**Title:** METHOD AND APPARATUS FOR LOCATING TUMORS

**Abstract**

A lesion can be accurately located, its size and its biological potential estimated prior to surgery by measuring the interstitial fluid pressure of the lesion. A pressure-sensing biopsy needle, which is an inner pressure-sensing needle (2) within an outer needle (1), rapidly measures the interstitial fluid pressure of tissue and allows the operator to determine the location and estimate the size of a lesion. The interstitial fluid pressure of the lesion can be correlated with the biological potential and is used to determine whether surgical removal of the lesion is warranted. When surgical removal of the lesion is desired the inner pressure-sensing needle (2) is removed leaving the outer needle in situ, and a hookwire (15) is inserted into the tissue through the accurately placed outer needle (1) thus transfixing the lesion.
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METHOD AND APPARATUS FOR LOCATING AND DIAGNOSING
TUMORS PRIOR TO NEEDLE BIOPSY

Background of the Invention

This invention was made in the course of work supported in part by the
United States Government, and the Government has certain rights in the invention.

This invention relates to the localization and diagnosis of lesions \textit{in vivo}.

"Lesion" as used herein is a pathologic change in tissue, such as for example a
tumor. Lesions that are too small to be found by palpation are conventionally
located using imaging techniques and surgically removed. For example, breast
lesions can be detected by mammogram as much as four years earlier than by
physical examination. However, a mammogram is unable to distinguish a benign
from a malignant lesion, and detection of a lesion by mammography must be
followed by biopsy. Because a mammogram has a positive predictive value of 20-
30\%, a large proportion of breast biopsies following mammography prove to be
for nonmalignant lesions. A reduction in the number of breast biopsies performed
for benign disease would be extremely important and beneficial.

In conventional mammogram-assisted screening for breast disease, a
mammogram of the breast is made, and the resulting image is inspected for
lesions. If a small lesion appears, a radiopaque needle is inserted into the breast in
a region as near as can be estimated to the lesion. Then the region is imaged with
the needle in place, the resulting image is inspected, and the needle is relocated as
necessary to place it within the lesion. Once the needle appears to be positioned
within the lesion, the surgeon follows the needle to the lesion and removes the
lesion and surrounding tissue, and the pathological status of the lesion can be
determined. Because the imaging procedure provides only an estimate of the
proximity of the biopsy needle to the lesion, it may often be necessary, in the
interest of removing all the lesion, to remove a substantial quantity of normal
surrounding tissue as well.

The positioning of a biopsy needle in soft tissue as a marker for lesions has
been found to be unreliable, because the biopsy needle can move during the
p. 781) describe inserting a hookwire into the lesion \textit{via} the lumen of the hollow
needle used during the imaging procedure to localize the lesion. After the hookwire is in place the needle is withdrawn, leaving the hookwire in a position estimated to be closest to the lesion. This needle-hookwire approach has been used successfully to provide a more secure marker for breast biopsies (Meyer et al., 1982, Arch. Surg., Vol. 117, pp. 65-68). However, once the hookwire is implanted in the tissue, it cannot be removed without tissue damage except by surgery.

Since the development of needle-hookwire assembly by Kopans et al., other breast biopsy needles have been developed. For example, biopsy needles have been designed with retractable barbs to anchor the biopsy needle in tissue, and to facilitate the removal of the needle in case of incorrect positioning, or in case it is desirable to remove the localization needle during surgery without requiring surgical removal of excess tissue (U.S. Patent Nos. 4,986,279; 4,799,495). In each of these biopsy needle localization systems, the proximity of the biopsy needle to a lesion is estimated by imaging techniques.

The effectiveness of therapies currently used for the treatment of lesions, as for example solid tumors, is limited by the capacity of the therapeutic to reach the target in vivo in adequate quantities. In animal studies, solid tumors have been shown to contain a greater volume of interstitial fluid—that is, of fluid in the extracellular and extravascular space, than normal tissues contain, suggesting that tumors should be readily infiltratable by therapeutic macromolecules. However, additional animal studies have demonstrated that the interstitial fluid pressure ("IFP") is higher in tumors than in normal tissues, resulting in poor perfusion of tumors by therapeutic molecules and a radially outward convection of interstitial fluid from tumors (reviewed in Jain, 1987, Cancer Res., Vol. 47, pp. 3039-3051).

