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(54) **Title**: A DIAGNOSTIC MEDICAL DEVICE FOR ENDOSCOPIC USE

(57) **Abstract**: The present invention provides a diagnostic device suitable for attachment to the external surface of an elongate medical instrument, such as an endoscope,comprising: a) an inner radially-expandable element located within the lumen of a separate, outer, radially-expandable element, wherein said outer expandable element is fitted with a plurality of RF electrodes on its outer surface; and b) a harness unit containing one or more conduits for connecting the lumen of the inner expandable element with a source of pressurized inflation fluid, together with electrical wiring that is capable of connecting said RF electrodes either directly or indirectly with external power, control and/or computational units.

A DIAGNOSTIC MEDICAL DEVICE FOR ENDOSCOPIC USE

FIELD OF THE INVENTION:

The present invention relates to the field of medical instruments. More particularly, the present invention relates to a diagnostic medical device for tissue analysis that may be used in conjunction with an endoscope or other elongate medical instrument.

BACKGROUND OF THE INVENTION:

It is well known that the electrical properties of a malignant tissue differ from those of healthy tissue. More particularly, the impedance of malignant or non healthy tissue has long known to differ from the impedance of healthy tissue. Most of the scientific effort in this field has been focused on a technique known as Electrical Impedance Tomography (EIT). Investigators have measured the electrical properties of various body organs with the purpose of trying to map the different types of tissue by measuring their electrical properties.

Various different diagnostic methods and tools based on the measurement of the electrical properties of pathological tissues have been described in the art. Thus, US20070260156 discloses a method, apparatus and probe for examining tissue for the presence of target cells, particularly cancerous cells, by subjecting the tissue to be examined to a contrast agent containing small particles of a physical element conjugated with a biological carrier selectively bindable to the target cells. Energy pulses are applied to the examined tissue. The changes in impedance and/or optical characteristics of the examined tissue produced by the applied energy pulses are detected and utilized for

determining the presence of the target cells in the examined tissue.

US20050021019 discloses a method and apparatus for examining a substance volume to characterize its type, particularly useful for examining tissue to characterize it as cancerous or non-cancerous. This is achieved by applying a polarizing magnetic field through the examined substance, applying radio frequency (RF) pulses locally to the examined substance volume in order to invoke electrical impedance (EI) response signals corresponding to the electrical impedance of the substance, and magnetic resonance (MR) responses signals corresponding to the MR properties of the substance. The EI and MR response signals are then detected and used in the characterization of the examined substance volume type.

However, the abovementioned prior art publications do not describe a method or device that may be used to efficiently diagnose malignant tissue throughout a whole open body cavity such as the colon, female reproductive system or esophagus. A particular problem that has not been adequately addressed by prior art approaches relates to the fact that the cross-sectional geometry of body cavities and passages is generally non-uniform along their length. Furthermore, the surface of the walls that form the boundaries of said cavities and passages are, in most cases, irregular, and often present an undulating hill-and-vale type of surface to electrodes, probes and sensors that are brought into contact therewith. As a result of these geometrical and topographical irregularities, the non-homogeneous pressure of the measuring means on the tissue of the body cavity wall will typically result in large errors in the electrical property being measured.

It is therefore an object of the present invention to provide a method and means for the effective and efficient *in vivo* diagnosis of pathologically-involved tissue in the wall of a body cavity or passage.

It is a further object of the present invention to provide a method and means for the *in vivo* diagnosis of abnormal tissue in a body cavity in which contact of the measuring device with the tissue being analyzed is maintained despite the non-homogeneous nature of the topography of said tissue.

Other objects and advantages of the present invention will become apparent as the description proceeds.

SUMMARY OF THE INVENTION:

The present inventors have found that a dual-balloon RF device that is capable of being fitted around the external surface of an endoscope or other elongate medical device may be used to provide diagnostic information regarding the presence or absence of malignant lesions in the wall of a body cavity such as the large intestine. The use of the dual-balloon structure, with RF electrodes attached to the outer balloon, enables several technical problems associated with membrane-bound electrodes in this context to be solved.

Consequently, the present invention is primarily directed to a diagnostic device that is suitable for attachment to the external surface of an endoscope (such as a colonoscope) or any other elongate medical instrument (such as a catheter or cannula) in a circumferential manner, wherein said diagnostic device comprises an inner radially-expandable element located within a separate, outer, radially-expandable element. A

plurality of electrodes, at least some of which are capable of transmitting RF signals, are present on the outer surface of said outer expandable element. In one preferred embodiment, the leads of said electrodes are connected to an electrical circuit board that is located in close proximity to said expandable elements. In another embodiment, the circuit board may be located remote from the device, i.e. part of the external unit that includes the control, computation and inflation fluid source elements. Finally, in certain other embodiments, the device of the present invention does not include such a separate circuit board, and the electrodes are connected directly with the external power, control and/or computational units.

The device further comprises a harness unit which contains *both* one or more conduits for connecting the lumens of the expandable elements with a source of pressurized inflation fluid (such as water, saline or air), *and* electric wiring for connecting the aforementioned electrical circuit board with external electrical power and/or control units. It should be noted that the term "harness unit" is used herein as a collective term to include all of the various conduits, wires and cables that are required for connecting the device of the present invention with the various external control units, computation units, inflation fluid reservoirs and pumping apparatus, all of which will be described in more detail hereinbelow. Consequently, while this collective term includes within its scope discrete, well-defined harness units, it may also be taken to mean simply a bundle of the aforementioned wires and conduits.

In one preferred embodiment of the device of the invention, the inner radially expandable element is an essentially

closed radially-expandable balloon, the only opening(s) in which being in fluid connection with the aforementioned inflation fluid conduit(s). In another preferred embodiment, the outer expandable element comprises a flexible membrane. In a further preferred embodiment, the outer expandable element is provided in the form of a balloon. In one preferred embodiment only the inner expandable element is in fluid connection with the inflation fluid conduit. In another preferred embodiment, however, the space between the inner and outer expandable elements is also in fluid connection with a conduit that is capable of being connected with a source of inflation fluid.

In one preferred embodiment, the aforementioned plurality of electrodes comprises an array of individual electrodes having defined mutual separation distances. In another preferred embodiment, the plurality of electrodes comprises an array of coaxial electrodes.

In another aspect, the present invention also provides a diagnostic system comprising:

a) a diagnostic device suitable for attachment to an endoscope, as disclosed hereinabove;

b) an RF impedance measuring unit;

c) a computation unit, comprising suitable hardware and software for analyzing the output of said RF impedance measuring unit; and

d) a source of inflation fluid and pumping means for causing said fluid to move into and out of the fluid conduits contained within said diagnostic device.

In another, highly preferred embodiment, the diagnostic system further comprises an automatic pressurization unit for

automatically controlling the inflation pressure within the lumen(s) of the expandable elements.

Details of the arrangement of the various parts of the system and of the connections therebetween will be described hereinbelow.

