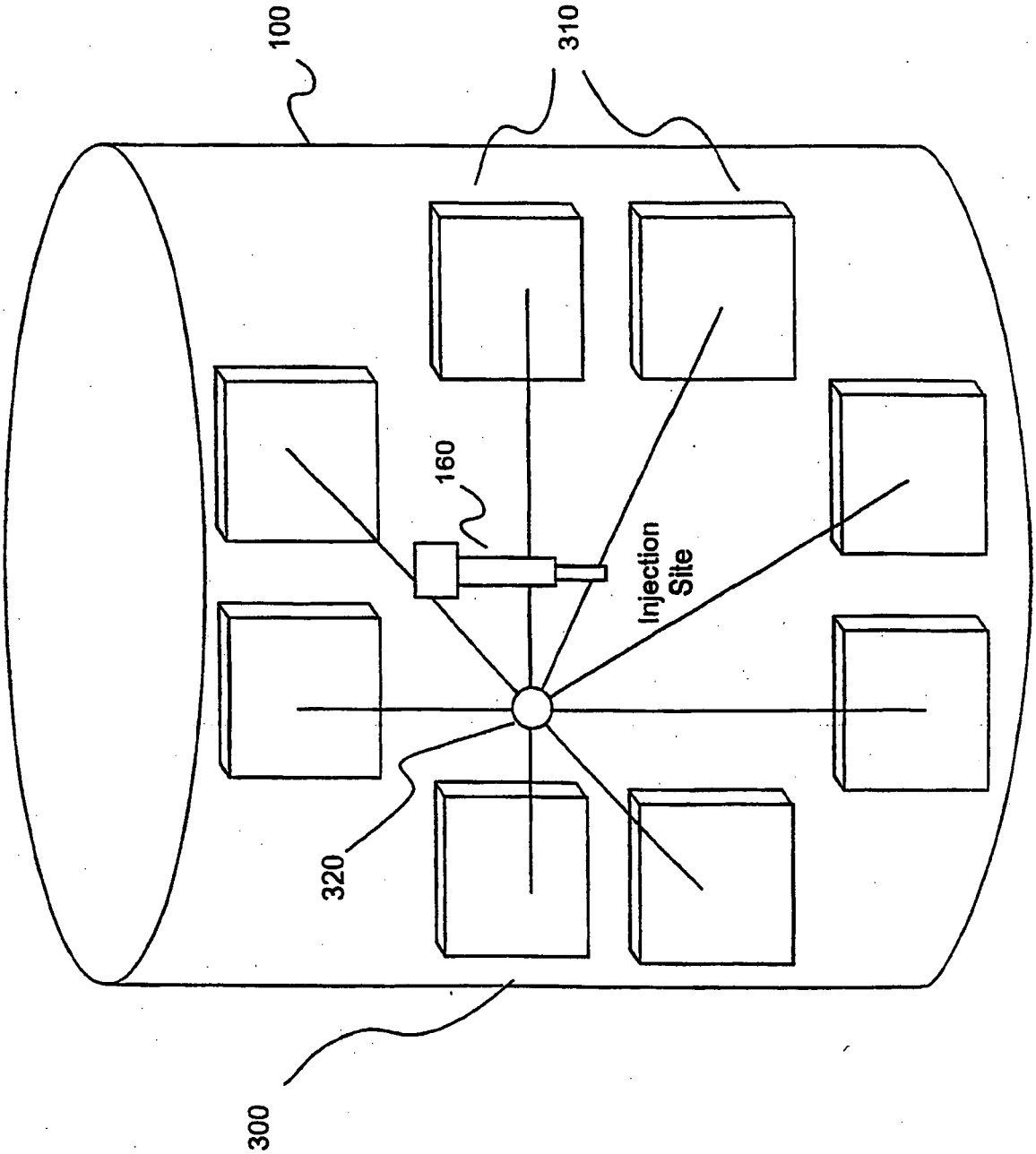


Fig. 5

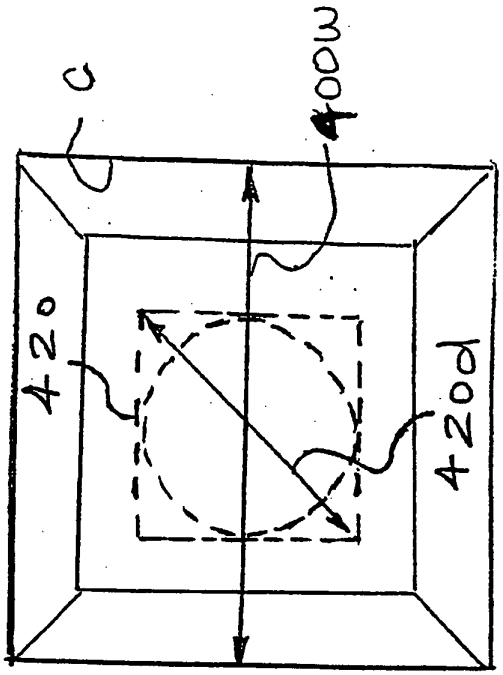


FIG. 7D

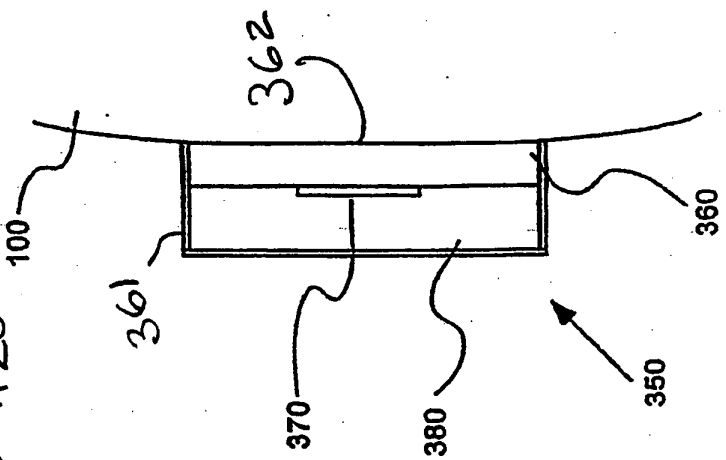


Fig. 6

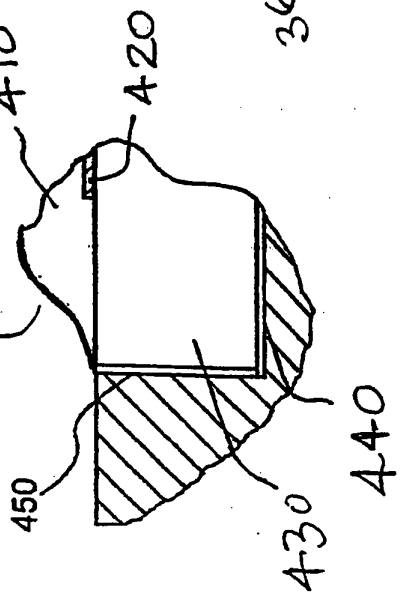


FIG. 7E

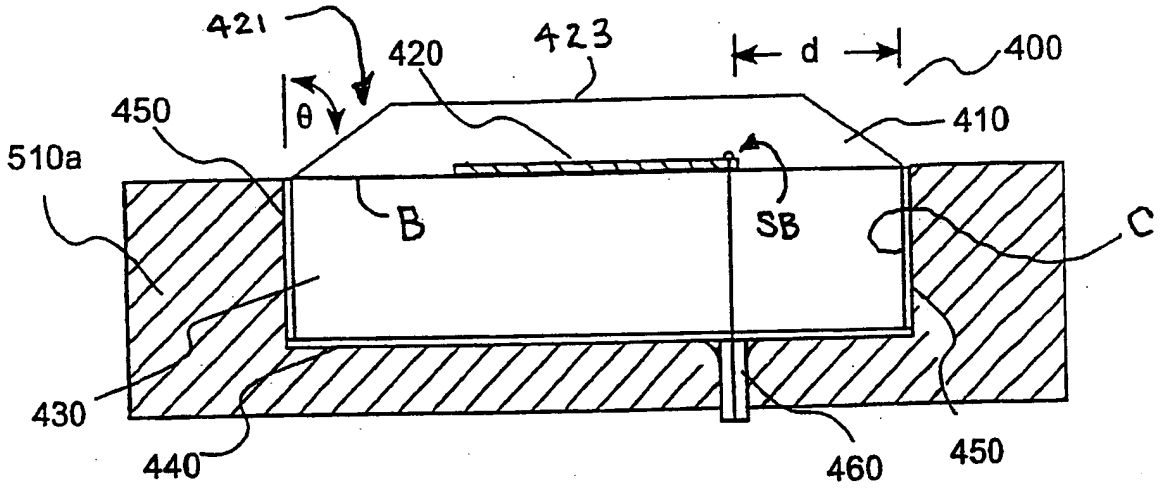


Fig. 7A

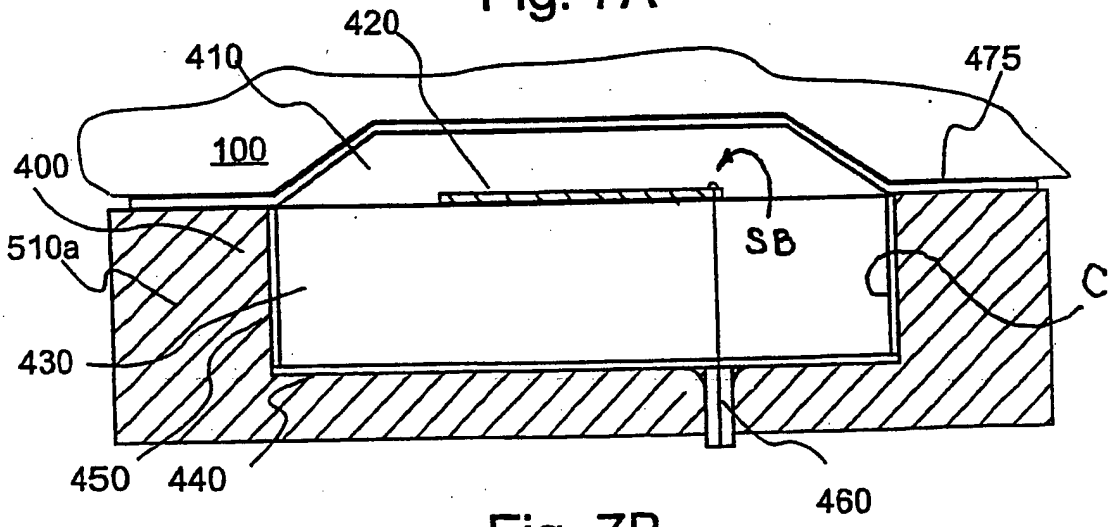


Fig. 7B

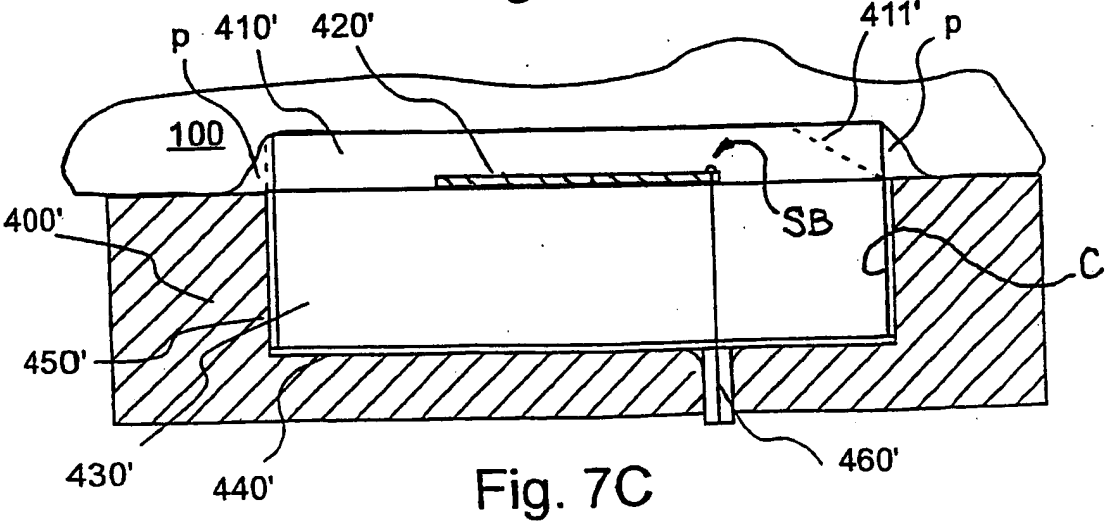