An examination of the microvascular network of rat mammary adenocarcinoma tumors was conducted to aid in understanding the distribution of blood flow and its influence on the exchange and uptake of relevant molecules in chemotherapy, immunotherapy, or radiation treatment (Less et al., 1991, Cancer Res., Vol. 51, 265-273). The results of this study indicated that the bifurcation geometry and network structure in tumor vasculature may be one mechanism
responsible for the increased resistance to blood flow reported in tumors (Sevick et al., 1989, Cancer Res., Vol. 49, pp. 3506-3512).

The elevated IFP of tumors was first described by Young et al. (1950, Jour. Pathol. Bacteriol., Vol. 62, pp. 313-333) after taking "tissue pressure"

measurements in rabbits. Each of three methods for measuring local interstitial pressure, known as the needle method, wick-in-needle method, and micropipet method, has advantages and limitations. In the needle method, a needle filled with physiological saline and coupled to a pressure measuring device is inserted into tissue. In the wick-in-needle method, fibers of polyester or other multifilamentous material are placed within the lumen of the needle in order to provide a large surface area continuum with the interstitium and reduce occlusion. Both of these methods can cause tissue distortion. In the micropipet method a micropipet connected to a servo-null pressure-measuring system is used, reducing some problems presented in the needle and wick-in-needle methods, but the micropipets are susceptible to breakage.

The IFP of subcutaneous tumors was measured in rats using micropipets (Boucher et al., 1990, Cancer Res., Vol. 50, 4478-4484). This study describes a steep IFP gradient that begins at the surface of the tumor, or the skin/tumor interface, and quickly reaches a plateau value in the tumor mass within 0.2-1.1 mm of the tumor surface. These results confirmed an earlier mathematical model of interstitial fluid transport in tumors (Jain et al., 1988, Cancer Res., Vol 48, pp. 7022-7032) which proposed that very little filtration of macromolecules into tumors occurs even from blood vessels which pass through the tumor, and that the convective outward flow of the interstitial fluid pushes solutes toward the periphery. These conclusions are also supported by work from Dvorak et al. (1988, Am. Jour. Pathol., Vol. 133, pp. 95-105) who demonstrated that small molecules can readily penetrate tumors, and large macromolecules are limited to the tissue-tumor interface. The inability of therapeutic drugs to reach the center of tumors has grave implications for cancer therapies, and based upon these results Boucher et al. (1990) proposes methods by which drug delivery to tumors could be enhanced.
The wick-in-needle technique was developed by Fadnes et al. (1977, Microvasc. Res., Vol 14, pp. 27-36). Fadnes et al. describes a thin hypodermic needle open at the end and having a side-hole, its lumen filled with multifilamentous nylon thread and connected by polyethylene tubing to a pressure transducer. Fadnes et al. describes using this pressure-sensing needle to compare the subcutaneous IFP in anesthetized rats under normal and dehydrated conditions. The interstitial fluid pressure of human melanomas and uterine cervix carcinomas was measured using the wick-in-needle technique in studies that demonstrated for the first time in humans that IFP is higher in tumors than in normal tissue.

Boucher et al. (1991), Cancer Res., Vol. 51, pp. 6691-6694, demonstrated that the IFPs of large human melanomas far exceed the values expected from measurements of rodent tumors or human xenografts. Roh et al. (1991), Cancer Res., Vol. 51, pp. 6695-6698, demonstrated that a lowering of the IFP in some cervical tumors during fractionated radiation therapy correlates well with therapeutic outcome.

Both Boucher et al. and Roh et al. conclude that the IFP of tumors will be valuable for designing future cancer therapies and predicting treatment outcome.

