Tissue vitality is monitored by means of a sensor attached to the tissue. Preferably, the sensor is attached to the tissue at the end of a surgical intervention, for example after anastomosis of the colon. The sensor is attached to the tissue with a sensitive surface facing the tissue, e.g. at a point of anastomosis. The sensor is designed to measure for example (partial) carbondioxide or oxygen pressure of the tissue, or the amount of oxygenated hemoglobin in the tissue. The sensor is incorporated in a sensing device with a wireless transponder circuit to read sensor output data from a wireless transponder circuit. As a result the sensor can subsequently be used to read out information about tissue vitality, even if the sensor itself is located in an inaccessible location, such as the inside of the colon, without physically perturbing the tissue.
Title: Tissue vitality monitoring system and method and surgical technique.

The invention relates to a tissue vitality monitoring system and method.

Background of the invention

Many patients die every year as a result of leakage of esophagus, gastrointestinal and hepato-pancreatico-biliary anastomoses. An anastomosis is the surgical joining of parts of the bowel or of other organs to make them continuous and is an ongoing problem, showing a high morbidity and mortality and involving tremendous costs. In general, on average 3-12% of all gastrointestinal anastomoses leak, with the highest occurrences for leakage being observed for rectum resection (10%), pancreas surgery (8%) and esophagus resection (5%). More specifically, in the case of leakage of rectum (terminal part of the large intestine) anastomoses, statistics show a mortality of 10-20% and a morbidity of 30-50%. In conclusion, anastomotic leakage is the main, yet unsolved reason for the major lethal risk in abdominal surgery.

If a leakage problem is detected it is mostly treated via surgery. The state of the patient (already weakened by the first operation) deteriorates because by the time leaks are discovered, which is in most cases after four or more days, a threatening abdominal infection is present, which makes the surgical repair of the anastomosis hazardous.

To date there are limited tools available to the surgeons to assess the quality of the anastomosis during operation and during the post-operative phase. The medical world needs an aid to detect leakage both during the operation and during the critical recovery period. Considering the large number of complications this could lead to a major advance.

One example of a technique to detect leakage of an anastomosis is to fill the abdomen with a saline solution, while the colon is immersed in it. If air
bubbles develop at the anastomotic site there is clear indication that the
anastomosis is leaking. Unfortunately, such an examination is time consuming
and not very accurate. Moreover, it does not offer the certainty that the
anastomosis will not leak at a later stage.

To detect subsequent leakage of an anastomosis patients are surveyed by
evaluating clinical, radiological and endoscopic parameters with limited
sensitivity such as pain, fever, ileus, CT imaging, urine production (volume)
and blood tests.

In the prior art there is consensus that the quality of the arterial and
venous circulation (tissue perfusion) in the organs that are anastomosed is of
utmost importance for the normal healing of anastomoses. Among various
techniques for tissue perfusion measurement, thermal dilution methods based
on the bio-heat equation were recently developed. They appear to be more
quantitative, easy to control and less expensive than other existing techniques.

These techniques include the self-heated thermistor method (see J. C. Chato, “
A method for the measurement of thermal properties of biological materials”,
16-25) and the thermal pulse decay technique (H. Arkin, K. R. Holmes, V.
Rupinskas, “Pulse decay method for measuring the thermal conductivity of

A common shortcoming of the above methods is the use of invasive probes
that have to be used to heat and acquire temperature information. A non-
invasive method to measure tissue perfusion using the phase shift between an
applied sinusoidal heat flux and the skin surface temperature response has
been proposed in J. Liu, Y. Zhou, Z. Deng, “Sinusoidal heating method to no
invasively measure tissue perfusion”, IEEE Transactions on Biomedical
Engineering, vol. 49, no.8, 2002, pp. 867-877. For perfusion estimation, the
induced thermal field needs to be weak enough so that it does not affect the
regional blood flow. In practice, the heat flux was generated with a heat plate
consisting of copper wires, while the surface temperature response was
measured with a thermocouple. The method was tested in experiments on the human body as well as non-perfused materials, showing promising results. Nevertheless, further investigations are necessary to simplify the present measurement instrument.