Fig. 7C

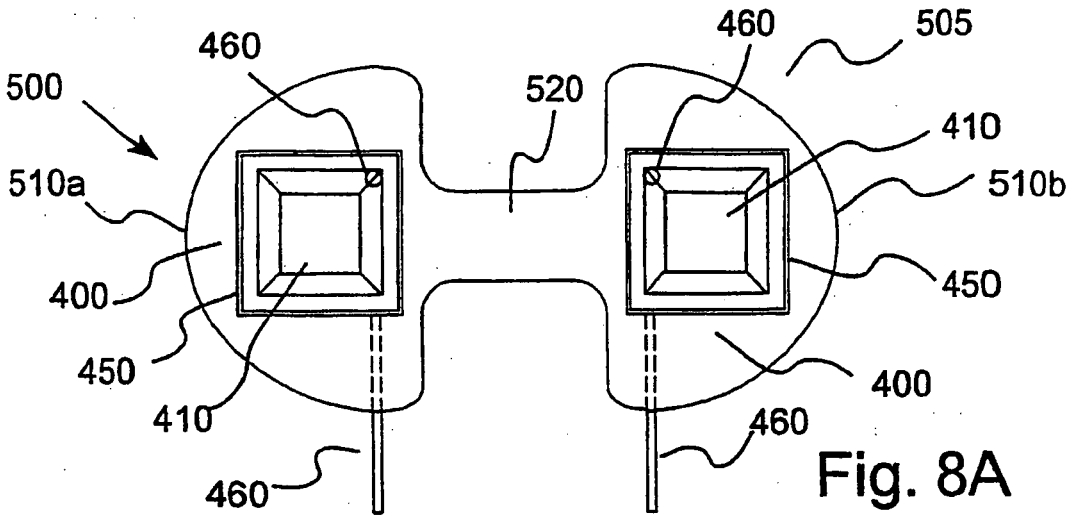


Fig. 8A

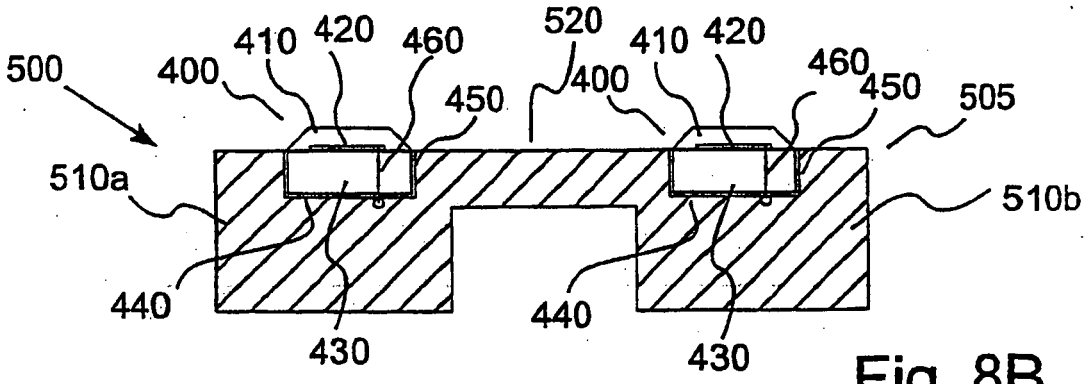


Fig. 8B

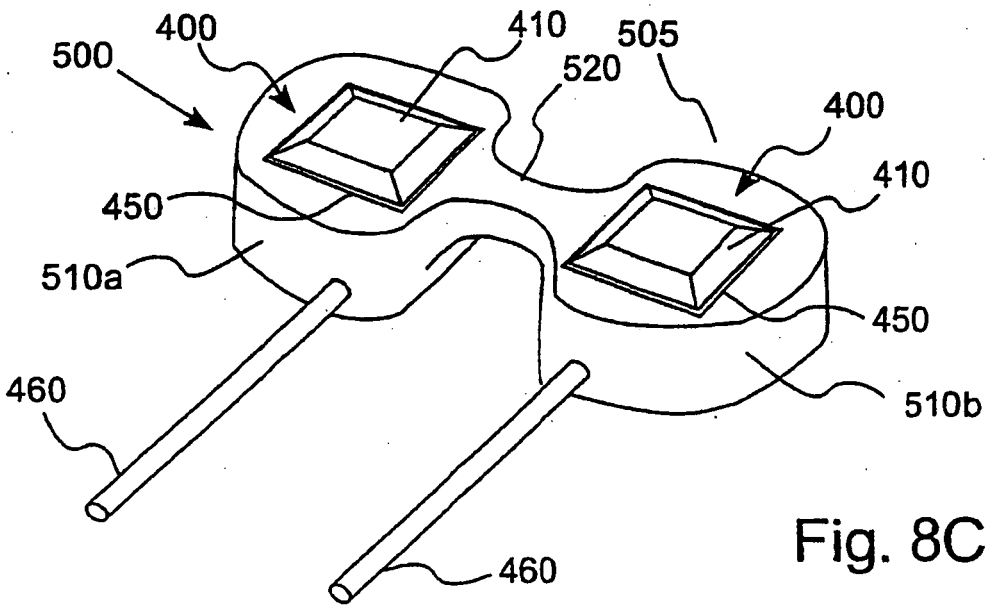


Fig. 8C

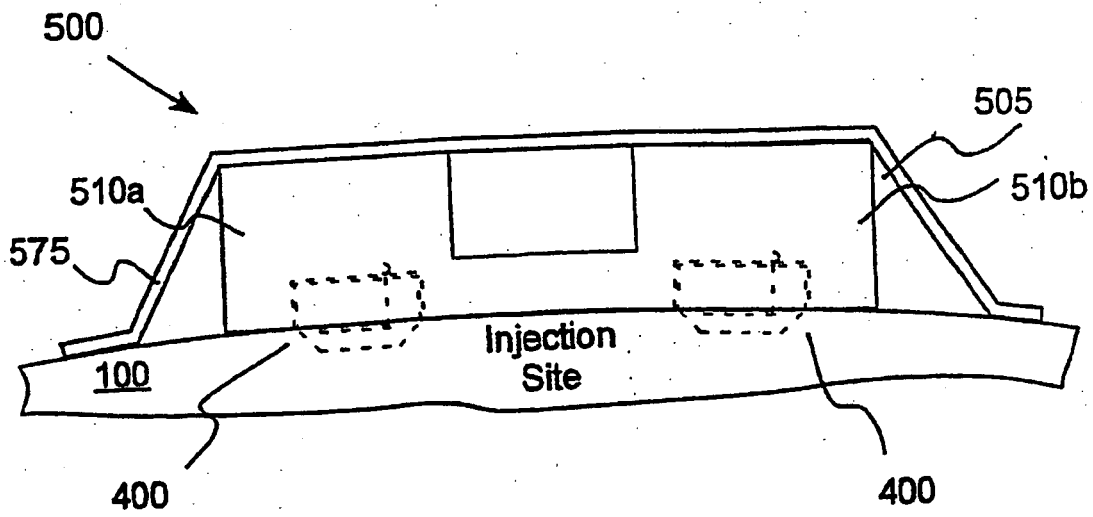

500
505
510a
510b
575
Injection
Site
100
400
400

Fig. 8D

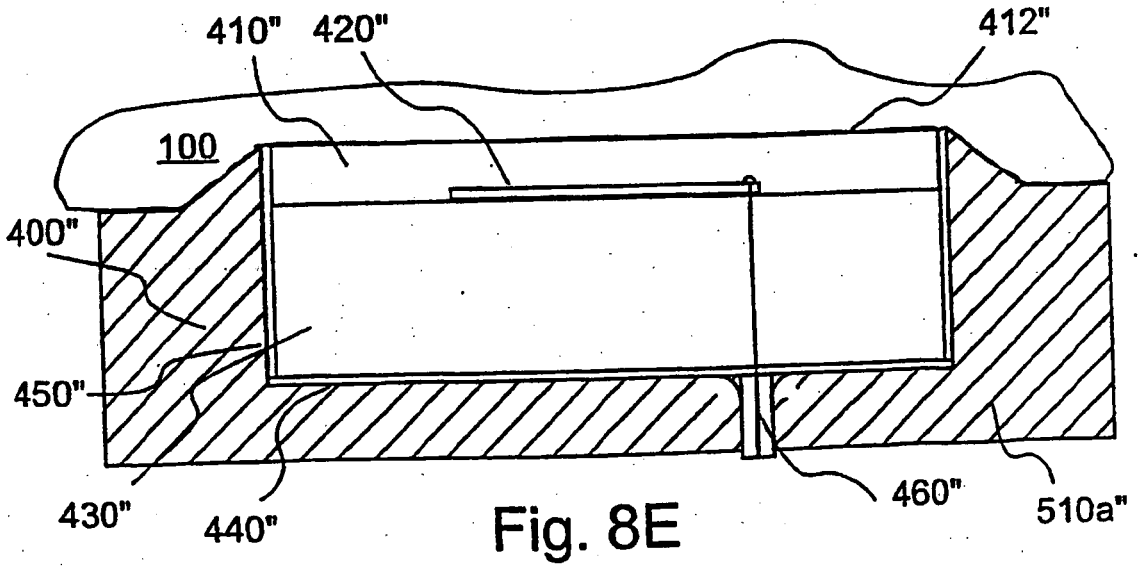

410"
420"
412"
100
400"
450"
430"
440"
460"
510a"