K.P. Wang, U.S. Pat. No. 4,799,494, describes a needle assembly for collection of lung tissue. The needle assembly includes a blunt hollow outer needle having a side-hole for tissue collection, and a non-removable inner hollow needle attached to a solid wire, slidably engaged within and snugly fitting the lumen of the outer needle, used for piercing the tissue. The lumen of the outer needle is connected to a crude balloon pressure sensor. The '494 patent states that the localization of the needle tip in the lung lesion to be sampled results in a pressure decrease detectable at the balloon.

Summary of the Invention

We have discovered that a lesion can be accurately located within a tissue mass by measuring, at several points in a path through the tissue mass, a selected parameter that is known to measure differently in lesions (or at least in some types of lesions) and in normal tissues; and we have developed apparatus for carrying out such measurements, particularly of interstitial fluid pressure.

Using the method, the location and, at least to some extent the size and the boundary of a lesion can be determined accurately and without a requirement for
repeated reimaging of the tissue mass. Moreover, some selected parameters can, depending upon the extent of deviation of their measure from normal, provide information regarding the pathological condition of the lesion; for example, some parameters deviate more from normal in malignant tumors than in benign lesions.

In one aspect, the invention features a method for locating a lesion within a tissue mass, including measuring a parameter at a plurality of points in at least one path through the tissue mass, the measure of the parameter in lesions being different from the measure in normal tissue.

In preferred embodiments, the parameter is interstitial fluid pressure, and more than one parameter may be measured at one or more of the points; the method may further include a step of inserting a tissue marker, such as a hookwire, into the lesion along a portion of the path, to mark the lesion for subsequent removal.

Typically, the method of the invention may be used to mark the location of, and if desired to gain additional information as to the condition of, a lesion located by imaging or by palpation.

In another general aspect, the invention features apparatus for measuring a tissue parameter at a number of points along at least one path through the tissue mass, including an insertion tube, sharpened at a distal end and made sufficiently rigid so that it can be inserted distal end foremost into the tissue mass along the path, and, insertible with the insertion tube, a sensor capable of providing a measure of the tissue parameter at a point in the tissue mass along the path.

According to the invention, apparatus for locating a lesion in a tissue mass includes such apparatus for measuring a selected tissue parameter at a number of points along one or more paths through the tissue mass; at any point in the tissue mass a measure by the sensor of the selected parameter that is distinguishably different from that in normal tissue indicates that the point is within a lesion.

In preferred embodiments the tissue parameter is interstitial fluid pressure and the sensor includes a pressure sensor. The wall of the insertion tube includes a port near its distal end, and the sensor includes a sensor tube, containing filaments, slidably engageable within the lumen of the insertion tube; the sensor tube is distally closed and has a port near its distal end, and the ports are
positioned so that when the sensor tube is engaged within the insertion tube lumen the ports can be substantially aligned to provide fluid communication between the lumen of the sensor tube and the tissue adjacent the ports; and the sensor tube lumen is operationally connected to a pressure measurement device such that it is responsive to fluid pressure within the sensor tube lumen.

The apparatus of the invention makes use of a thin-walled fine-gauge distally sharpened needle for the insertion tube, so that by use of the apparatus the method of the invention can be carried out without anesthesia. The pressure-sensing apparatus according to the invention can be used to accurately determine the interstitial pressure within a lesion in approximately 10 minutes’ time. The invention provides for reliable measurements of interstitial fluid pressure in any variety of types of lesions in any of a variety of tissues with a minimum of discomfort to the patient.

The invention can provide for estimating the location, size and biological potential of a lesion by measuring the interstitial fluid pressure, by passing the insertion tube, with the associated sensing device, into tissue that has been shown by palpation or imaging techniques to contain a lesion (such as a tumor), in a path that is estimated to pass through the lesion, and measuring the pressure at multiple points along the path. “Biological potential” as used herein encompasses all pathological types of lesions, including benign lesions.

The higher IFP of a lesion allows the operator, making several measurements along the path, to determine when the insertion needle has both entered and exited the lesion. The IFP of a lesion can additionally be indicative of its biological potential. In malignant lesions the IFP is elevated above the IFP of normal tissue and the IFP increases with lesion size. In benign lesions, on the other hand, the IFP may be comparable to that of normal tissue.