In a further aspect, the present invention also provides a method for diagnosing the presence of malignant tissue within the wall of a body cavity or passage, wherein said method comprises the steps of:

a) introducing into said body cavity or passage a first radially-expandable element containing an array of electrodes on its outer surface;

b) causing the radial expansion of said expandable element, such that said electrodes contact said body cavity wall;

c) passing an RF current between pairs of electrodes;

d) calculating the complex impedance of the body cavity wall region that is in contact with said electrodes;

e) determining from the change in impedance in certain areas of the body cavity wall that said areas are putative sites of malignant and/or pre-malignant tissue.

In one preferred embodiment of the method of the invention, the body passage is the colon, and the expandable element bearing the electrodes is attached to a colonosocope.

In another particularly preferred embodiment of the method, a second, inner radially-expandable element is placed within the lumen of the first radially-expandable element, such that the expansion of said second expandable element causes the electrodes on said first expandable element to be brought into contact with the body cavity wall.

In a further particularly preferred embodiment, the method further comprises the step of automatically maintaining the electrodes in contact with the body cavity wall by means of operating an automatic pressurization system.

BRIEF DESCRIPTION OF THE DRAWINGS:

- Fig. 1 is a block diagram illustrating the main elements of the present invention.
- Fig. 2A illustrates an array of single electrodes in one preferred embodiment of the device of the present invention.
- Fig. 2B illustrates an array of coaxial electrodes in one preferred embodiment of the present invention.
- Fig. 3A provides an external view of a preferred embodiment of the device of the present invention with the inner balloon in its deflated state.
- Fig. 3B depicts a longitudinal section view of the same device as shown in Fig. 3A, with the inner balloon in its deflated state.
- Fig. 4 provides a longitudinal section view of the same device as shown in Fig. 3B, with the inner balloon in its inflated state.
- Fig. 5 is a schematic external view of a preferred embodiment of the device of the present invention with the inner balloon in its fully inflated state.
- Fig. 6 is a block diagram of the main electronic components of the present invention.
- Fig. 7 is a block diagram depicting the main elements involved in control of the inflation/deflation of the inner balloon of the present invention.

- Fig. 8 is a photographic view of a region of the colonic wall being analyzed by a device of the present invention. The location of the putative lesion is indicated by the white lines.

DETAILED DESCRIPTION OF THE INVENTION:

The present invention relates to a device that uses RF energy to detect the electrical properties of tissue. As mentioned hereinabove, the electrical properties of pathologically-involved tissue (such as malignant tissue) differ from those of healthy tissue. More particularly, the impedance of malignant or other non-healthy tissue may differ from the impedance of healthy tissue. A key feature of one preferred embodiment of the device of the present invention is its unique double balloon structure, which permits the low crossing profile endoscopic delivery of the measuring electrodes to the body cavity wall to be analyzed. Then, active expansion of the inner balloon (or other expandable element) is employed in order to bring said electrodes into contact with the body cavity wall tissue, and to maintain this contact throughout the duration of the measurement process. While the device of the present invention will be described in relation to its use in the large intestine, it may, of course, be used in other body passages such as the esophagus, small intestine and female reproductive system.

The measurement of electrical impedance may be performed in several different ways. The most common technique is the two electrodes technique, wherein a constant RF current is passed between two electrodes. The electrodes are brought in touch with the tissue to be analyzed and the voltage across the electrodes is measured. By having both voltage and current as a function of time one can easily calculate the complex

impedance of the tissue. Sometimes this function is divided into its real part- the resistance, and the complex part- the capacitance. Resistance and capacitance measurements show different behavior between pathologically-involved tissue (such as malignant tissue) and healthy tissue.

In prior art studies, various types of digestive tract tissue were measured for their electrical properties [*Davies RJ et al., Biophys. J. 52: 783-790 (1987); Gonzalez-Correa CA et al., Physiol. Meas. 24: 291-296 (2003)*]. The results of these studies indicate that a resistance difference of 21% was measured between healthy colon epithelial cells and the same type of colon epithelium after 20 weeks of carcinogen administration. This difference is a cell to cell electrical properties difference. A real-time in vivo measurement of tissue electrical properties will be different since in addition to the cell to cell changes, it would sense geometrical changes. By this it is meant that while the colon wall, for example, is quite homogenous having a flat nearly uniform thickness and layers, a polyp has a different shape, thereby resulting in a substantially different impedance between two points on the sides of the polyp than of the impedance between two points with the same distance in between, on the surface in the absence of a polyp. This effect adds to the cell to cell difference, thereby enhancing the probability of detecting abnormalities in the colon.

However, measurements of this type are subject to errors caused by inhomogeneous pressure of the electrodes on the tissue measured. Thus, the essence of the device of the present invention is that is able to maintain a homogeneous, predetermined pressure of all electrodes on the area of tissue to be measured.

The present invention relates to a device that serves as an attachment to a generic endoscope or other elongate medical instrument (such as a catheter) that provides the clinician with a tool for detecting suspicious polyps, wherein said attachment is mounted on the generic endoscope before each procedure, and is introduced into the patient's body together with said endoscope. The present invention is also directed to a system that comprises the aforementioned device together with electronic equipment that assists in performing the measurements for detection and that perform analysis. This latter part of the system is located external to the body.

As shown in block diagram form in Fig. 1, the present invention comprises the following main components:

I. An intra body unit (10) fits over the distal end of the generic endoscope and comprises:

   1. a flexible membrane (11) covered with an array of metallic electrodes;

   2. an inner expandable element (12) located inside the first membrane (11);

   3. an electrical circuit board (13);

   4. a main harness unit (14) for carrying both fluid pressure and electronic signals from inside the body to the external unit and *vice versa*.

II. An external unit (20) that comprises:

1. an RF impedance measuring unit (21);

2. a computing unit (22) which analyzes the signals;

3. a monitor (23);

4. a controllable automatic pressurization unit (24) which controls fluid pressure, air pressure or any gas pressure used to inflate said membranes.

The flexible membrane (11) in the intra body unit (10) is usually a toroid shaped balloon or any other flexible membrane that is made of a flexible material such as medical grade silicone rubber, or durable polyurethane, or a non-compliant material such as nylon 12. The membrane (11), hereinafter also referred to as the outer balloon is optionally manufactured by blow molding technique or dip method. The characteristic wall thickness of this outer balloon can vary from 5 microns to 100 microns. The membrane (11) is flexible and stretches while being pushed outwards by the inner expandable element (12), which is commonly provided in the form of a balloon (constructed of materials such as silicone rubber, polyurethane or nylon 12), and hence is also referred to hereinafter as the inner balloon.

The membrane (11) is covered with an array of metallic electrodes. When introduced into the patient's body, the membrane (11) is in a non-expanded conformation as shown in Fig. 3a and 3b. When the clinician wishes to begin the measurement process, the membrane (11) is expanded, thus pushing the electrodes against the inner wall of the digestive track. Optionally, the electrodes are designed to

be recessed inside the membrane (11). When the membrane (11) expands the electrodes bulge outwards.

In one preferred embodiment, the electrodes are made of communication wire and the distal end comprises a small metal plate. The metal plate is made of a conductive metal e.g. stainless steel, copper or gold, and its width and length dimensions are generally between 0.5 mm and 3 mm. The plate may have a circular disk shape or a spherical shape, a half spherical shape or any other geometry, which might ensure better contact with the measured tissue being diagnosed. It is to be recognized that the aforementioned electrode shapes and sizes are provided for the purpose of illustration only, and should not be construed as limiting the invention in any way. The electrodes are optionally made of a single conducting material each.