Fig. 8E

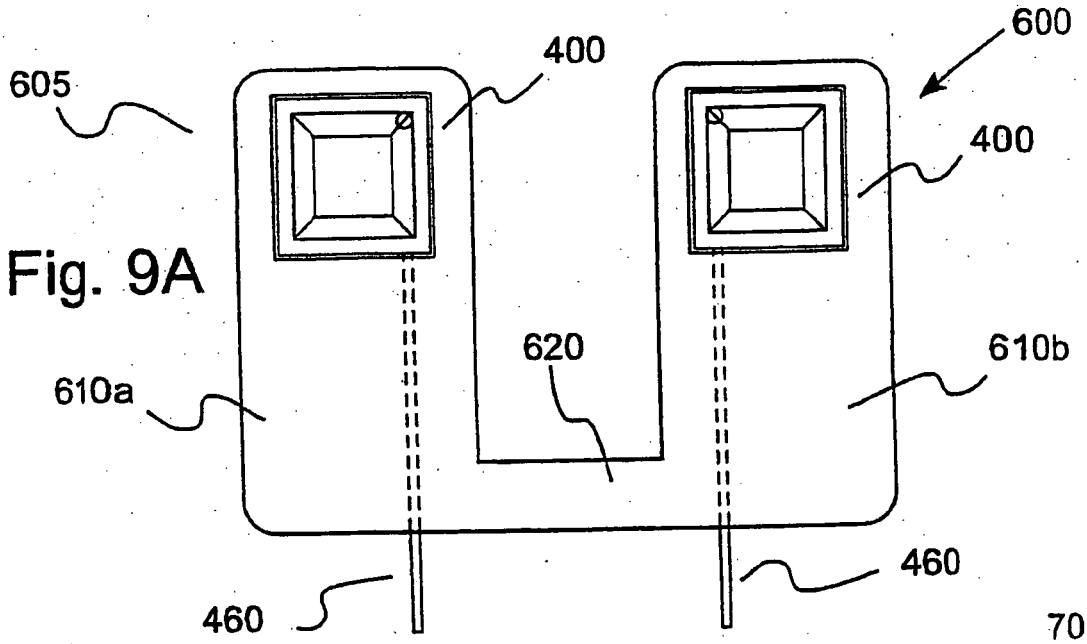

600
605
400
400
620
610b
610a
460
460

Fig. 9A

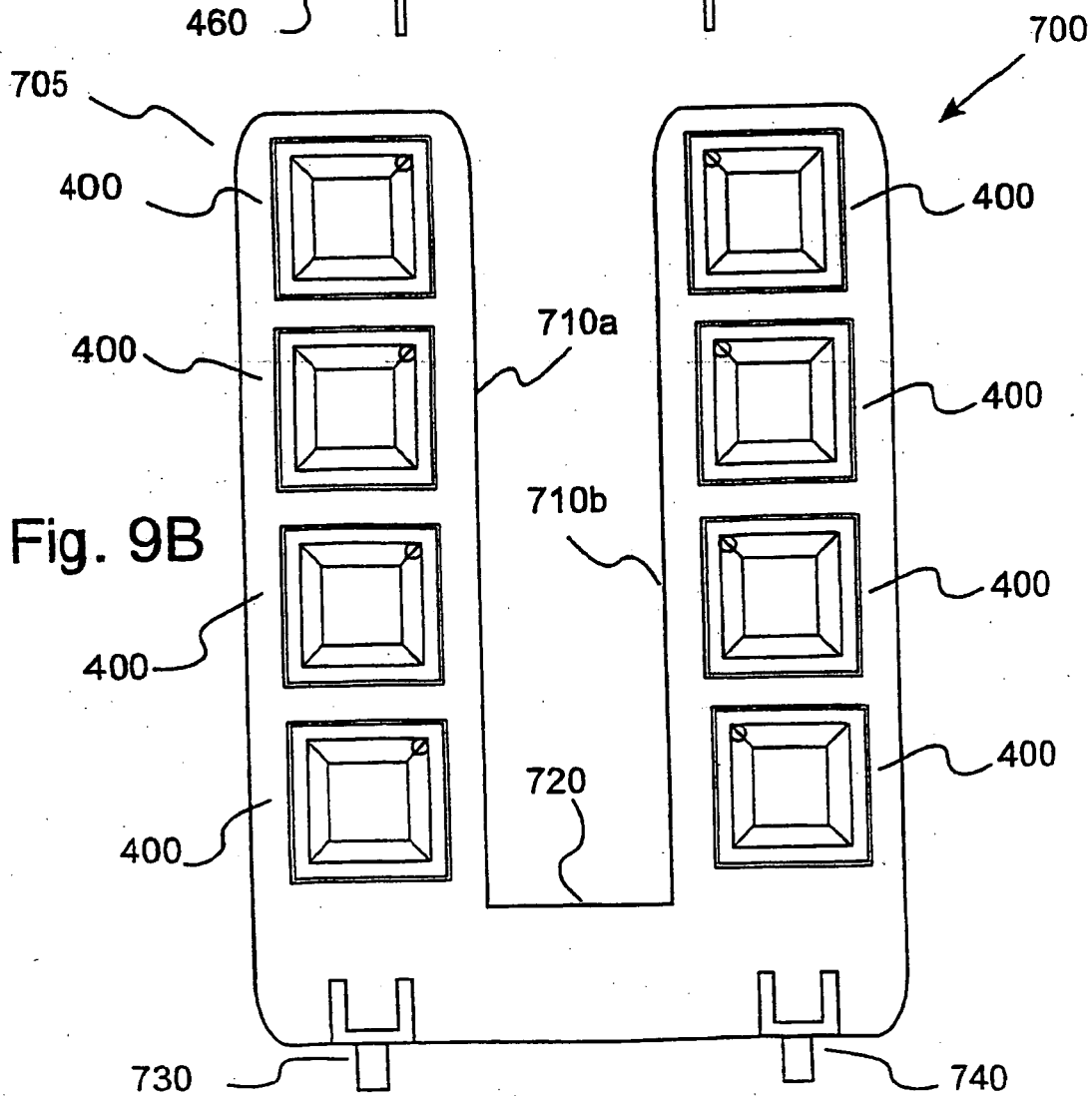

700
705
400
400
710a
400
400
710b
400
400
720
400
730
740

Fig. 9B

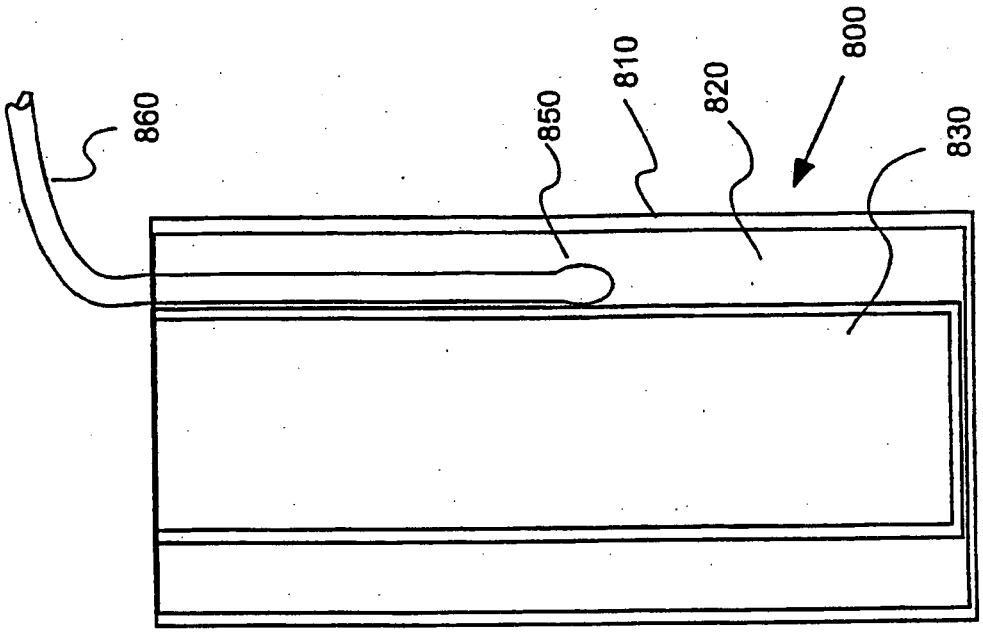