Another technique, mainly developed to measure tissue perfusion for mammography investigations makes use of the ultrasound contrast agent interruption as well as decorrelation methods. This is disclosed in J. B. Fowlkes, "An examination of ultrasound measured tissue perfusion on breast cancer", Optics and acoustics, 1998 - http://www.stormingmedia.us/20/2033/A203333.html. Contrast interruption allows control of contrast-agent flow in selected vessels and is used in conjunction with common ultrasound imaging methods that measure the contrast agent signal level. On the other hand, contrast decorrelation measures contrast motion through the ultrasound beam. With certain modifications, this technique may directly assess perfusion in a real-time imaging application of flow in ultrasound accessible tissues.

In some areas of medicine, tissue perfusion is investigated using the PET (positron emission tomography) and SPECT (single photon emission computed tomography) techniques, but these are very costly and cannot be used to provide continuous measurements for anastomotic leakage. Other imaging techniques such as angiography or nuclear magnetic resonance imaging are invasive and use expensive equipment.

A less costly device, used in different hospitals, is the Laser Doppler flowmeter. The device is employed for the real-time measurement of microvascular blood flow. Laser Doppler Flowmetry (LDF) works by illuminating the tissue under observation with low-power laser light from a probe containing optical fibre light guides. Laser light from one fibre is scattered within the tissue and some is scattered back to the probe. Another optical fibre collects the backscattered light from the tissue and returns it to a monitor. Most of the light is scattered by tissue that is not moving but a small percentage of the returned light is scattered by moving red blood cells. The
light returned to the monitor undergoes signal processing whereby the emitted and returned signals are compared to extract the Doppler shift related to moving red blood cells. This method is non-invasive and was employed for intra-operative use (see for example A. Vignali, Luca G., Marco B., Giovanni M.B., L. Malvezzi, C. Valerio, “Altered microperfusion at the rectal stump is predictive for rectal anastomotic leak”, Dis. Col. Rect. Vol. 43(1), 2000, pp.76-82). However, the device is rather large and therefore it becomes inconvenient to place it on tissue in clinical practice. Moreover, the pressure exerted by the probe on tissue has proven to influence the measurements. This is mainly because the clinician cannot hold the probe completely still and any small hand movements would press on the capillaries, closing them.

It is also known to monitor heart activity, oxygen or glucose level in the veins etc. by means of implanted sensing devices. Typically such devices are permanently implanted (or at least until they are replaced) and connected to a readout interface from which sensor data can be read out.

The above-described techniques are used in certain medical areas and for certain interventions, but all have disadvantages for the proposed application of monitoring vitality of tissue, in particular of anastomoses and more particularly of anastomoses of the colon. Some of the techniques are rather expensive, some use probes that are not easy to handle, cannot measure continuously or are invasive.

US patent No. 6,241,743 discloses application of an oxygen sensor in an implanted anastomosing ring for veins. In one embodiment this ring contains a sensor for measuring oxygen content of blood that flows through the anastomosed artery. WO02060244 discloses the implantation into mice of temperature sensors from which data can be read with a wireless transponder. These sensors are not directed at anastomosed tissue.

A known sensor to measure oxygen is the Clark (polarographic or amperometric) electrode, which uses a cathode that is held at a polarising voltage, causing the reduction of oxygen. The anode is commonly made of
silver. The current flow from the anode to the cathode is proportional to the oxygen content of the solution. Miniature silicon-based Clark cells have been developed making them suitable for use in tissue measurements, where they are affixed to the skin of human subjects. Polarographic electrodes have been widely used for monitoring tissue oxygen but a number of disadvantages remain unresolved. At low oxygen pressures, the electrodes consume a significant quantity of oxygen by the electro-chemical reduction reaction. As a result, the electrode tends to underestimate the level of tissue oxygen if left in place, an effect, which is most evident under conditions of tissue hypoxia.

Moreover, the silver of the anode slowly consumes so that the working life of these miniature Clark cells is only a few hours. An optimised version of the standard Clark cell was developed by Arquint et al. (Ph. Arquint, A. v.d. Berg, B.H. v.d. Schoot, N.F. de Rooij, “Integrated blood-gas sensor for PO2, pCO2 and pH, Sensors and Actuators B, 13-14 (1993), pp. 340-344). The sensor can be continuously operated for more than two weeks, in blood, but there were no tests performed in tissue.