In one embodiment of the present invention the electrodes are made of a conducting elastomer painted on the balloon surface. Conducting elastomers are usually composed of a polymer containing a thin powder of Aluminum, silver or carbon.

The electrodes are attached to the membrane (11) or preferably fixed into groves prepared in it. Optionally, a non flexible elastomer for instance Mylar or Kapton is used to print the electrodes on the non flexible elastomer, and attach it or glue it to the flexible membrane (11). Printing electrodes or conductors on Mylar or Kapton is usually done by attaching a thin layer of copper to the elastomer and shaping it by etching. Each electrode is attached to the balloon by adhesion or implanted inside the wall of the balloon during manufacture. Electrodes are glued to the

balloon using a biocompatible adhesive having a good adhesion both to the balloon material and to the metal electrodes. If, for instance the balloons are made of silicone- a silicone adhesive will preferably be used.

In the embodiment in which the electrodes are implemented inside the balloon wall, each electrode is embedded in a cavity made of the balloon material such that the outer side of the electrode, which faces the cavity wall being measured, is uncovered while the opposite surface of the electrode is coated with balloon material or glue.

When the outer balloon is in its non-inflated state as shown in Fig. 3A, the electrodes are recessed into the balloon envelope as shown in Fig. 3B. When the outer balloon is inflated - either independently or stretched by the inner balloon (as will be explained hereinafter) - the electrodes bulge outwards from the balloon surface, as shown in Fig. 4 and Fig 5. The detection probe, which comprises the generic endoscope with the present invention attachment, should have a minimal cross profile in its deflated state, and when inflated it should reach at least 40 mm in diameter using relatively low pressure (between 50 mbar and 100 mbar).

The electrodes are arranged on the balloon surface in a symmetrical array. Preferably, the electrodes are evenly spread over the balloon circumference in "circles" where each circle is located on the balloon surface and is perpendicular to the generic endoscope longitudinal axis such that each of the electrodes on each circle are pressed upon the circular open body cavity being measured. The number of electrodes in each circle might be the same or it may vary at different circles. Figs. 4 and 5 illustrate a typical example of the

device of the invention in its inflated state with the electrodes (310) bulging outwards from the surface of the outer balloon (11).

In a preferred embodiment of the present invention, when membrane (11) is inflated, an RF current is passed between each pair (201) of adjacent single contact conducting electrodes (200) at a time, as shown in Fig. 2A. Voltage is simultaneously measured and resistance and capacitance are calculated. This is usually known in the art the "two electrode impedance scheme". The distances between the electrodes change according to the inflation pressure of the membrane (11) and the original size of the body cavity. The tissue analysis accordingly takes this change in distance into account, as will be further explained hereinafter.

In another embodiment one can use what is called "the four electrode scheme" in which current is passed through two of the electrodes and voltage is measured across two other electrodes. Both techniques are familiar to the skilled artisan in this field and a fuller description may be found in the technical literature [for example: *Bayford RH, Annu. Rev. Biomed. Eng. (2006). 8:63-91*].

In another preferred and very useful embodiment of the present invention the electrodes are arranged in a coaxial manner, as shown in Fig. 2B, in which there is an outer circular electrode (210) and an inner circular electrode (211) at the center of said outer circular electrode wherein both electrodes are printed on the membrane (11). The distance between the inner and outer coaxial electrodes is constant and is not a function of the size of the inflating membrane. An RF current is passed between the inner and outer

circular electrodes. Thus the tissue of the body cavity between the electrodes is diagnosed. Voltage is simultaneously measured and resistance and capacitance are calculated.

In another embodiment of the invention the electrodes function as small antennas. RF pulses are transmitted and impedance in front of each antenna is measured by measuring the returned RF wave. When performing the measurement in this manner, it is not necessary that the electrode physically touch the tissue. Electromagnetic waves emitted by the electrode are partly absorbed by the tissue and partly back-reflected. The back- reflected wave is measured- giving information about the electrical properties of the tissue in front of the electrode. In this case, the electrodes may be covered with a thin layer of polymer. Electromagnetic waves pass through the polymer and then into the tissues whose properties are to be measured.

The RF wavelength can be chosen in a way that it would penetrate a few millimeters of feces and even a few millimeters of tissue. Using a high frequency gives a good return wavelength but the electronic design would have to be more complicated. Using a low frequency requires a more simple electronic design but would give a poorer return wavelength due to a large penetration of the transmitting signal into the body cavity. The optimal frequency is thus a compromise between penetration depth of the RF field into the tissue, and ease of design. The higher the frequency, the smaller is the penetration field. When using longer wavelengths, the system would measure deep beyond the colon wall, for example, and other tissues might interfere with that measurement. On the other hand, when going to shorter

wavelengths and higher frequencies, electrical errors caused by the high frequency come into effect. This includes common high frequency problems such as leakages between cables and straw capacitance. Thus, in one preferred embodiment, frequencies lower than about 100KHz are used. A database of penetration of wavelength into all types of human tissues is given in the publication: "Dielectric Properties of body Tissues", Italian National Research Council, Institute for applied physics-Nello Carrara, Florence, and may be used to optimize frequency selection for the particular clinical application of the presently-disclosed device and method.

The electrode-carrying membrane (11) is preferably comprised of a sealed balloon. However, any other flexible non sealed configuration of a flexible electrode carrying membrane also falls within the scope of the invention. An advantage of using a sealed balloon during colonoscopy is that said balloon presses the fecal material, thereby flattening it and enhancing the sensitivity of the device. In addition, the pressure exerted by the balloon causes stretching of the colonic wall, such that the previously undulating, convoluted surface becomes flat, thereby enhancing the field of view of the colonoscope camera, and thus ~~fecal material also~~ aiding the regular colonoscopy procedure

The inner expandable element (12), located inside the outer membrane (11), serves as an inflation means for pressing the outer electrode membrane (11) against the inner wall of the body cavity. The function of the inner balloon is to ensure an even pressure on the outer membrane against the cavity wall, thereby enabling even contact of all of the electrodes with the tissue of the body cavity wall.

The inner expandable element (12) is preferably comprised of a flexible material and optionally, comprised of the same material as the outer balloon. The inner expandable element (12) is pressurized and is preferably a sealed membrane, such as a balloon.

This dual-balloon structure provides a workable solution to the previously unsolved problem of providing a balloon that is capable of functioning both as an optimal carrier for a sensitive electrode array measuring device, and as an expansion device for causing said electrode array to be in constant contact with the uneven inner wall surface of the body cavity, and applying constant pressure on it. The combination of the inflatable inner balloon and the electrodes attached to the outer membrane ensures that all electrodes are pressed against the tissue with constant pressure. In addition, the separation of function between the electrode carrier balloon and the expansion balloon prevents the problem of fluid leakage around the electrodes and their electrical connections that would otherwise occur if the latter were to be mounted on the external surface of a single expansion balloon. In such a case, the incomplete sealing of the (single) membrane would adversely affect the pressurization of the membrane on the cavity wall, making it harder for the membrane to press upon the cavity, and thereby reducing the effectiveness and/or accuracy of the electrical measurements. It may therefore be appreciated that, by means of optimizing the relative mutual position and wall thickness of the two balloons, the dual-balloon structure of the present invention is able to press against the inner cavity wall in an optimal way such that even one or more electrodes were to be damaged or not sealed properly, the device would still function in an adequate manner.