Insertion of the sensor through the lesion along more than one path allows the IFP and the entry and exit points to be determined along more than one transect of the lesion. The size and extent of the lesion and its biological potential can then be estimated. Preferably, the IFP of the lesion is measured in two different locations, and the IFP is recorded first of normal tissue then repeatedly at close intervals or continuously as the needle is advanced into the lesion and exits
the lesion into normal tissue again. The pressure reading for the excursion of the insertion needle along each path takes approximately 10 minutes, and the entire procedure takes approximately 20 minutes to complete.

For example, where palpation or mammography has shown that a lesion is present in the breast, the interstitial fluid pressure of the lesion can be determined as described above, and if the interstitial fluid pressure indicates a benign lesion then the patient will not need to undergo surgery. If, on the other hand, the pressure measurement indicates a malignant lesion, a hookwire can be very accurately placed within the lesion as a marker for the subsequent surgical removal.

**Description of the Preferred Embodiments**

**Drawings**

Fig. 1.1 is a longitudinal section of part of a pressure-sensing needle assembly, according to the invention, showing the positions of the components.

Fig. 1.2 is a cross-sectional view thru 1-1' of the pressure-sensing needle assembly of Fig. 1.1.

Fig. 1.3 is a cross-sectional view thru 2-2' of the pressure-sensing needle assembly of Fig. 1.1.

Fig. 1.4 is a longitudinal section of a needle assembly, according to the invention, showing a hookwire within the lumen of the insertion needle.

**General Description**

In the method according to the invention, the location of a lesion within a tissue mass is accurately determined by measuring a parameter, known to measure higher or lower within such lesions than in normal tissues, at a plurality of points in one or more paths through the tissue mass. Any one or more of a variety of parameters can be measured according to the invention; in particular, elevated interstitial fluid pressure within a lesion can be a reliable indicator not only of the location and size of the lesion, but also of its biological potential; for example, malignant tumors can have interstitial fluid pressures elevated to a greater degree than benign tumors. Moreover, apparatus for introducing the sensor into the tissue mass can be provided with two or more sensors, capable of detecting more than one parameter. Some such parameters can be selected to aid in locating the lesion
or in diagnosing its pathological condition, and others can provide information that
may be useful to medical personnel who subsequently treat the lesion.

An accurate sensor for carrying out the method of the invention can
conveniently be associated with a fine-gauge, thin-walled tube, made sufficiently
rigid and sharpened so that it can be passed into the tissue mass without causing
intolerable discomfort to the subject; a sharpened hollow needle such as a fine-
gauge biopsy needle may be suitable, for example. Where initial imaging methods
indicate the presence of a lesion within a tissue mass, the hollow sharpened needle
with the associated sensor is inserted into the tissue mass along a direction
estimated to pass into the lesion, and measurements are made at close intervals. If
the measurements do not indicate that the sensor has passed into a lesion, the
needle and sensor can be withdrawn and reinserted along a different path. These
steps can be repeated until the lesion has been located and sufficient information
has been obtained to provide an indication for biopsy; repeated reimaging is
unnecessary. Once the sensor indicates that the needle has passed into a lesion, it
can be passed further into the tissue mass and further measurements can be made
along the path, until the measurements indicate that the sensor has passed through
and out from the lesion into normal tissue. A record of the positions along the
path where the measurements were made can provide an estimate of the dimension
of the lesion along the line of the path. Then the needle can be partly withdrawn,
so that its open tip is again within the lesion. Then a marker, such as for example
a hookwire, can be introduced via the needle to a point within the lesion near the
needle tip, and the needle can be withdrawn, leaving the marker in place.

By way of example, an embodiment of apparatus for lesion localization and
diagnosis according to the invention is described below, including a pressure
sensor insertible into a thin-walled hollow insertion needle. The pressure sensor
itself includes, a hollow tube containing filaments, dimensioned and configured so
that it slides within the lumen of the hollow insertion needle in sealed relation to
the needle wall. The filament-containing sensor tube is closed at its distal end; and
the walls of the sensor tube and of the insertion needle are each provided with a
port near the distal end, and the ports are alignable to provide communication
between the interstitial fluid surrounding the insertion needle and fluid within the
lumen of the sensor tube. A pressure measuring device is operatively connected to the sensor tube so that it is responsive to the hydrostatic pressure within the sensor tube lumen, providing a measure of the interstitial fluid pressure in the tissue mass near the insertion needle adjacent the ports.