Another way to measure tissue oxygenation is based on the following concept: capillary oxygen pressure may approximate arterial oxygen pressure in areas of the skin where local blood flow exceeds the amount necessary for local tissue oxygen needs. This approximation may hold if the local area is heated. An electrode is attached to tissue and heated to 40°C, providing local vasodilatation. Oxygen from the capillaries can then diffuse through the skin into a Clark cell, for direct measurement. The disadvantages of this technique are the tissue burns that result from a prolonged application for more than 2-3 hours.

What is needed is a tissue vitality monitoring system that aids the surgeon during the operation to reduce the number of complications requiring a second operation (construction of an artificial anus/stoma) and/or, in cases where there are still complications, to give a fast warning so that the problem can be tackled quickly to save the patient or prevent irreparable damage.
Summary of the invention

Among others it is desirable to develop a measurement system and method able to provide readout of tissue vitality data, wherein individual readout operations do not require renewed physical access to the tissue.

Among others it is desirable to develop a measurement system and method able to provide readout of adequate tissue perfusion, wherein individual readout operations do not require renewed physical access to the tissue.

Among others it is desirable to develop a miniaturised measurement system able to provide readings of adequate tissue perfusion.

Among others it is desirable to develop a surgical technique that reduces the number of complications requiring a second operation and/or to give a fast warning of potential complications.

There is provided a surgical method that includes anastomosis of tissue and attachment of a wireless sensing device. The sensitive surface of the sensing device is placed facing the anastomosed tissue. The sensing device includes a wireless transponder circuit, preferably an RF transponder circuit that derives its power supply from the RF field from outside. Such devices are known per se for example from access control systems, wherein a transponder is provided on a card that is carried by authorized persons. Commercial applications of this technique to medical are available from Telemedtronic, and described in WO02060244. Subsequently, sensing data is read from the sensing device with a transmitting/receiving unit to monitor tissue vitality of the anastomosed tissue.

In an advantageous embodiment the method is applied to anastomosis of the colon and the sensing device is attached to colon tissue in the intestinal tract and the sensing device is affixed to the colon only by a soluble attachment such as a soluble suturing wire. Thus, the sensing device will be washed out
after a few days without further need for an intervention to remove the device. However, the method can be applied to any kind of tissue, in particular to wounds to monitor healing.

According to another aspect a method of monitoring parameters of tissue vitality is provided, the method comprising using a transmitter/receiver to read sensor output data from wireless transponder of a sensing device that is attached to the tissue with a most sensitive surface facing the tissue. Preferably the sensing device is arranged to sense oxygen and/or carbon-dioxide perfusion in the tissue. A high level of oxygen is indicative of healthy blood circulation. Accumulation of carbon-dioxide is indicative of the absence of healthy blood circulation. In one embodiment the sensing device senses the pressure of oxygen and/or carbon dioxide that diffuses from the tissue into part of the sensing device through the sensitive surface. In another embodiment the sensor senses absorption of light that returns to the sensing device through the sensitive surface from the tissue adjacent the sensitive surface. Preferably a plurality of measurements for different wavelength bands is used to determine the fraction of hemoglobin that is oxygenated.

Preferably, a plurality of sensors for different parameters is integrated together in the vitality-monitoring device.

Thus, a sensing device is used in the manufacture of a tissue vitality monitoring device and preferably for an anastomosed tissue vitality monitoring device, and more preferable for an anastomosed colon tissue vitality monitoring device.

Brief description of the drawing

These and other advantages and aspects will be illustrated by means of non-limitative embodiments using the following drawings.

Figure 1 shows a tissue vitality monitoring system
Figure 2-4 show sensing devices

Figure 1 shows a tissue vitality monitoring system (not drawn to scale) comprising a transmitter/receiver unit 10, and a wireless sensing device 12 attached to tissue 14. (Wireless, as used herein, means that measurement data can be read out of the device without using conductors between the sensing device and a readout device. As used herein, it does not exclude the use of wires inside the sensing device.). Sensing device 12 comprises a wireless transponder circuit 120, an interface circuit 121 and sensors 122, 124, 126, 128. Sensors 122, 124, 126, 128 each have an exposed surface through which they sense tissue parameters. These sensitive surfaces all lie on a sensing surface 129 of sensing device 12 (typically in a single plane). Interface circuit 121 couples sensors 122, 124, 126, 128 to transponder circuit 120.