Fig.11

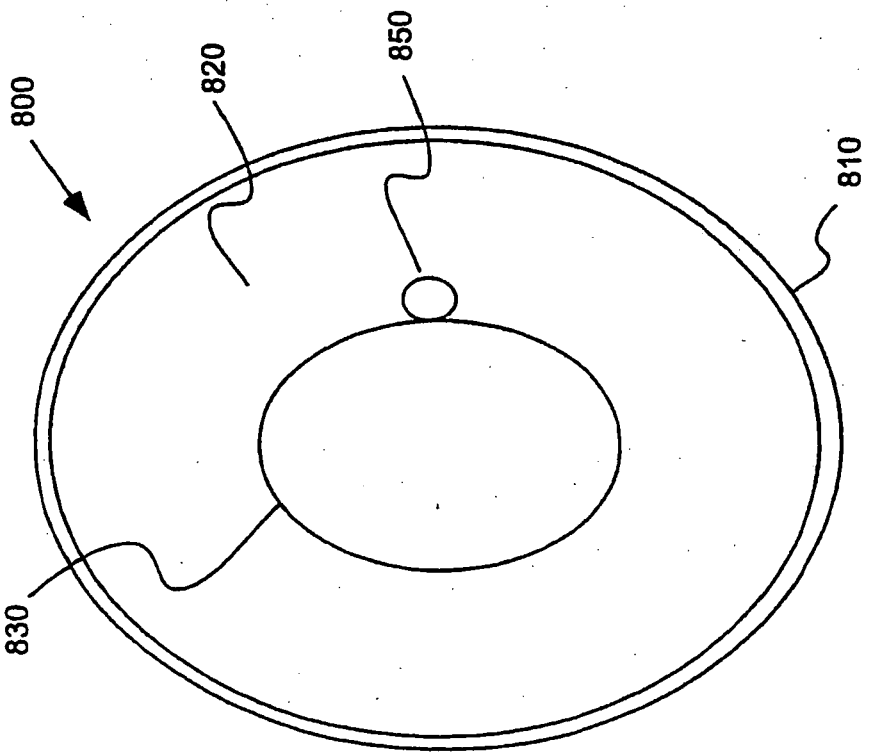


Fig. 10

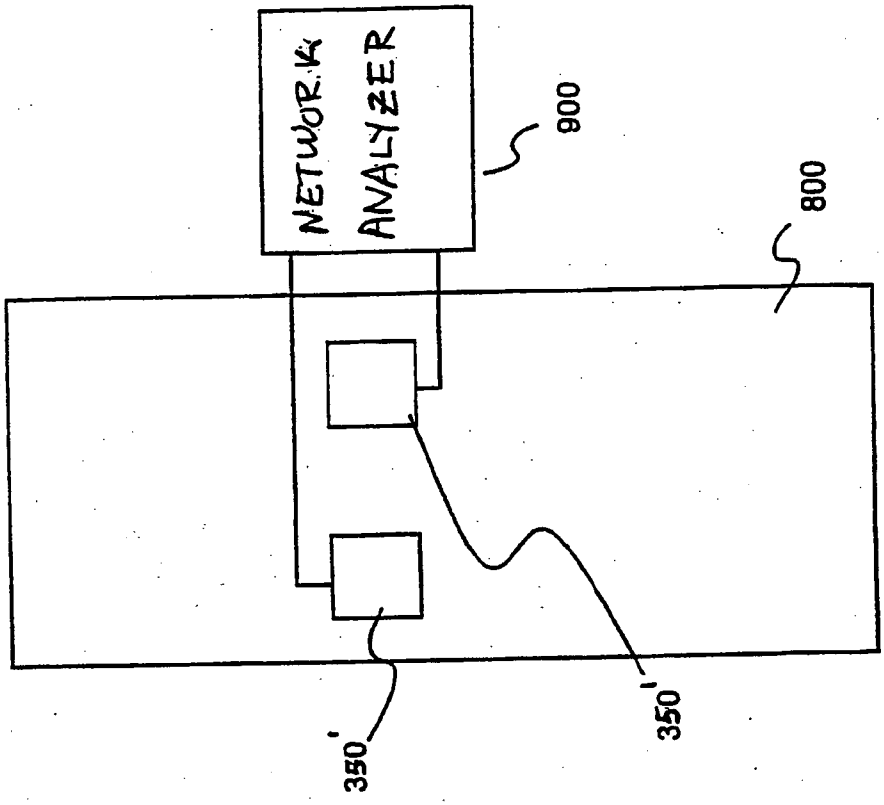

NETWORK
ANALYZER
900
800
350'
350'

Fig. 14

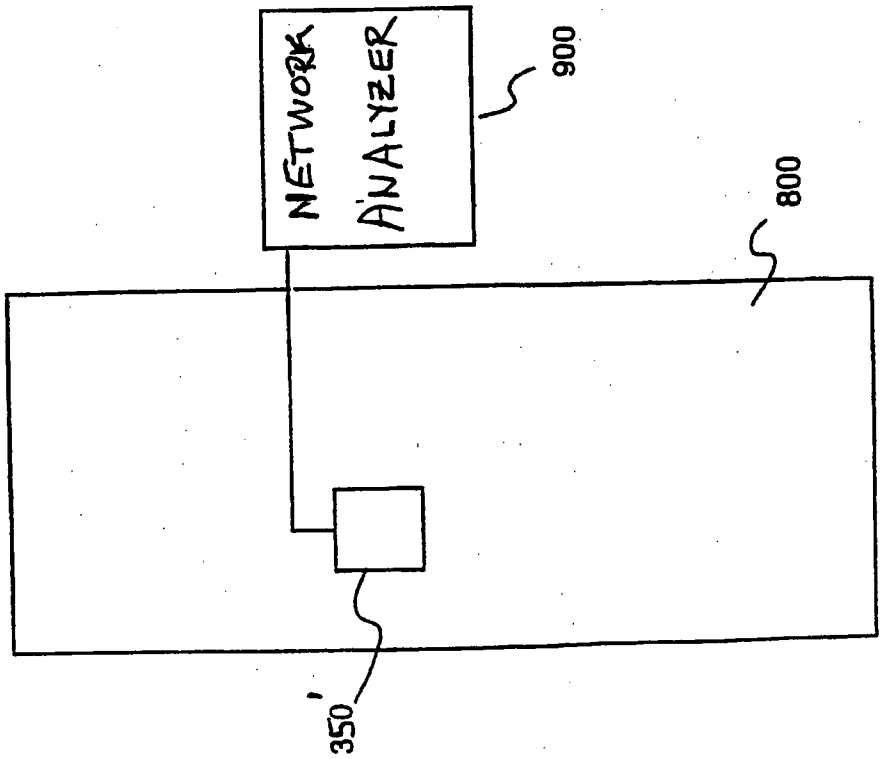

NETWORK
ANALYZER
900
800
350'