The balloon structure adjusts itself to the geometry of the cavity. In the case where the generic endoscope is a colonoscope, the balloon structure adjusts itself to the geometry of the cavity additionally relying on the low friction inside the human colon. The friction inside the colon is extremely low, due mainly to a layer of mucus covering the inner side of the colon.

Inflation of the inner balloon may be performed either in an intermittent manner - for example, whenever the physician detects a suspected area - or constantly during the entire procedure. While inserting the generic endoscope and moving it through the colon, the inner and outer inflatable membranes are both in a deflated state and the operator uses the endoscope in a regular manner. Upon noting a suspicious area, the operator can preferably inflate the inner balloon which in turn pushes the outer membrane outwards such that the electrodes touch the measured area and obtain an RF reading to determine the nature of the tissue. This measurement can be performed in parallel with the visual diagnosis and is useful especially in cases where the tissue is covered with feces or other debris.

In many cases (e.g. in the human colon and esophagus), the diameter of the body cavity being investigated is not constant, but rather varies along its length. In order to ensure an even pressure of the measuring balloon on the inner cavity wall, a pressurization unit (24) in the external unit (20) is connected to the inner balloon. An independent pressure sensor attached to the inner surface of the inner balloon is used for measuring the pressure within said inner balloon at all times and controlling it.

In another mode of operation the balloons are inflated for the entire length of time that the distal end of the endoscope is situated within the body cavity by an automatic pressurizing system, thereby ensuring constant contact of the outer electrodes with the changing inner wall of the cavity. The plurality of "circles" on the array of electrodes enhance the probability of finding malignant tissue because if one "circle" does not diagnose malignant tissue (due to a technical malfunction or another reason) the other "circles" are likely to detect it.

The electrical circuit board (13) is preferably attached to the distal end of the endoscope for switching the signal between electrode pairs. A multi-filament electric wire connects each electrode on the membrane (11) to the small electrical circuit board (13). This type of circuit board is commonly used in RF measuring systems.

Optionally, the circuit board (13) amplifies and processes the signals such that their transfer to the external unit (20) will be improved. The circuit board comprises an amplifier circuit (131), as shown in figure 6. The amplifier circuit (131) amplifies the measured signals and converts them to lower frequency signals. Lower frequency signals have lower losses and are easily transferred through commonly used electrical wires.

The electrical circuit board (13) comprises an electronic switching element (132) that switches the measuring signal between all pairs of electrodes. The circuit board (13) is connected to the main harness unit (14), and receives measuring RF current signals from the external RF impedance

measuring unit (21). The circuit board (13) switches them to the electrode pairs. The voltage across these pairs is measured and impedance calculated. All electrode pairs are connected to the switching component by small tiny conducting wires. Optionally, the wires can be replaced by a small harness or alternatively a small flexible Kapton or Mylar printed wiring arrangement. The switching element is a multiplexer or any other electronic element able to switch the incoming signals to the pairs of electrodes located each on the flexible membrane.

The main harness unit (14) connects between the detection probe and the proximal part of the endoscope carrying both fluid pressure and electronic signals from inside the body to the external unit (20) and *vice versa*. The harness is connected to the external unit (20) *via* a multipurpose connector allowing both the flow of the balloon filling liquid/air/gas and the continuousness of the electrical circuits.

The main harness unit (14) comprises a flexible inflation/deflation conduit constructed from expandable elastomer such as silicone polyurethane, or any other biocompatible elastomer. The conduit has an external diameter of 1 mm to 5 mm, which connects the external pump to the balloon and allows for the rapid inflation/deflation of the balloon.

The main harness unit (14) further comprises a multitier wire, which carries the RF signals from the electrical circuit board (13) to the external unit (20). Through the harness unit (14), a pair of electrodes at a time is connected to the impedance measuring unit (21).

The intra body unit (10) of the device is attached to the generic endoscope prior to its introduction into the body. The flexible membranes (11, 12) are attached to the generic endoscope a few centimeters from its distal end thus reaching each area before an image thereof is captured by the video camera. For example, the colonoscope is usually retracted proximally and the measurements are applied before it is captured by the video camera.

The attachment of the dual-balloon device to the generic endoscope is preferably performed by an attachment tool. The tool is placed inside the inner balloon which is stretched, thereby enabling it to be mounted on the external surface of the endoscope. The tool is thereafter disconnected and removed, and the device of the present invention is held in place by the radial forces exerted by the stretched inner balloon.

The harness unit (14) is connected to the outer side of the generic endoscope by flexible clips or any other means enabling the medical staff either to attach or remove it in an easy manner.

The RF impedance measuring unit (21) is optionally a commercial unit or a unit built especially for the frequency range needed. An example of a typical unit is called a Vector Impedance Meter, which drives constant current between the electrodes and at the same time calculates the complex impedance by measuring voltage. Commercial vector impedance meters include, for example, the E4980A unit supplied by Agilent Technologies. In another embodiment of the present invention it is possible to use a simple custom-built

impedance measuring circuit. Circuits of this type are well known and understood by the skilled artisan in this field.

Resistance and capacitance data from each pair of electrodes are digitized and collected. All data is transferred into a computing unit (22). The computing unit comprises a processor which analyzes the data and decides upon detection of a suspicious tissue. Impedance data from electrodes located along the balloon circumference are compared. Irregularities in the electrical impedance are identified, enabling the user to locate malignant tissue, such as polyps which are malignant or harmless, located inside the body cavity (e.g. the colon).

A special mathematical algorithm enables the differentiation between a normal and abnormal tissue. During the movement of a colonoscope inside the colon, for example, the diameter of the balloon changes frequently. This is since the balloon adjusts itself to the diameter of the colon, which is not constant. A momentary record of all impedance data at one location inside the colon might be different from one collected at another point. Therefore data from all electrode pairs is collected electronically at a rate that is faster than the mechanical movement of the colonoscope inside the tract. In a rapid movement, the colonoscope may reach a maximum speed of about 1cm/second. Measurement and data collection should be performed from all electrodes located at a single balloon circumference in about 0.25sec assuring that the electrodes move a maximal distance of 2.5 mm during a full set measurement.

Data is collected from electrode pairs and averaging the resistance and capacitance of all electrodes is performed.

That average serves as means of calibration (e.g. as an impedance reference) during the analysis of the signal received from each electrode pairs. The measurement method and algorithm are therefore not dependent on an absolute impedance reference number. This is very significant, since many methods of tissue impedance changes fail due to lack of an absolute impedance reference. The suggested method creates a momentary measured reference and is therefore effective in the variety of tissue impedance changes both between different patients and between different points along the body cavity.