Sensing device 12 has attached rings 16 (shown in side view) in a plane that is parallel to sensing surface 129 and/or lies in an extension of sensing surface 129. Rings 16 have eyes of a size to receive suturing wires that attach sensing device 12 to tissue 14 (e.g. a diameter of between 1 and 5 millimetre). In the attached position sensing surface 129 faces tissue 14 and is in contact with tissue 14. Rings may be provided for example on a backplate on which one or more semi-conductor devices are mounted that implement transponder circuit 120, interface circuit 121 and sensors 122, 124, 126, 128.

One example of an application of the tissue vitality monitoring system is during or in the aftermath of colon surgery. During a surgical intervention a part of the colon of a patient is removed and the ends of colon on either side of the removed part are joined to each other (anastomosed) using suturing wire or staples for example. Sensing device 12 is attached to the colon in the digestive tract (on the inside of the colon), with sensing surface 129 facing the anastomosed tissue (facing anastomosed tissue, as used herein, means facing tissue right at the point of anastomosis or so close to this point that the vitality of the tissue that is in contact with sensing surface 129 is
decisive for leakage from the anastomosis). Subsequently sensing data is read at least once from sensing device 12, using transmitter/receiver unit 10. Typically this is done a number of times during recuperation from the surgical intervention, or even before the time of completion of the surgical intervention. The resulting measurement data is provided to a doctor for analysis and decision whether a renewed intervention or treatment is necessary due to lack of vitality of the tissue.

Preferably, conventional soluble suturing wire, soluble staples or any other soluble attachment means are provided through rings 16 and through the wall of the colon. This means that it is a matter of time, typically 4-7 days, or about a week to at most a month, before the wire, or staple etc. dissolves so that sensor will be washed out through the colon. This has the advantage that no further surgical intervention is needed to remove sensing device 12 after it has determined that the anastomosis is healing properly or not. In this case the biocompatibility tests are less stringent than for permanent implants. As an alternative the sensing device 12 can be fixed on the outside of the colon, as a permanent implant, or on the outside of the colon and attached to a drain.

Transmitter/receiver unit 10 and wireless transponder circuit 120 may be implemented using known techniques. Typically, transmitter/receiver unit 10 is designed to emit an electromagnetic field that carries a query signal. Also typically, transponder circuit 120 is arranged to pick up energy from the field (or from an auxiliary field emitted by transmitter/receiver unit 10) and to power operation of sensing device from the picked up energy. Transponder circuit 120 is arranged to receive and decode the query signal and to generate a response signal (e.g. in the form of a modulation of absorption of the electromagnetic field) that encodes sensor output data requested by the query signal.

Transmitter/receiver unit 10 detects the response signal and decodes the sensor output data from the response signal. The sensor output data may
then be displayed by transmitter/receiver unit 10, or uploaded to a diagnostic system (not shown) and/or processed to provide more convenient data.

Sensors 122, 124, 126, 128 are designed to measure tissue parameters that are indicative of tissue vitality. Any type or combination of sensors suitable for this purpose may be used. Preferably sensors for in situ measurements of the quality of the arterial and venous circulation (perfusion) in the anastomosed tissue are used.

An example of a parameter that may be sensed as an indication of perfusion is oxygen pressure in the tissue, for example in terms of oxygen pressure of oxygen that diffuses from the tissue through the sensitive surface into part of the sensor body. Another example of a parameter that may be sensed as an indication of perfusion is oxygen saturation, i.e. the quantity of oxygen in the tissue, or more preferably the fraction of hemoglobin in the tissue adjacent sensing surface 129 that is oxygenated. Another example of a parameter that may be sensed as an indication of perfusion, is carbon dioxide partial pressure in the tissue.

In one embodiment an oxygen pressure sensor 122, an oxygen saturation sensor 124, a carbon-dioxide pressure sensor 126 and a temperature sensor 128 are used. In this case oxygen pressure sensor 122, oxygen saturation sensor 124, and carbon-dioxide pressure sensor 126 each have an exposed surface next to, or through, which these sensors sense oxygen and/or carbon dioxide. These sensitive surfaces all lie on a sensing surface 129 of sensing device 12 (typically in a single plane).