Fig. 12

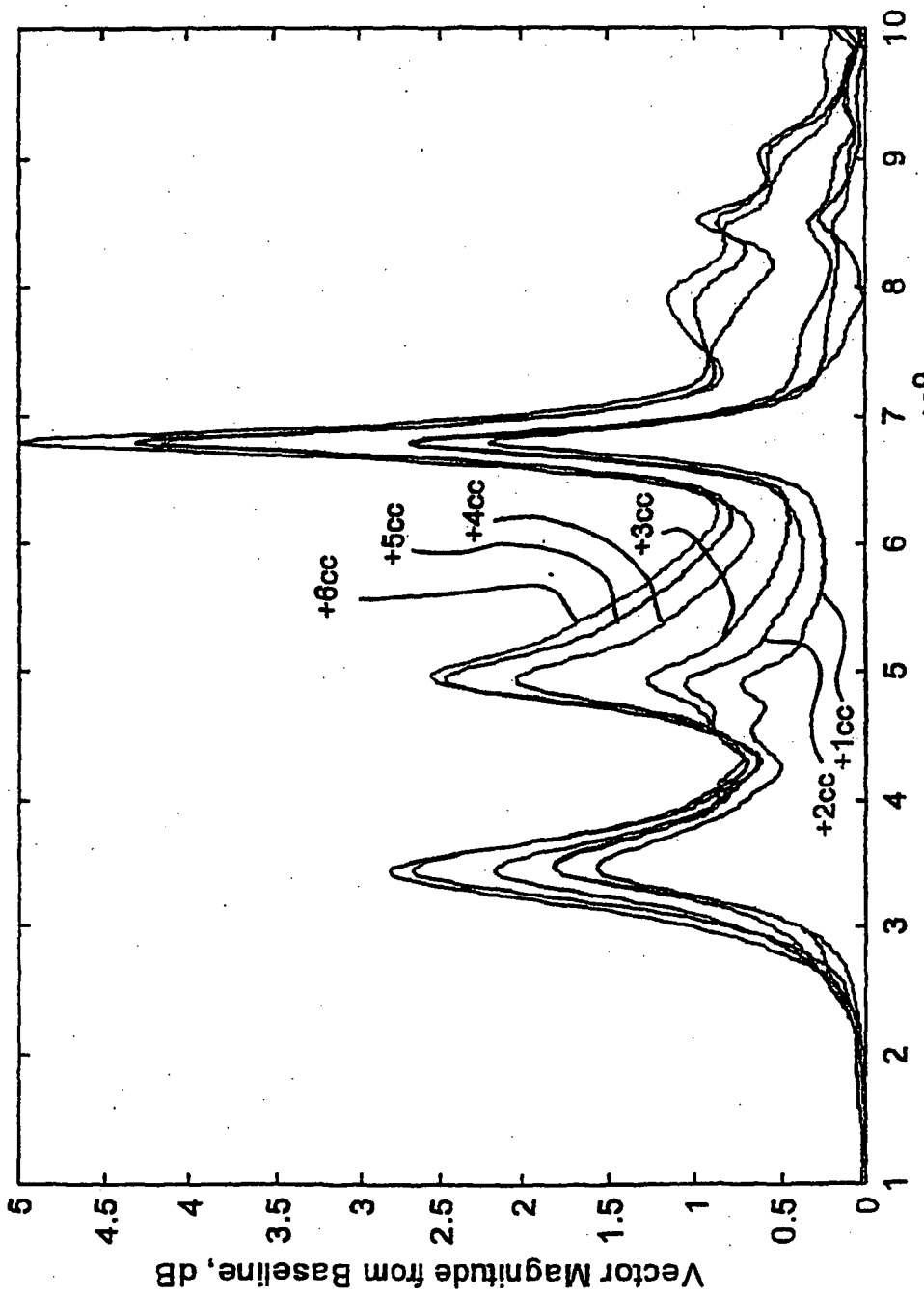

Vector Magnitude from Baseline, dB
Frequency, Hz
x10^9
+8cc
+5cc
+4cc
+3cc
+2cc
+1cc

Figure 13

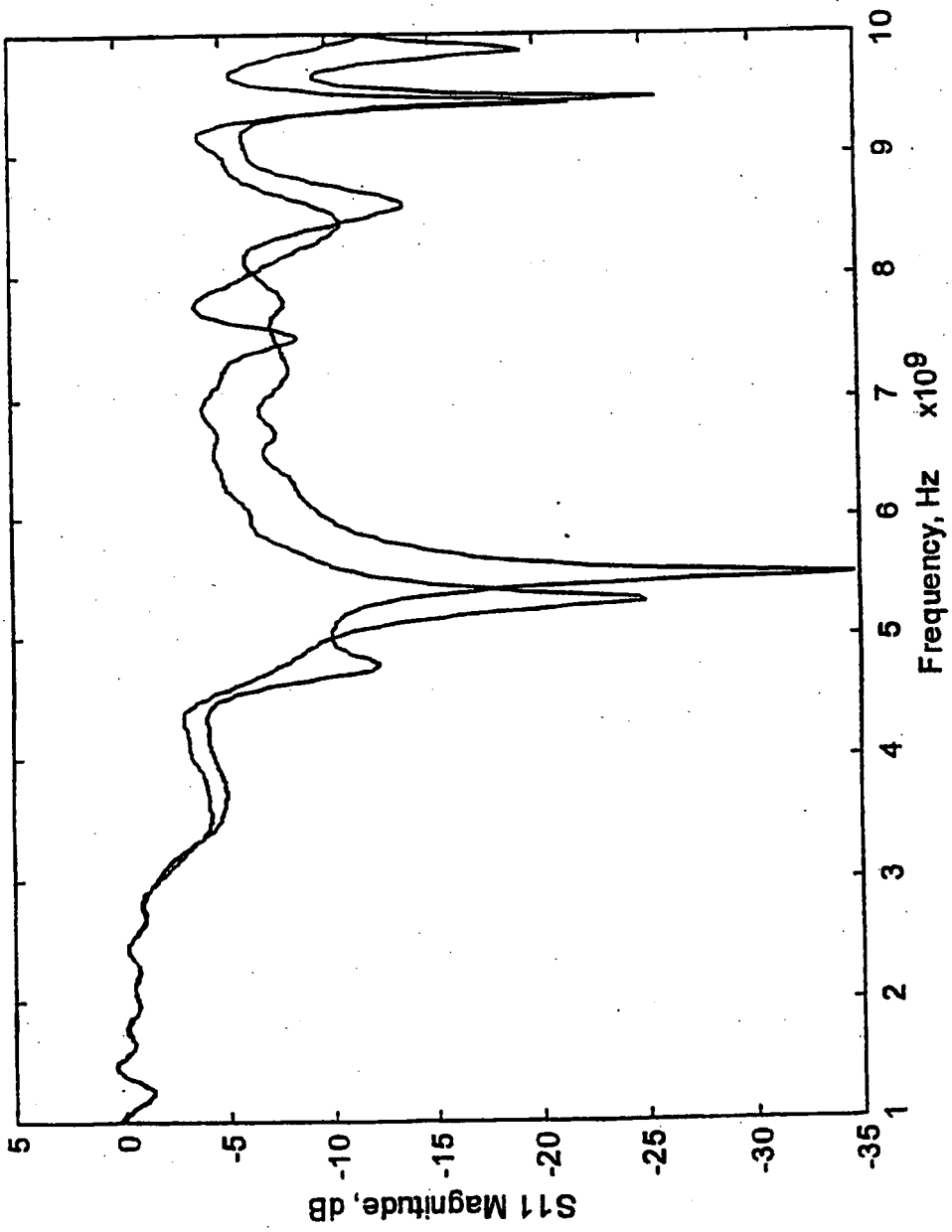

S11 Magnitude, dB
5
0
-5
-10
-15
-20
-25
-30
-35
1
2
3
4
5
6
7
8
9
10
Frequency, Hz
x10^9