5 Apparatus

The distal portion of an embodiment of apparatus for lesion localization and diagnosis according to the invention, including a pressure sensor insertible into a thin-walled hollow insertion needle, is shown by way of example in a diagram in Fig. 1.1, and in sectional views in Figures 1.2 and 1.3.

10 With reference now to Fig. 1.1, the pressure-sensing apparatus, a distal portion of which is shown includes a fine-gauge, thin-walled hollow insertion needle 1 and, shown in operative relation within insertion needle 1, a removable hollow inner sensor tube 2. Within the lumen 7 throughout the length of sensor tube 2 are filaments 6. Sensor tube 2 is operatively connected to a pressure measurement device (not shown in the Figs.) in such a manner that the pressure measurement device is responsive to hydrostatic fluid pressure within the lumen 7 of sensor tube 2. The distal tip 5 of sensor tube 2 is plugged, while the insertion needle 1 is left open. A port 3 in the wall of the insertion needle 1 and a port 8 in the wall of sensor tube 2 are substantially aligned when the insertion needle and sensor tube are in operational relation, as shown in the Figs.

In one embodiment, the insertion needle 1 is a 20 gauge stainless steel needle, and port 3 is a 2-3 mm hole, located 2 cm from the open sharp distal insertion needle tip 4. Sensor tube 2 is a stainless steel hollow needle, 23 gauge so that it fits snugly within insertion needle 1, and port 8 is a 2-3 mm hole, located about 2 cm from the distal sensor tube tip 5, which is sealed with solder. The sensor tube 2 contains within its lumen 7 and throughout its length 4-5 monofilamentous surgical suture fibers 6, preferably 6-0 ethilon or other monofilamentous nylon of the same size, which occupy the length of the inner needle 2.

30 Insertion needle 1 and sensor tube 2 are each provided at the proximal end (not shown in the Figs.) with a plastic hub for ease in manipulation by the user, as is well-known in the needle biopsy art. Alignment marks on the plastic hubs (not
shown) are provided to aid the user in holding the ports 3, 8 in alignment during use, as shown in Figs. 1.1, 1.3. When the ports 3, 8 are aligned substantially as shown in the Figs., they provide for direct communication between fluid in the sensor tube lumen 7 and the interstitial fluid in tissues outside the insertion needle 1 near the ports.

Sensor tube 2 is operatively connected to a pressure measurement device (not shown in the Figs.), such as the model P23XL pressure transducer available from Spectramed Inc., Oxnard, CA, by way of non-compliant sterilized plastic tubing filled with sterile heparinized saline, preferably 70 Units/ml, connected between the pressure transducer and the proximal end of the sensor tube. The pressure transducer is connected to signal processing means, such as, for example a preamplifier, and a recorder or other data storage device. In one embodiment the signal from the transducer is sent through a preamplifier, such as the model 114113-01 available from Gould Inc., Cleveland, OH, and the amplified signal is sent to a dual-channel chart recorder, such as the model 30-V7202-11 available from Gould Inc.; or the amplified signal is digitized and stored.

The lengths of the sensor tube 2 and insertion needle 1 are selected to be sufficiently long to reach to the expected path length within the tissue mass to the deepest measurement point. The lesion is located and the tip of the insertion needle is relocated within the lesion as described above, General Description, and the sensor tube is withdrawn from the insertion needle. Then, as shown in Fig. 1.4, a flexible hookwire 15 such as, for example, a 0.03 cm diameter hookwire having 22,600 kg/cm² tensile strength, 11.4 kg breakload or, for example, a 0.02 cm diameter hookwire having 20,000 kg/cm² tensile strength, 6.5 kg breakload, is inserted into the tissue by way of the lumen 9 of the properly emplaced insertion needle. Then insertion needle 1 is withdrawn from the site, leaving the hookwire 15 implanted in the lesion as an accurate marker of the position of the lesion. The portion of the hookwire that emerges from the wound (not shown) is taped to the subject’s skin until surgery. If desired, the outer needle 1 can be reintroduced over the hookwire during surgery to provide a firm guide for the surgeon’s knife.
Use

The pressure measuring apparatus according to the invention can be used for measuring the interstitial fluid pressure in tissues, and for locating lesions in the tissues, at any of various sites within the subject's body.