Figure 2 shows an illustrative example of an oxygen and carbon dioxide sensor 20 in the sensing device. Sensor 20 comprises a substrate 22 with a first and second photodiode 24a,b thereon. Respective layers of polymer material 26a,b are provided on photodiodes 24a,b. Between photodiodes 24a,b a well is provided. The well has skewed sidewalls 28a,b covered by reflective material. A LED 29 (Light Emitting Diode) is provided in well 25, positioned to emit light on either side of LED 29 towards skewed sidewalls 28a,b. The layers
of polymer material 26a,b extend from above photodiodes 24a,b at least to the emitting sides of LED 29. LED 29 and photodiodes 24a,b have anode and diode contacts (not shown) coupled to interface circuit 121 (not shown).

Each layer 26a,b comprises a gas permeable polymer and a fluorescent compound that is immobilized in the gas permeable polymer. In the respective layers 26a,b fluorescent compounds are used of which the dye will be quenched by contact with oxygen and carbon dioxide respectively. The dye in the polymer of a first one of the layers 26a is reactive to oxygen but not, or less, permeable for carbon dioxide. Conversely the dye in the polymer of the second one of the layers 26b is carbon-dioxide reactive but not, or less, reactive for oxygen. Materials of this type are described in Draaijer A., Konig J.W., Gans de O. Jetten J., Douma A.C. “A novel optical method to determine oxygen in beer bottles”, 27th Congress of the European Brewery Convention 1999

The surfaces of layers 26a,b form the sensitive surface of the sensor. The main (largest) surfaces of layers 26a,b are placed into contact with tissue 14. As a result oxygen and carbondioxide will diffuse from the tissue into layers 26a,b, establishing a concentration that depends on the pressure of free oxygen/carbon-dioxide in tissue 14. Typically the tissue will fold around the top and sides of layers 26a,b and against a remainder of surface 129 around layers 26a,b so that substantially no oxygen or carbon dioxide from other sources can diffuse into layers 26a,b. Alternatively layers 26a,b may be provided in a recess of sensitive surface 129 to seal off diffusion from outside.

During measurement interface 121 applies a voltage pulse between the anode and cathode of LED 29 to cause emission of a pulse of light with a wavelength of about 470 nm for example, which is reflected into layers 26a,b via skewed sidewalls 28a,b. The pulse excites the fluorescent molecules in layers 26a,b. Subsequently the fluorescent molecules decay to their unexcited state, emitting fluorescent light. The excited state (caused by an excitation light pulse) of a fluorescent molecule is deactivated by a collision process with oxygen, which has the effect that the fluorescence decreases. As a result, the
fluorescence decay time depends on the concentration of oxygen and carbon
dioxide that has diffused into layers 26ab respectively.

Measurement interface 121 measures the conductivity of
photodiodes 24a,b to measure the intensity of the fluorescence from layers
26a,b as a function of time. The oxygen concentration in such sensors can be
determined in two ways: by measuring the fluorescence intensity or by
measuring the fluorescence lifetime. Using the latter method has the
advantage that the measurement is independent of the source intensity,
detector efficiency and fluorescent probe concentration. Measurement interface
121 sends data indicative of the measured intensities or a decay time that it
has computed from the intensities to transmitter/receiver unit 10 via
transponder circuit 120.

Using this principle, the sensor system can be miniaturised to the
dimensions required by in situ monitoring of anastomoses. Preferably the size
of the sensor is made so small that it does not significantly interfere or
jeopardize functioning of the anastomosed tissue. Preferably, therefore the
diameter of the sensor is less than one centimetre, more preferably less than
half a centimetre or even less than a millimetre. It is important to note that
the quenching process does not consume oxygen or carbon dioxide, so that the
measurements can easily be repeated over an extended period of time. Thus,
simple LED excitation and photodiode detection can be used to construct a
simple oxygen sensor.

The sensor of figure 2 can be manufactured using conventional
photolithographic micro-electronics manufacturing techniques, followed by the
application of layers 26a,b. Alternatively, the LEDS and/or any other parts
may be manufactured separately and placed in the sensor.

Figure 3 shows an alternative Carbon-dioxide pressure sensor 30.
This type of sensor is known per se from an article titled "A swelling hydrogel-
based PCO2 sensor", by S. Herber, W.Olthuis and P. Bergveld and published
in Sensors and Actuators B 91 (2003) pages 378-382. This sensor comprises a
cavity 34 filled with a bicarbonate solution. A top of cavity 34 is closed off with a carbon-dioxide permeable membrane 36. A porous metal screen 35 is provided in cavity 34, attached to substrate 22 on opposite sides of cavity 34. A hydrogel 32 provided between a bottom of cavity 34 and screen 35, that is filled with a bicarbonate solution next to hydrogel 32. Hydrogel 32 contains microspheres that respond to changes in pH by swelling or shrinking, dependent on the direction of change in pH. A strain gauge 38 is attached to the bottom of the cavity.