Figure 15

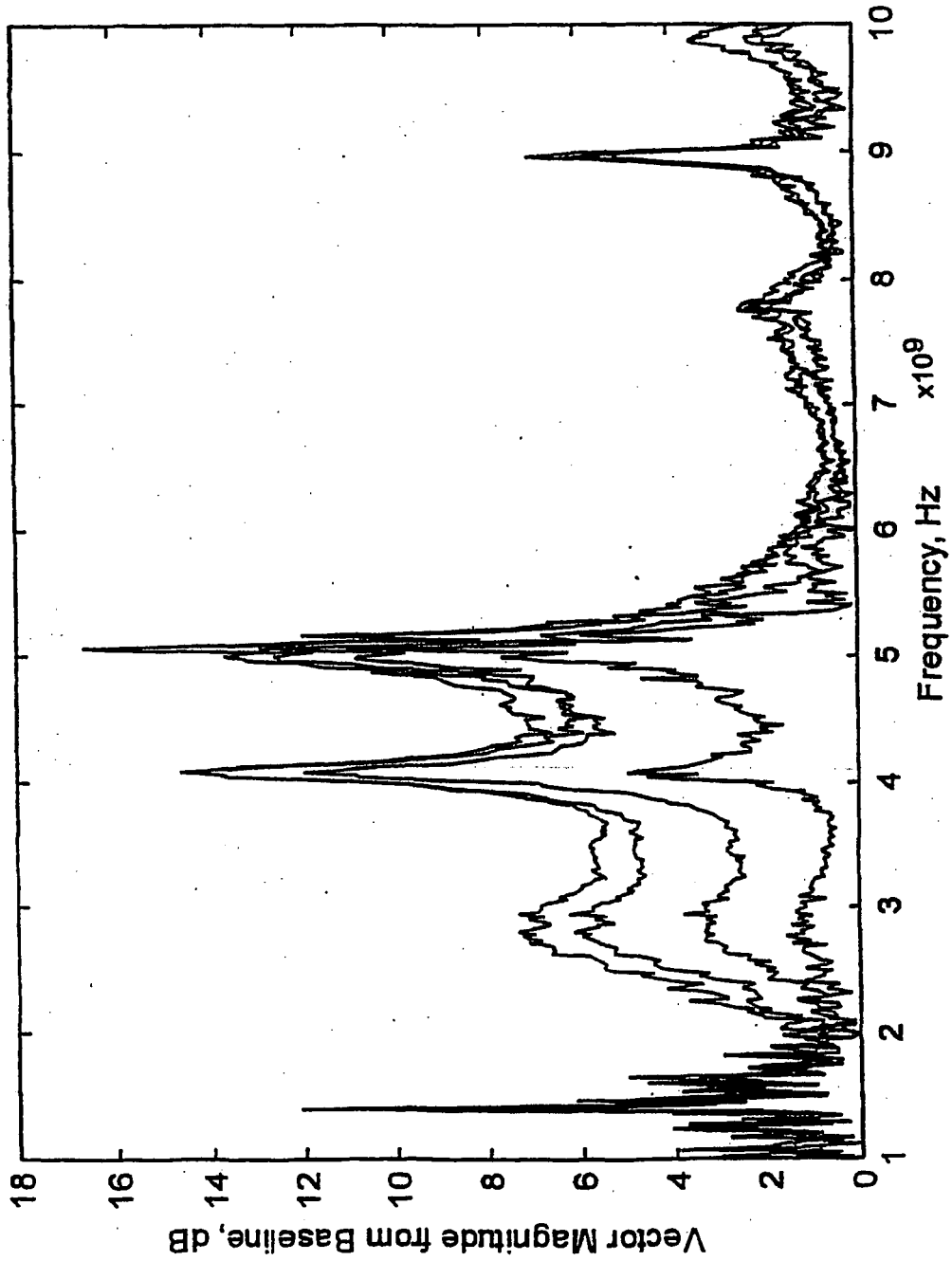

Vector Magnitude from Baseline, dB
0
2
4
6
8
10
12
14
16
18
1
2
3
4
5
6
7
8
9
10
Frequency, Hz
x10^9

Figure 16

Fig. 17

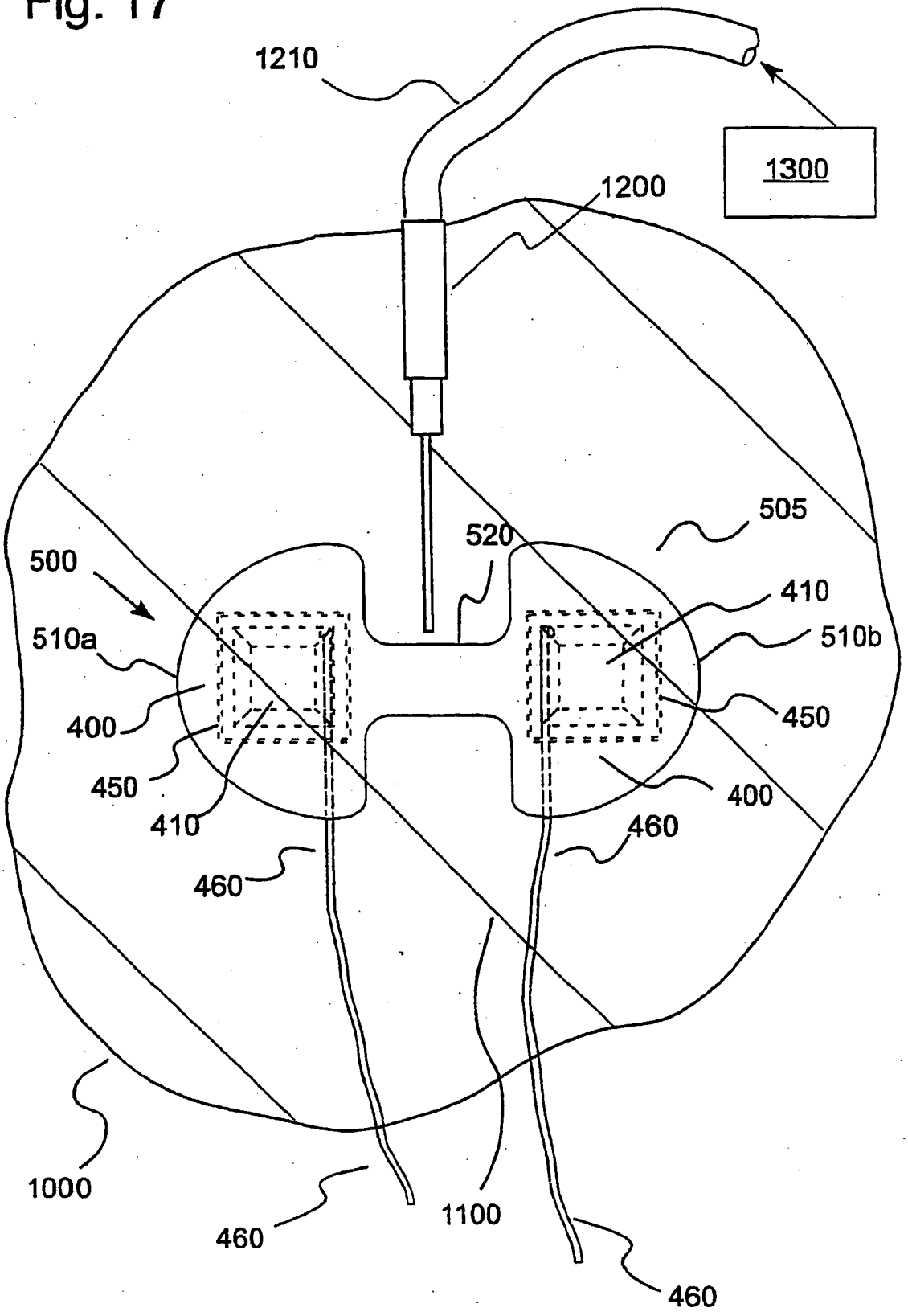

1210
1300
1200
505
520
500
410
510a
510b
400
450
450
400
410
460
460
460
1000
460
1100
460