Preferably the apparatus is calibrated just prior to use. Such calibration can conveniently be performed using a water column, and a zero reference point is preferably obtained by placing the sensor tube tip and insertion needle tip at skin level. The user then introduces the insertion needle, containing the sensor tube in proper alignment as indicated by the alignment marks on the hubs, into the tissue mass at a point where the ports can be expected to be situated in normal tissue. Then proper communication between the saline in the lumen of the sensor tube and the interstitial fluid in the tissues can be checked as follows. First the plastic tubing connecting the pressure transducer with the sensor tube is compressed with a screw clamp. This displaces a small amount of fluid within the tubing and the lumen of the sensor tube, which should cause a transient rise in the pressure measured by the transducer; the fluid should, provided that there is proper fluid communication, quickly thereafter pass from the sensor tube through the ports into the surrounding tissues, allowing the pressure measurement to return quickly to normal. The clamp is then released, decompressing the tubing and causing a transient decrease in the pressure at the transducer, which should again quickly return to normal. The pressure sensing tube lumen may be considered to have proper fluid communication with the interstitial fluid of the tissues if, following compression and decompression in such a test, the stable value measurements are within 15% of each other.

The apparatus is then advanced into the tissue and the interstitial fluid pressure is continuously recorded (or recorded at closely-spaced intervals). As the apparatus enters a lesion, and the interface between normal tissue and a malignant lesion interface is pierced, the passage through the interface of the ports is expected to be observed as a sharp and marked increase in pressure. The depth of the needle at the interface is recorded, and then the needle is advanced further into the tissue through the lesion. As the apparatus reaches the distal lesion/normal tissue interface, the passage through the interface by the ports as they leave the
lesion mass is observed at the lesion/normal tissue interface as a sharp and marked
decrease in the measured interstitial fluid pressure, the pressure rapidly falling
from the internal pressure of the lesion to the expected pressure of normal tissue.
Using this method a series of measurements along a path requires approximately 10
5 minutes to complete.

Proper fluid communication between the needle and the interstitial fluid of
the lesion can be confirmed by compressing and decompressing the tubing while
the needle is stationary within the lesion. One may wish to complete this
additional step when the measured IFP within a lesion is very low or comparable
to the pressure in normal tissues, in order to ensure the accuracy of the
measurement, particularly as a low IFP within a lesion can be indicative that the
lesion is benign.

The procedure outlined above can then be repeated using another pressure
sensing assembly at a different location within the lesion. Two independent
measurements of the IFP within a lesion can improve the accuracy of the
diagnosis, and determination of the entry and exit points of the needle along two
(or more) paths within a lesion will allow a more accurate estimation of the size of
the lesion.

Once the location of the lesion has been accurately determined the sensor
20 tube is withdrawn from the insertion needle, leaving the insertion needle in situ,
and a hookwire is inserted via the insertion needle lumen into the tissue at the
insertion needle tip. The insertion needle is then withdrawn from the tissue mass,
leaving the hookwire implanted in the lesion as an accurate and secure marker of
the location of the lesion.

Other Embodiments

Other embodiments are within the following claims.

For example, measuring devices other than the fiber-containing tube
described above could be used in association with the insertion needle to
measure the interstitial pressure. Available pressure measuring devices that can be
adapted for use in the invention include devices based upon the piezoelectric effect
or upon flexion of fiber optic devices. Such alternate pressure measuring devices
may have the benefit of significantly reducing the length of time required to
accurately determine the interstitial fluid pressure.