... Hydrogel 32 contains microspheres that respond to changes in pH by swelling or shrinking, dependent on the direction of change in pH. In operation, a carbon dioxide pressure balance is established between the tissue and the solution. Changes in the carbon dioxide in the hydrogel changes the pH of the solution, which results in swelling or shrinking of the microspheres. In turn this results in a change in the force that the hydrogel exerts on the bottom of the cavity. A resulting deformation is measured by strain gauge 38.

Figure 4 shows an oxygen saturation sensor 40 which is designed to measure differences in the light absorption spectrum of deoxygenated and oxygenated hemoglobin. The construction of sensor 40 is similar to that of figure 2, with LEDs 44a,b and photodiodes 46. The main difference is that no special polymer material is provided on top of photodiodes 46 between the photodiodes 46 and the tissue (or at least no material that generates a significantly amount of light or affects light absorption that affects the measurements). A plurality of wells 42a,b is provided with LEDs 44a,b constructed to emit light in different wavelength bands. Photodiodes 46 are realized using vertically stacked p-n junctions each optimised for a different wavelength or wavelength band.

Oxygenated blood has a rich red colour whereas when the oxygen saturation level is low, the colour is darker. The oxygen saturation level can be determined by measuring the absorption at two wavelengths, 800 nm and 660 nm. The change in absorption is most obvious for light of wavelengths of
660 nm. At 800 nm the absorption is the same for both oxygenated and deoxygenated blood and this can be used as a reference level for the measurements.

In operation the sensor measures light scattering and absorption of light from LED's 44a,b in the tissue at a plurality of wavelengths. Thus absorption due to hemoglobin with and without oxygenation is determined. When activated by transponder circuit 120, interface circuit 121 causes LEDs 44a,b to emit light in different wavelength bands and senses the output current or voltage of photodiodes 46 to measure the intensity of the scattered light from the tissue. Transponder circuit 120 returns the measurement results, or data obtained by interface circuit 121 after processing the measurement results, to transmitter/receiver unit 10. From the two measurements the oxygen saturation can be obtained.

Although an arrangement with two LEDs has been shown, it should be realized that a greater number of LEDs may be used, for a correspondingly greater number of wavelength bands. This allows for absorption measurement for more than two wavelengths which may be used to improve measurement accuracy and/or to eliminate contributions of molecular species other than hemoglobin. Also, although the use of two stacked photodiodes is disclosed, it should be appreciated that alternatively one photo diode may be used while the LEDs are alternately activated, or that photodiodes that lay next to each other on the surface may be used. The use of stacked photodiodes has the advantage that device size is reduced and that effects due to tissue inhomogeneity are reduced. Although separate LEDs have been shown, it should be used that alternatively other types of light emitting devices may be used, including light emitting devices whose wavelength band can be shifted under electronic control to observe absorption in different wavelength band.

Preferably interface circuit 121 measures the output current or voltage of the photodiodes to detect the light as part of absorption and/or for quantitative pressure measurements. However, it should be noted that
alternatively some form of threshold light intensity detection may be used, optionally combined with controlled variation of the emission intensity of the LEDs, to measure absorption for example. Similarly, threshold detection may be used to measure decay times.

As may be noted each of the illustrated sensors can be realized on the same type of sensor surface, using similar manufacturing techniques. This makes it possible to integrate a plurality of different sensors on a miniaturized device that can be introduced into the colon and washed out of the colon without additional problems for the patient.

The sensor device for colon tissue oxygenation preferably includes an oxygen saturation (SO2) sensor, an oxygen pressure (PO2) sensor, a carbon-dioxide pressure (PCO2) sensor. A temperature sensor is preferable integrated as well. The measurement of temperature can be used as an indicator of local infection. Optionally a pH sensor may be integrated as well. The measurement of pH can be used as an indicator of tissue condition. Preferably these four sensors are integrated in a single chip, made as small as possible and packaged in a biocompatible manner that allows simple and fast attachment during the operation. Transponder circuit 120 and interface circuit 121 may be integrated on the same chip with the sensors, but preferably they are integrated on a separate chip or chips, that may be mounted against the back of the chip on which the sensors are integrated (i.e. on a face opposite sensitive surface 129). It should be realized that alternatively a simplified device may be used wherein one or more of the sensors have been omitted. The remaining sensors may provide sufficient information to monitor vitality of the tissue.