The above algorithm compensates also for technical errors created by the changing diameter. In one of the embodiments described using single electrodes, the distance between electrodes changes as a function of balloon diameter. In another embodiment - the coaxial electrode arrangement - the distance between electrode pairs is constant, and the compensation algorithm can be applied for other reasons.

The electrode carrying membrane (11) is designed to have a constant thickness, ensuring that when it expands, the distance between all pairs of electrodes is the same during expansion. This is important for calculating average reference impedance and looking for variations from that reference number.

In the event that, due to a manufacturing problem for example, the distance between electrode pairs would not reach the needed accuracy, a pre- calibration process may be applied. In this process, the membrane (11) is inflated, introduced into a dielectric liquid, and distances calibrated by performing a dielectric measurement. Correction factors

may be introduced into the analysis algorithm compensating for the distance variation such that when performing an in vivo measurement with the device, the manufacturing variations are compensated for.

Results of the impedance measurement are displayed on a monitor (23). In one preferred embodiment, the impedance measurements are combined and displayed on the regular video image supplied by said monitor. Since the device allows the detection of a suspicious area, one can mark a circle on the screen and highlight the sector of the circle at which a suspicious tissue is detected. To have a reference angle between the suggested device and the video system, a small marking rod could optionally be attached to the device- extending towards the view field of the video camera thereby enabling the doctor to initialize the angle reference scale. This step provides information regarding the exact sector at which the suspicious tissue is located. Fig. 8 provides an example of such a monitor image of the large intestine, wherein a suspicious region is indicated by the white lines, and the marking rod by the black line.

An automatic pressurization unit (24) keeps the inner balloon at all times at a pre-determined pressure. The pressure may be of any appropriate liquid-fluid, air or any gas. The pressure used is typically around 60mbar, a pressure commonly used by physicians during colonoscopy procedures. Since the colon diameter varies, the balloon diameter should change accordingly. This means that the pressurization system at some instances has to fill the balloon quickly to the wanted pressure and at other point- pump out the extra liquid/gas. This has implications for pumping speed, filling speed and tubing diameter, which are designed accordingly. Pressure

sensors sense the balloon pressure at all times. A typical pressure sensor that may be employed is a sensor of the type commonly used in blood pressure measurements (for example Omron MEMS sensors or capacitive diaphragm sensors).

The layout of the automatic pressurization unit (24) is shown in Fig 7. A microcontroller (242) obtains the pressure measurements within the inner balloon from sensor (241), which may be located inside the balloon (as illustrated in Fig. 7) or at any other point in the balloon inflation/deflation line. According to the measured sensor readings, the pressurization unit either causes release of liquid/gas by activating a pumping unit (243) or causes filling of the balloon with fluid using a pressure pump (244). Optionally, the pressurization unit comprises an additional pressure container pre-filled by the slow pump and acting quickly whenever a balloon fill is needed in a short time. This option is useful in case the primary pump reaction is too slow.

The use of the device and system of the present invention thus ensures a higher probability of tumor detection during a diagnostic medical procedure.

When using the present device, the colonoscopy (or other endoscopic) procedure will become much easier to perform, since said device is able to alert the physician ahead of time regarding any suspicious tissue. The common miss-rate of polyps during colonoscopy stands at about 24%. Using the present device, the detection of polyps and other lesions, sometimes missed by the physician - for example flat polyps

or any other kind of polyp - will be higher making the procedure much more efficient.

The present invention also provides a method for diagnosing malignant tissue in a body cavity such as the colon, or other body passage including (but not limited to) the esophagus or the female reproductive system. According to said method, RF energy is used to detect the electrical properties of tissue. A constant RF current is passed between two electrodes, which are brought in touch with the measured tissue and the voltage across the electrodes is simultaneously measured. By having both voltage and current as a function of time one can easily calculate the complex impedance of the tissue.

Generally, a decrease in impedance of about 10 - 20% is indicative of the presence of a polyp other lesion in the colonic wall. In other cases, an increase in impedance of a similar magnitude will indicate the presence of a lesion.

In one preferred embodiment, the present method involves the use of a device that may be attached to a generic endoscope, wherein said device comprises an expandable or inflatable membrane with an array of electrodes attached to it.

The method includes inflating the membrane with the array of electrodes attached, such that each of the electrodes on the membrane are pressed upon the circular open body cavity by the inflation of said membrane. The electrical properties of the tissue between the electrodes are measured and calculated thus diagnosing polyps and malignant tissue.

In another preferred embodiment of the method of the present invention, said method involves the use of a measuring device

that comprises two balloons, as described hereinabove, and measured, calculated and diagnosed as explained herein above.

The method of the present invention may be used to diagnose the presence of many different types of lesion in the tissues that form the walls of body cavities. These lesions include (but are not limited to) neoplastic conditions (such as various types of colonic malignancies), and pre-malignant lesions (such as colonic polyps).

While some of the embodiments of the invention have been described by way of illustration, it will be apparent that the invention can be carried out in practice with many modifications, variations and adaptations, and with the use of numerous equivalents or alternative solutions that are within the scope of a persons skilled in the art, without departing from the spirit of the invention, or the scope of the claims.

CLAIMS

1. A diagnostic device suitable for attachment to the external surface of an elongate medical instrument, comprising:
a) an inner radially-expandable element located within the lumen of a separate, outer, radially-expandable element, wherein said outer expandable element is fitted with a plurality of RF electrodes on its outer surface; and
b) a harness unit containing one or more conduits for connecting the lumen of the inner expandable element with a source of pressurized inflation fluid, together with electrical wiring that is capable of connecting said RF electrodes either directly or indirectly with external power, control and/or computational units.

2. The device according to claim 1, wherein said device further comprises an electrical circuit board located in proximity to said expandable elements, wherein the leads of the electrodes are connected to said circuit board.

3. The device according to claim 1, wherein the inner radially expandable element is a radially expandable balloon, having one or more openings which are in fluid connection with the inflation conduit.

4. The device according to claim 1, wherein the outer expandable element comprises a flexible membrane.

5. The device according to claim 4, wherein the flexible membrane is provided in the form of a balloon.

6. The device according to claim 5, wherein the outer balloon is in fluid connection with an inflation conduit.

7. The device according to claim 1, wherein the plurality of electrodes comprises an array of single electrodes having defined mutual separation distances.

8. The device according to claim 1, wherein the plurality of electrodes comprises an array of coaxial electrodes.

9. The device according to claim 1, wherein said device is suitable for attachment to the external surface of an endoscope.

10. The device according to claim 1, wherein the endoscope is a colonoscope.

11. A diagnostic system comprising
a) a diagnostic device according to any one of claims 1 to 10;
b) an RF impedance measuring unit;
c) a computation unit comprising suitable hardware and software for analyzing the output of said RF impedance measuring unit; and
d) a source of inflation fluid and pumping means for causing said fluid to move into and out of the fluid conduits contained within said diagnostic device.

12. The system according to claim 11, further comprising an automatic pressurization system for automatically controlling the inflation pressure within the lumen(s) of said expandable elements.