Figure 18

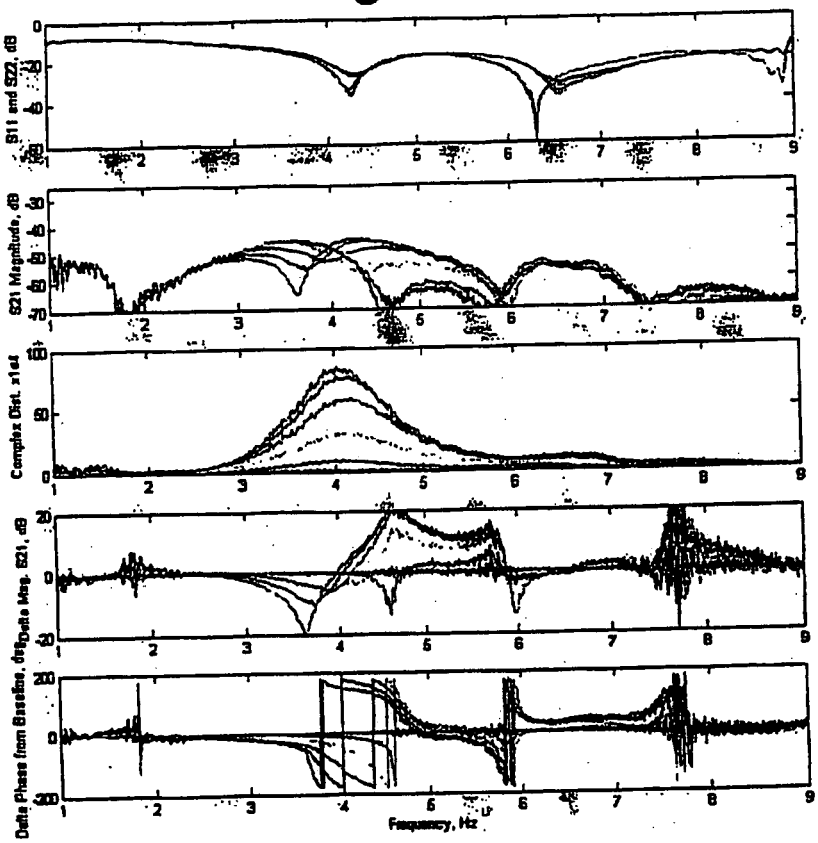


Figure 19A Figure 19B Figure 19C

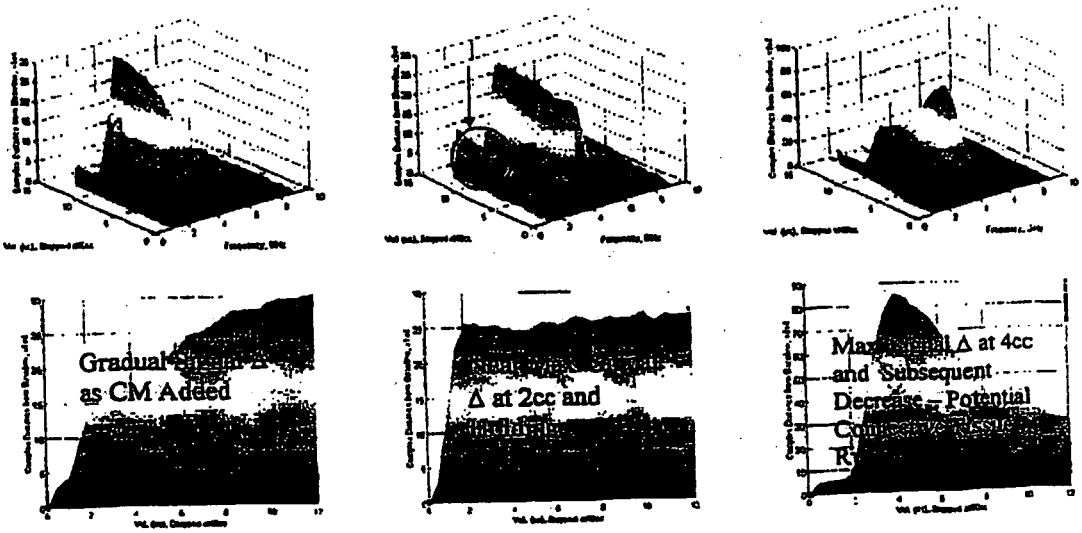


Fig. 20

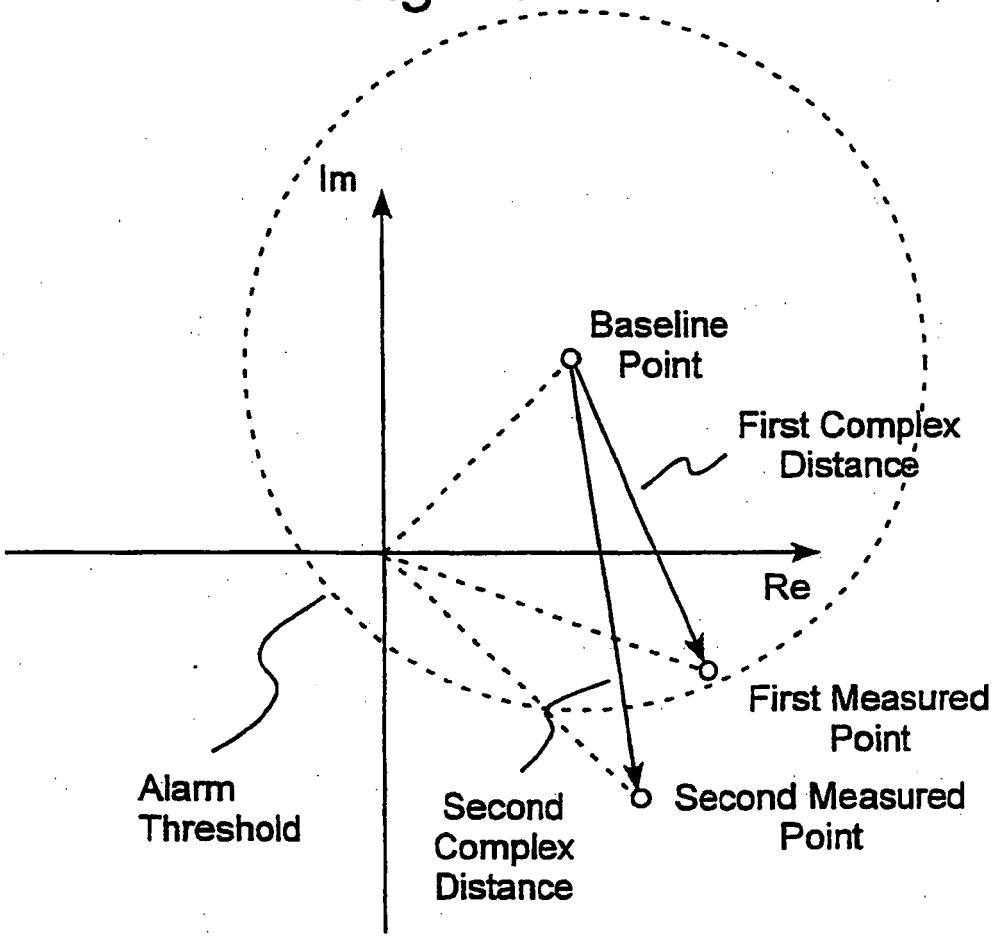

Im
Baseline Point
First Complex Distance
Re
First Measured Point
Alarm Threshold
Second Complex Distance
Second Measured Point