Although an embodiment has been shown wherein rings are provided to attach the sensing device to the anastomosed tissue, it should be realized that alternative means for attachment are possible. For example the sensing device could be provided attached to a piece of soluble suture, so that it can be attached to the tissue by suturing. As an example the sensing device could be
provided attached to a soluble suturing staple, so that it can be attached to the tissue by stapling.

Preferably the size of the sensor is made so small that it does not significantly interfere or jeopardize functioning of the anastomosed tissue.

Preferably, therefore the diameter of the sensor is less than one centimetre, more preferably less than half a centimetre or even less than a millimetre.

During analysis the measurement results may be compared with reference data for vital and/or non-vital tissue, to produce a forecast the start of the healing process. By using a novel transponder, there is no need for a battery to power the sensor system and the data can be transmitted wireless to the outside of the patients' body. These sensors will remain at the anastomotic site in order to monitor the healing process for 4-7 days.
Claims

1. A method of monitoring tissue vitality, the method comprising using a transmitter/receiver to read sensor output data from a wireless transponder circuit of a sensing device that comprises a sensor that is attached to the tissue with a sensitive surface facing the tissue.

2. A method according to Claim 1, wherein the sensing device is a device attached to an interior mucous membrane of a colon.

3. A method according to Claim 1, wherein the sensing device is a device attached to anastomosed tissue.

4. A method according to any one of the preceding Claims, wherein the sensor is of a type that senses oxygen perfusion in the tissue.

5. A method according to any one of the preceding Claims, wherein the sensor is arranged to detect a degree of presence of a molecular species in the tissue adjacent the sensitive surface.

6. A method according to any one of the preceding Claims, wherein the molecular species is oxygen.

7. A method according to any one of the preceding Claims, wherein sensing device is arranged to sense light absorption by oxygen-hemoglobin complexes in the tissue adjacent the surface.

8. A method according to any one of the preceding Claims, wherein the sensing device is arranged to sense a plurality of mutually different parameters of the tissue.

9. A method according to Claim 8, wherein the parameters comprise a quantity of oxygen adjacent the surface and a pressure of oxygen released from the tissue through the surface.

10. A method according to Claim 8, wherein the parameters include at least two of a quantity of oxygen adjacent the sensitive surface, an oxygenized/non-oxygenized hemoglobin ratio adjacent the sensitive surface, a
pressure of oxygen released from the tissue through the sensitive surface, carbon dioxide pressure near the sensitive surface, tissue pH at the sensitive surface and tissue temperature at the sensitive surface.

11. A tissue vitality monitoring system, comprising a wireless transmitter/receiver and a wireless tissue vitality sensing device that comprises a transponder circuit arranged to communicate with the transmitter/receiver and an oxygen perfusion sensor with a sensitive surface that is part of a tissue contact surface of the sensing device, the sensor having a signal output coupled to the transponder interface.

12. A tissue vitality monitoring system according to Claim 11, wherein the tissue vitality sensing device comprises sensors for sensing at least oxygen saturation in tissue adjacent the tissue contact surface and partial pressure of oxygen that passes into a part of the sensor through the tissue contact surface.

13. A tissue vitality monitoring system according to Claim 11, wherein the tissue vitality sensing device comprises a plurality of sensors, for sensing at least two of oxygen saturation, oxygen pressure, carbon dioxide pressure, pH and temperature.

14. A tissue vitality monitoring device comprising a wireless transponder circuit and a sensor for sensing a physiological parameter at and/or adjacent to a tissue contact surface of the sensing device, the sensor having a signal output coupled to the wireless transponder circuit.

15. A tissue vitality monitoring device according to claim 14, wherein the tissue vitality monitoring device is an anastomosed tissue vitality monitoring device.