13. A method for diagnosing the presence of malignant tissue within the wall of a body cavity or passage, wherein said method comprises the steps of:
a) introducing into said body cavity or passage a first radially-expandable element containing an array of electrodes on its outer surface;
b) causing the radial expansion of said expandable element, such that said electrodes contact said body cavity wall;
c) passing an RF current between pairs of electrodes;
d) calculating the impedance of the body cavity wall region that is in contact with said electrodes;
e) determining from the change in impedance in certain areas of the body cavity wall that said areas are putative sites of malignant and/or pre-malignant tissue.

14. The method according to claim 13, wherein the expansion of the first radially-expandable element is caused by the expansion of a second, inner radially-expandable element placed within the lumen of said first radially-expandable element.

15. The method according to claim 13, wherein the body passage is the colon, and wherein the expandable element bearing the electrodes is attached to a colonoscope.

16. The method according to claim 13, wherein said method further comprises the step of automatically maintaining the electrodes in contact with the body cavity wall by means of operating an automatic pressurization system.

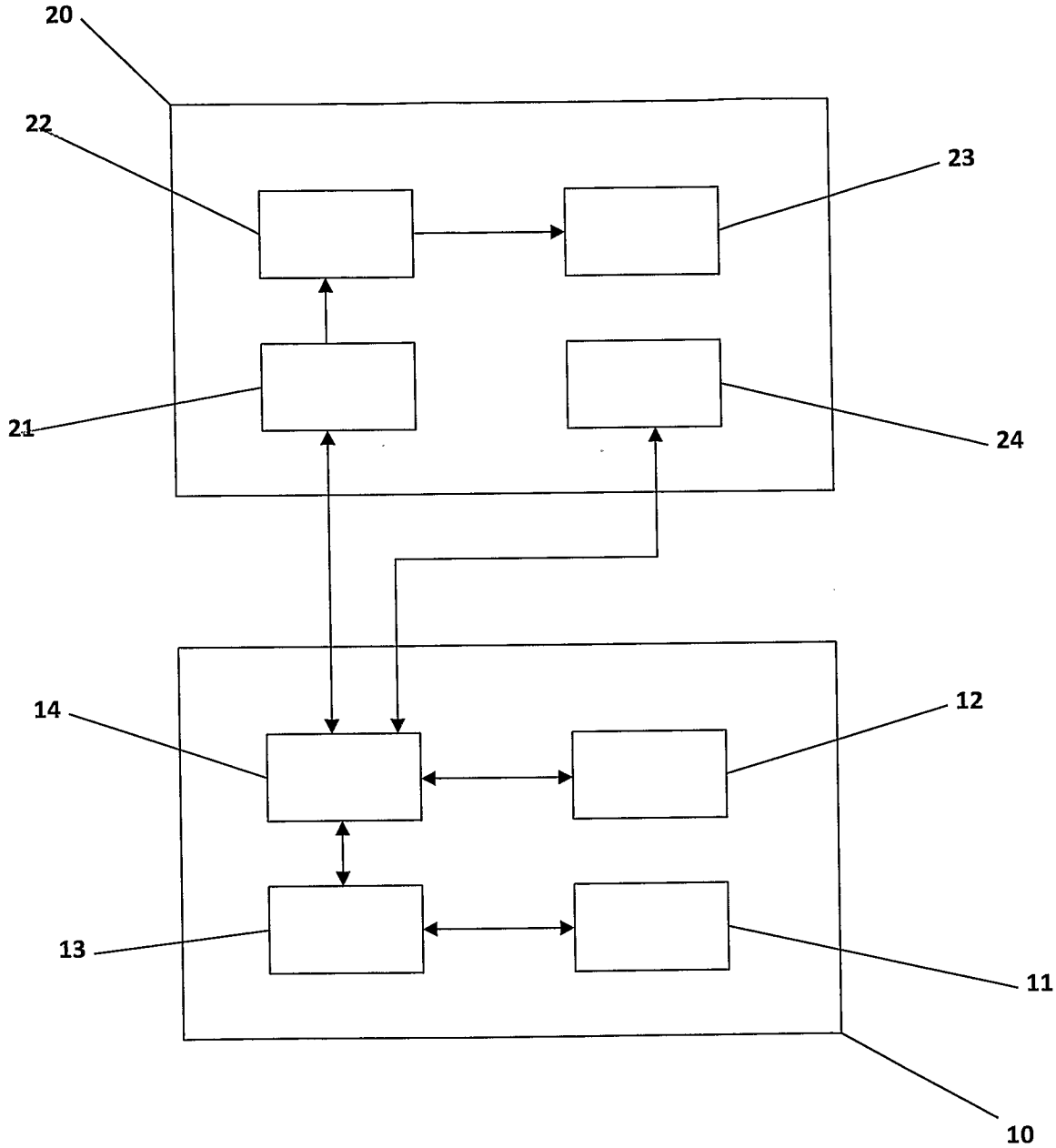

FIG. 1

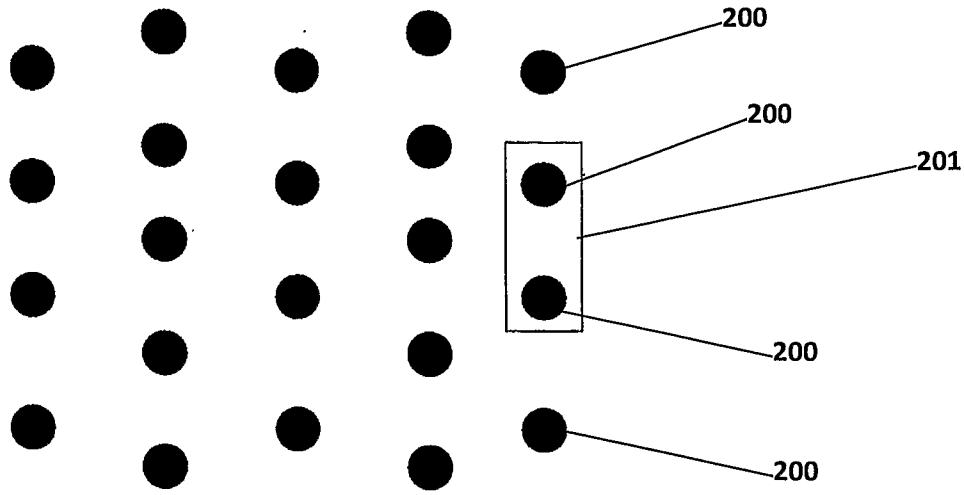

Fig. 2A

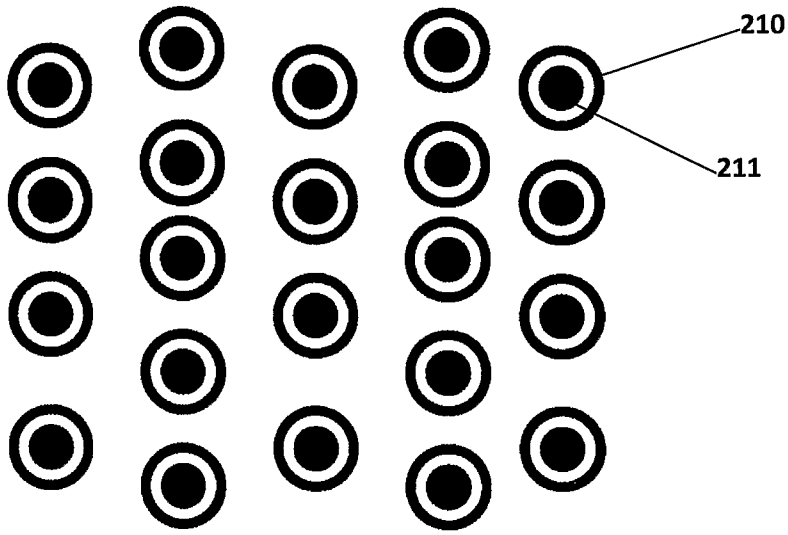

Fig. 2B

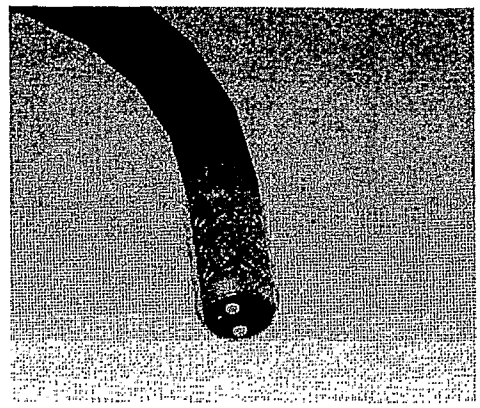

Fig. 3A

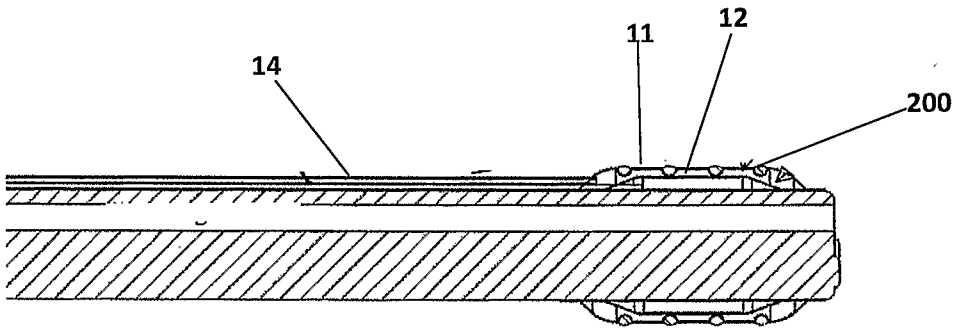

Fig. 3B

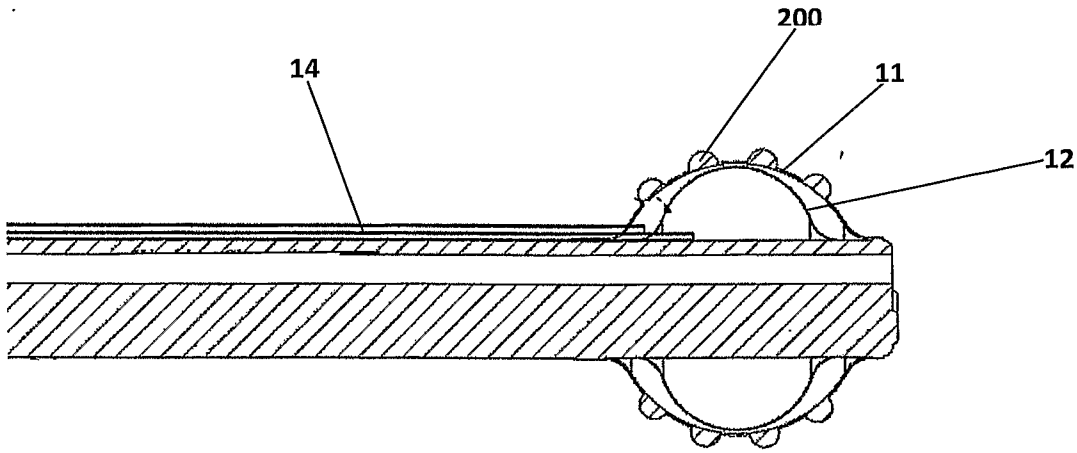

Fig. 4

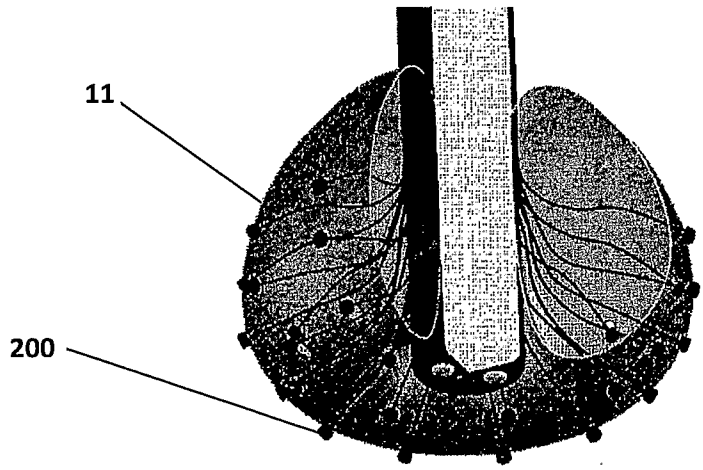

Fig. 5

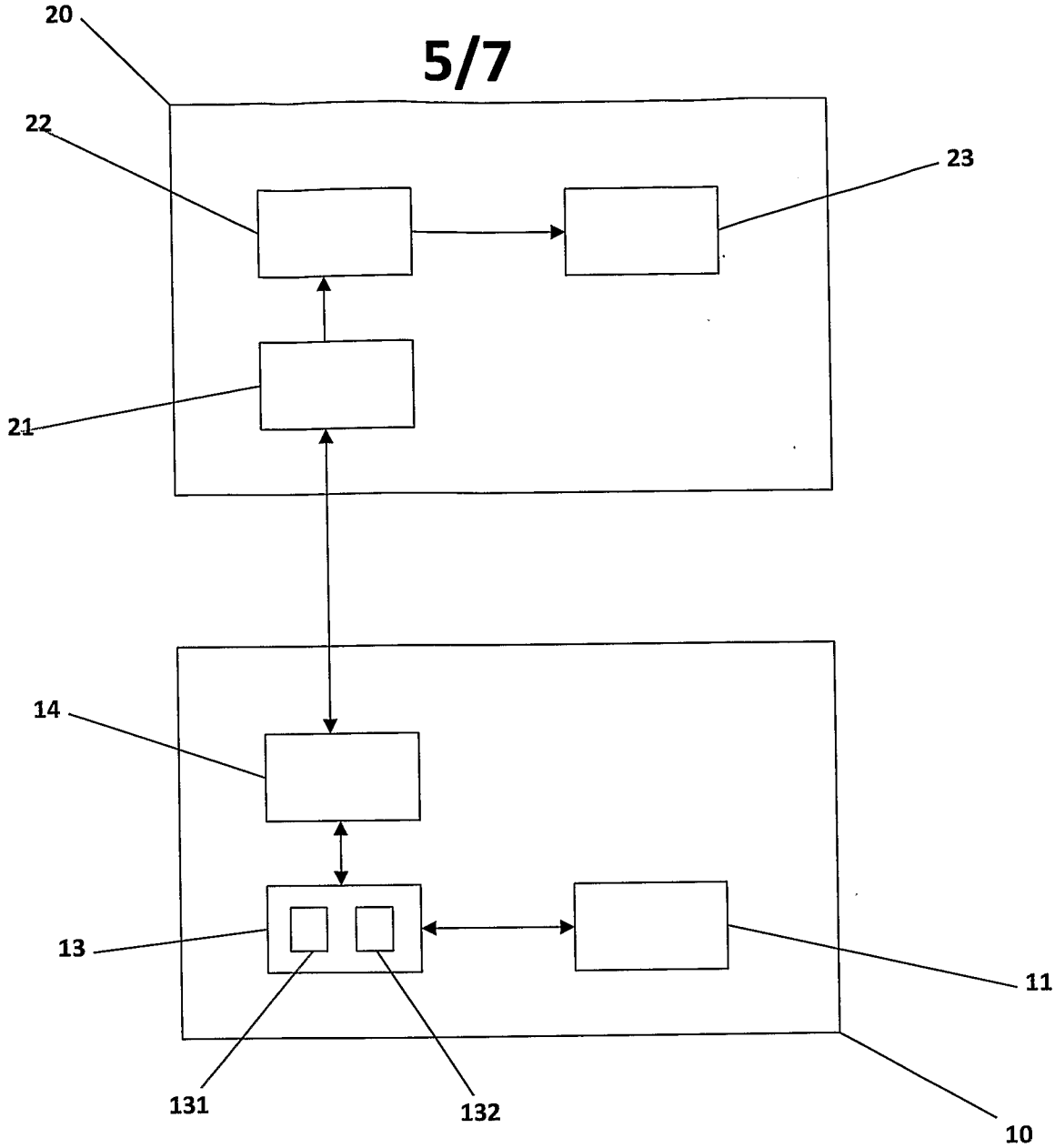

FIG. 6

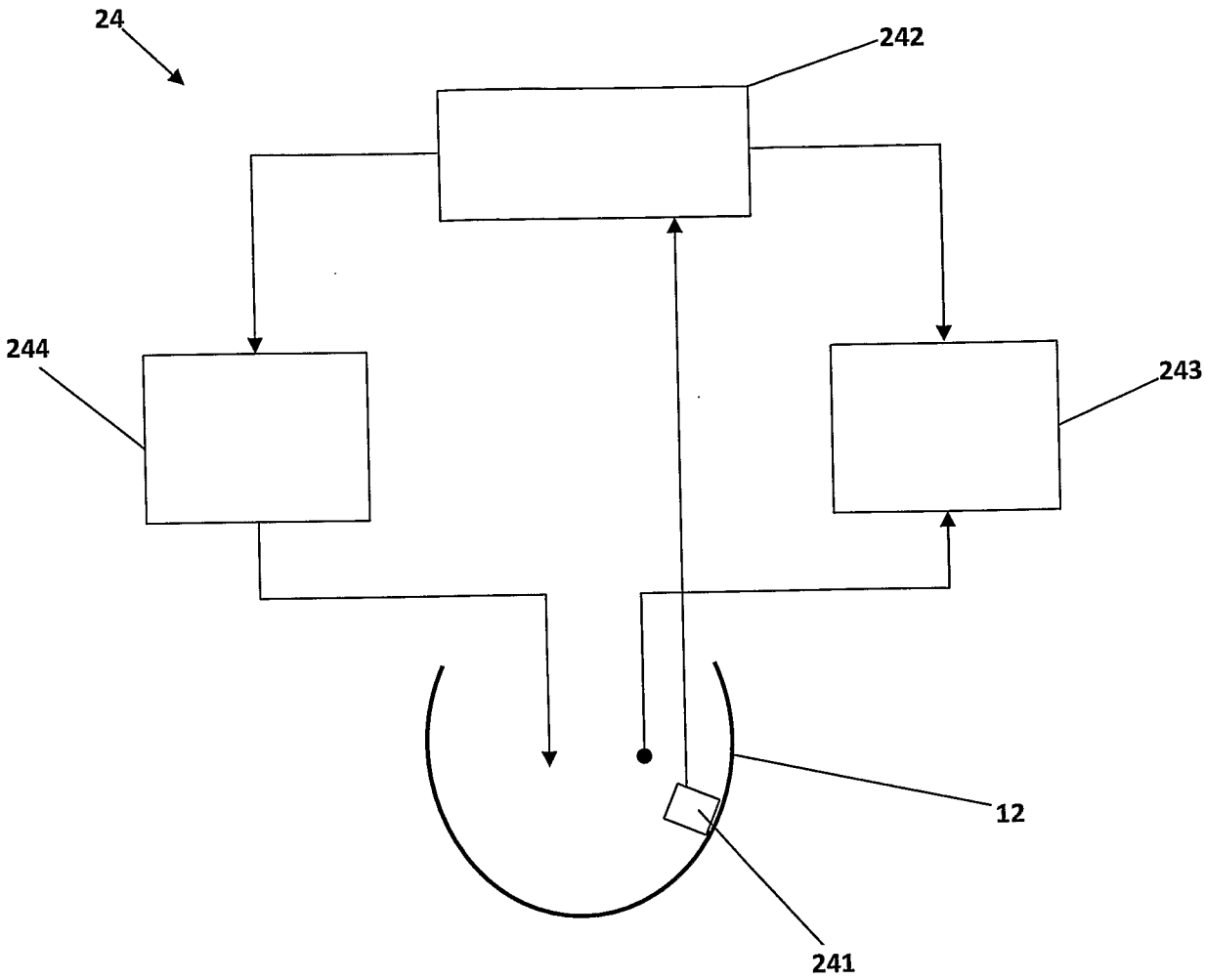

FIG. 7

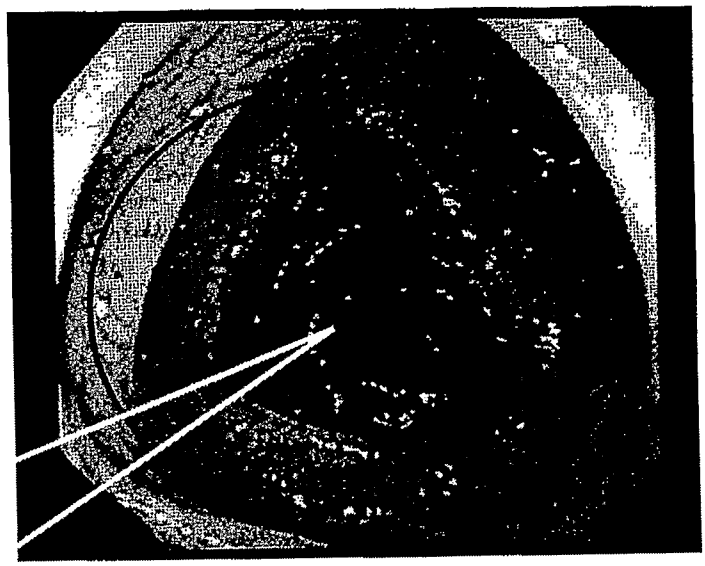

Fig. 8