Figure 21A

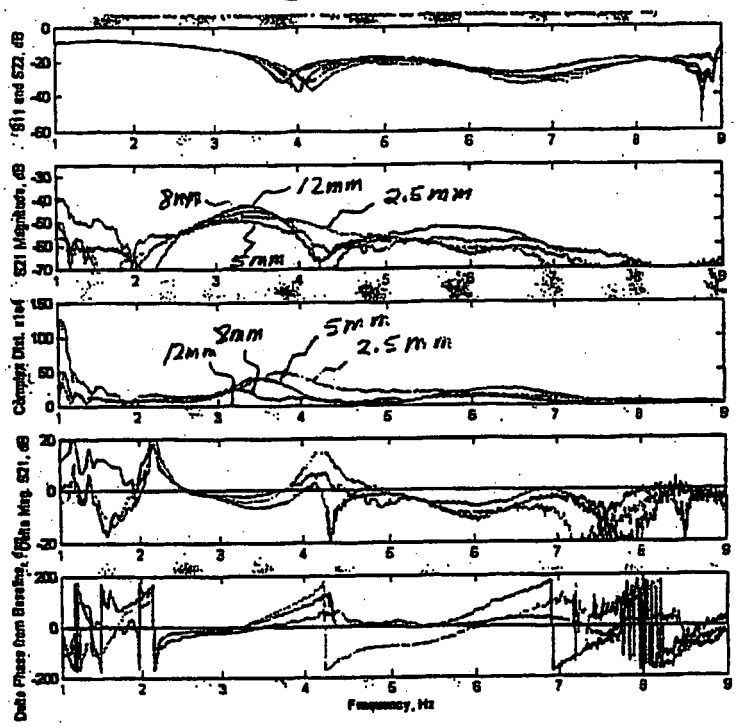


Figure 21B

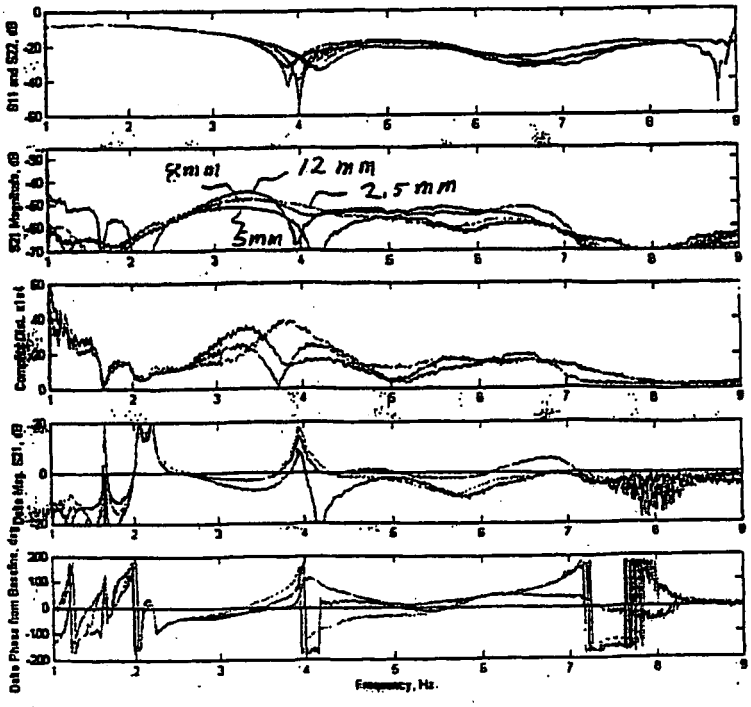


Figure 22A

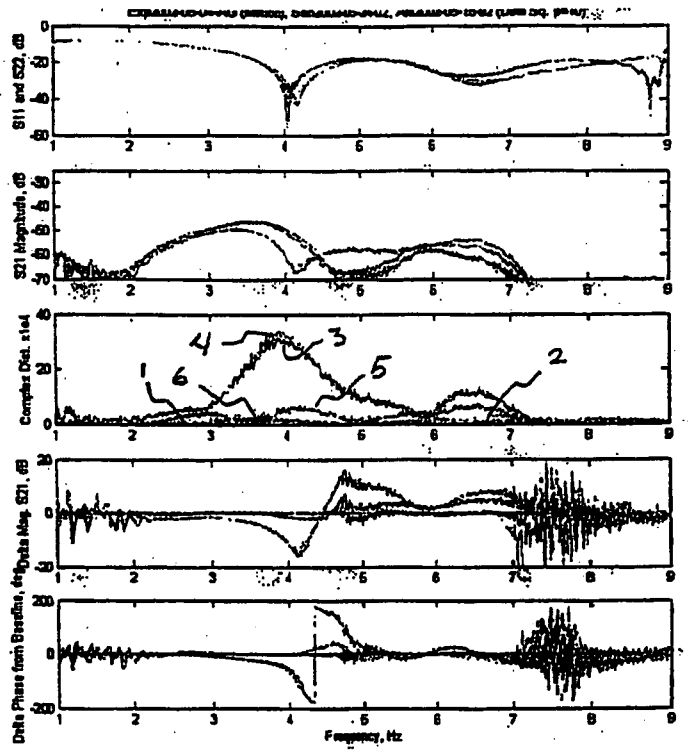


Figure 22B

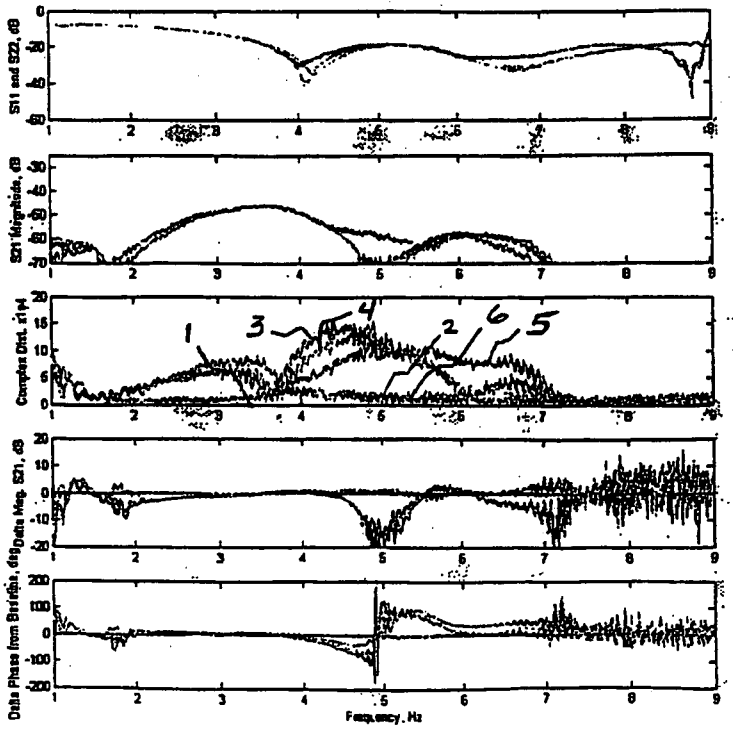


FIG-23

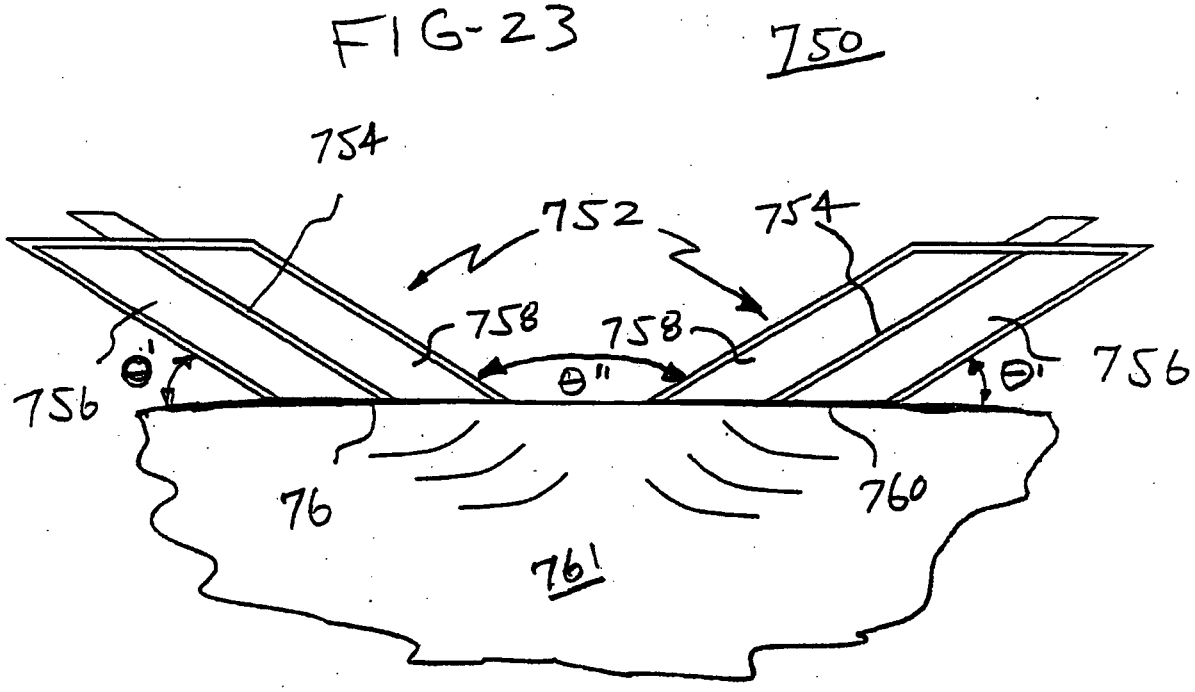
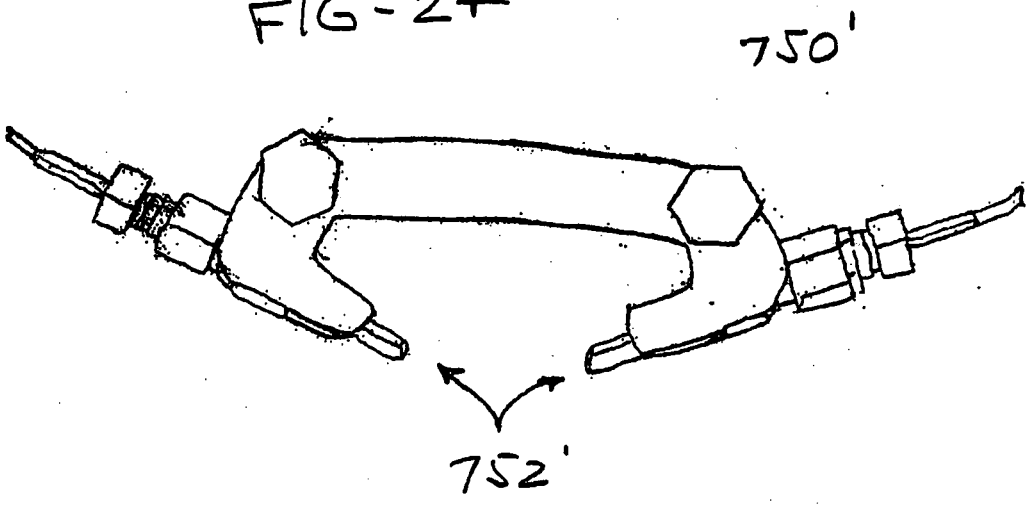


FIG-24



REFERENCES CITED IN THE DESCRIPTION

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专利名称(译)	用于生物组织应用的电磁传感器		
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代理机构(译)	布朗ROBIN FORSYTHE		
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摘要(译)

一种检测身体组织中的液体水平变化的方法包括以下步骤：在一段时间内将大约300MHz至大约30GHz的频率范围内的电磁能量施加到身体的第一体积;测量结果信号;并且将信号与参考信号进行比较以确定在该时间段期间组织中的液位是否已经改变。