16. A tissue vitality monitoring device according to claim 14 or 15, wherein the sensor is an oxygen perfusion sensor.

17. A tissue vitality monitoring device according to claim 16 wherein the sensor comprises a sensing device for sensing a quantity of oxygen adjacent to the tissue contact surface and a sensing device for sensing a pressure of oxygen released from the tissue through the tissue contact surface.
18. A tissue vitality monitoring device according to claim 14 or 15, wherein sensing device is arranged to sense light absorption of oxygen-hemoglobin complexes in the tissue adjacent to the surface.

19. A tissue vitality monitoring device according to claim 16, wherein the sensing device comprises a plurality of sensors, for sensing at least two of a quantity of oxygen adjacent to the sensitive surface, an oxygenized/non-oxygenized hemoglobin ratio adjacent to the sensitive surface, a pressure of oxygen released from the tissue through the sensitive surface, carbon dioxide pressure near the sensitive surface, tissue pH at the sensitive surface and tissue temperature at the sensitive surface.

20. A tissue vitality monitoring device according to claim 14, wherein the sensor comprises a gas permeable polymer adjoining the tissue contact surface, fluorescent material immobilized by the polymer, a light source directed at the fluorescent material, the light source having an emission band including a wavelength that excites fluorescence of the fluorescent material, and a light detection device directed at the fluorescent material.

21. A tissue vitality monitoring device according to claim 14, comprising a light source directed to emit light through the tissue contact surface and a light detector arranged to receive scattered light of the light source from the tissue through the tissue contact surface.

22. A tissue vitality monitoring device according to claim 14, comprising a light source arrangement directed to emit light through the tissue contact surface and a light detector arrangement arranged to receive scattered light of the light source arrangement from the tissue through the tissue contact surface, wherein the light source arrangement and/or the light detector arrangement are arranged to emit and respectively detect light from distinct wavelength bands separately.

23. A tissue vitality monitoring device according to claim 22, wherein the wavelength bands comprise bands wherein oxygenated and non-oxygenated hemoglobin absorb light in respective, mutually different ratios.
24. A tissue vitality monitoring device according to claim 14, comprising a light source directed to emit light through the tissue contact surface and a light detector arranged to receive scattered light of the light source from the tissue through the tissue contact surface.

25. A tissue vitality monitoring device according to any one of claims 14 to 24, comprising attachment means attached directly or indirectly to the sensor for attaching the sensor with the tissue contact surface facing the tissue.

26. A tissue vitality monitoring device according to any one of claims 14 to 24, comprising a first and second eye attached directly or indirectly to the sensor for receiving surgical suturing wire.

27. A surgical method comprising anastomosis of tissue and attachment of a sensing device with a wireless transponder interface to the anastomosed tissue, with a sensitive surface of the sensing device facing the anastomosed tissue, followed by reading sensing data from the sensing device with a wireless transmitter/receiver, to monitor tissue vitality of the anastomosed tissue.

28. A surgical method according to Claim 27, wherein the sensing device is attached to colon tissue on the inside of the intestinal tract and wherein the sensing device is affixed to the colon solely via a soluble attachment.
Fig. 3

Fig. 4
**INTERNATIONAL SEARCH REPORT**

**A. CLASSIFICATION OF SUBJECT MATTER**

NL2005/000508

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

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

A61B

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

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

EPO-Internal, WPI Data, PAJ

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

<table>
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<th>Category*</th>
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Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents:
  *A* document defining the general state of the art which is not considered to be of particular relevance
  *E* earlier document but published on or after the international filing date
  *L* document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
  *O* document referring to an oral disclosure, use, exhibition or other means
  *P* document published prior to the international filing date but later than the priority date claimed
  *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
  *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
  *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

Date of the actual completion of the international search

17 March 2006

Date of mailing of the international search report

28/03/2006

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
NL – 2280 HV Rijswijk
Tel: (+31-70) 340-2040, Tx. 31 651 epo nl,
Facs: (+31-70) 340-3016

Authorized officer

Birkenmaier, T

From: PCT/ISA/210 (second sheet) (April 2008)
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# INTERNATIONAL SEARCH REPORT

## Box II  Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. **X** Claims Nos.: 1-10, 27, 28 because they relate to subject matter not required to be searched by this Authority, namely:
   
   Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgery

2. √ Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. √ Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III  Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)

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

1. √ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. √ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. √ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. √ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**

- The additional search fees were accompanied by the applicant’s protest.
- No protest accompanied the payment of additional search fees.
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