Measurements of indicia other than IFP which show the presence of a lesion
at a given point in tissue, and therefore of the location of the lesion within the
tissue mass, can be used in place of or in addition to IFP measurements. Other
parameters which can be measured include, for example, interstitial fluid pH or
oxygen tension ("pO₂"). Preliminary results indicate that the extracellular pH of a
malignant lesion can be lower than that of normal tissue, and that the pO₂ of a
malignant lesion can be lower than that of normal tissue. Measurements of such
parameters, preferably simultaneously with and at the same measurement points as
the pressure measurements, can corroborate the diagnosis provided by the pressure
measurements. Moreover, the choice of therapeutic method for treating a lesion
can be substantially benefitted by measuring certain tissue parameters within the
lesion other than pressure. Some therapeutic compositions are known to be more
or less effective than others at the particular pH or at the pO₂ encountered within a
given lesion. For instance, a lesion having a low interstitial pH could immediately
be treated with drugs which are known to be more effective in acidic
environments. Thus the knowledge of the environment within a lesion will provide
the clinician with information which allows decisive and effective implementation
of drug or radiation therapies.

The assembly according to the invention, as described generally and
particularly above, can readily make use of a sensor device, capable of measuring
one or more parameters other than pressure, adapted for introduction by way of an
association with (as, for example, within the lumen) an insertion needle. For
instance, once the lesion has been located as described above, the pressure sensor
tube can be withdrawn and a fiber-optic sensor put in its place, capable of
measuring pH, pO₂, pCO₂, and the temperature within the lesion. A fiber optic
sensing device capable of taking such measurements and adaptable for use
according to the invention has been developed, for example, by Puritan-Bennet
Corp., (see, e.g., *IEEE Spectrum*, January 1992, pp. 61 et seq.).
Claims

1. A method for determining the locus of a pathologic change within a tissue mass, said pathologic change being characterized by a difference, with respect to normal tissue, in at least one tissue parameter comprising steps of inserting into the tissue mass a sensor portion of apparatus capable of measuring said tissue parameter, using said apparatus to measure said tissue parameter at a plurality of points in at least one path through the tissue mass, and determining the biological potential of the pathologic change in said tissue mass, non-normal measures of said tissue parameter being within the locus of the pathologic change.

2. The method of claim 1 wherein said parameter is interstitial fluid pressure.

3. The method of claim 1, further comprising measuring at least one further tissue parameter in at least said point in at least one said path.

4. The method of claim 1, further comprising inserting a tissue marker into the lesion along a portion of the path.

5. The method of claim 4, said tissue marker comprising a hookwire.

6. Apparatus for measuring a tissue parameter at a plurality of points in at least one path through the tissue mass, comprising
   an insertion tube, sharpened at a distal end and made sufficiently rigid so that said insertion tube can be inserted distal end foremost into the tissue mass along the path, and,
   insertible with said tube, a sensor capable of providing a measure of the tissue parameter at a point in the tissue mass along the path.

7. Apparatus for locating a lesion in a tissue mass, comprising
   an insertion tube, sharpened at a distal end and made sufficiently rigid so that said insertion tube can be inserted distal end foremost into the tissue mass along a path, and,
   insertible with said tube, a sensor capable of providing a measure of a selected tissue parameter at a plurality of points in the tissue mass along the path,
   whereby a measure at a point in the tissue mass of the selected tissue parameter provided by said sensor that is distinguishably different from measures
of the selected tissue parameter in normal tissue indicates that the point is within a lesion.

8. The apparatus of claim 6 or 7, the tissue parameter being interstitial fluid pressure, wherein said sensor comprises a pressure sensor.

9. The apparatus of claim 8, the wall of said insertion tube including a first port near said distal end,

    said sensor comprising a sensor tube slidably engageable within the lumen of said insertion tube,

    said sensor tube being closed at a distal end, the wall of said sensor tube having a second port near said distal end, said first and second ports being positioned in relation to said respective distal ends such that when said sensor tube is engaged within said insertion tube lumen said ports can be substantially aligned, to provide fluid communication between the lumen of said sensor tube and the tissue adjacent said insertion tube port,

    said sensor tube lumen containing a plurality of filaments, and

    said sensor tube lumen being operationally connected to a pressure measurement device such that said pressure measurement device is responsive to fluid pressure within said sensor tube lumen.