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[Continued on next page]

(54) **Title:** TUMOR DEMARCATION USING TARGETED FLUORESCENT PROBE AND PHOTONIC NEEDLE

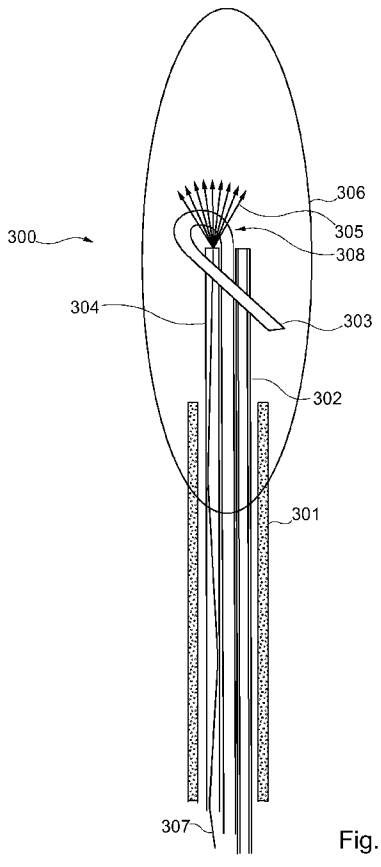

Fig. 3d

(57) **Abstract:** The present invention refers to the field of image-guided percutaneous needle biopsies, in particular to a light guiding hook wire comprising a light-guiding optical fiber (LGM, LGHW) for transferring light from one end on which a beam of input light are incident to another end placed in a cancerous tissue region around the tip of the hookwire, thereby providing an output light assignable to the intensity of the input light; and a liquid guiding device for providing a liquid to the region of interest. The present invention further refers to a method for excising non-palpable pathological tissue regions in the interior of a patient's body, especially tissue regions indicative of breast or prostate cancer, by using such a hookwire. A targeted contrast agent fluorescent in the visible or near-infrared spectrum of light can be used to mark cancerous tissue anomalies, and a light-guiding optical fiber (LGM, LGHW) may provide the light needed for an excitation of this tissue.

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Tumor demarcation using targeted fluorescent probe and photonic needle

FIELD OF THE INVENTION

The present invention relates to image-guided percutaneous needle biopsies, in particular to a light guiding hookwire, a surgical or biopsy needle (in the following also referred to as "photonic needle") comprising a light-guiding optical fiber for transferring light from one end on which a beam of input light is incident to another end placed in a cancerous tissue region around the tip of said needle, thereby providing an output light assignable to the intensity of the input light, and a liquid guiding device for providing a liquid to the region of interest. The present invention further relates to a method for excising non-palpable pathological tissue regions in the interior of a patient's body, especially tissue regions indicative of breast or prostate cancer, by using such a surgical or biopsy needle. A targeted contrast agent fluorescent in the visible spectrum of light can be used to mark cancerous tissue anomalies, and a light-guiding optical fiber may provide the light needed for an excitation of this tissue.

BACKGROUND OF THE INVENTION

Current radiologic imaging techniques make it possible to display a localized focus of cancerous tissue deep within the internal organs of a patient. A typical example for this is mammographic visualization of cancerous tumors in the breast of a woman. In order to accurately diagnose and effectively treat the cancer, it may be necessary for a surgeon to excise a portion of the diseased tissue for microscopic examination and histological analysis.

Needle localization with open surgical biopsy is an accurate, safe, and effective technique for diagnosis of lesions of the breast found by X-ray, CT, MR, sonography or hybrid radiography/MR imaging. Current equipment and techniques of imaging and needle placement allow localization and excision of lesions with a low failure rate. Complications are very rare, and the procedure can be successfully performed in most patients. As many cases of lesions detected by imaging are currently diagnosed by core biopsy, case selection for needle localization has changed. Many cases will be more challenging because of lesion location, failure to successfully perform core biopsy and lesion visualization secondary to removal by core biopsy. Thorough understanding of needle

localization techniques will aid in successful completion of these difficult cases. Although the role of needle localization and open surgical biopsy is changing, as alternative techniques for diagnosis become available, it remains an integral part of mammographic and ultrasonographic imaging. Nonetheless, a recurrent problem for a surgeon consists in that searching for a small cancerous tumor or lesion, even with the aid of modern imaging techniques and modalities, often turns out to be extremely difficult. In addition to that, this may cause considerable damage to non-pathological tissues surrounding a lesion and often fails in the attempt.

With the introduction of screening mammography, the median tumor size has decreased considerably, and approximately half of diagnosed breast cancers in surgical practice are non-palpable. Traditionally, non-palpable breast lesions are excised with a hook wire as a guiding tool, which greatly facilitates image-guided needle biopsy and surgical resection by providing radiologists with a long wire marker having a small hook portion or spur at one end to be placed into the tissue under radiological control. Once the wire hook has been inserted into a tissue region of interest, an X-ray image is taken to document the exact relationship of the hook portion to the target lesion. The wire length thereby serves as a marker and guides the surgeon to a suspected lesion or node. Presuming that the wire guide has been accurately positioned, an image-guided needle biopsy based on X-ray, MRI, CT, sonography or hybrid radiography/MR imaging can be performed rapidly and accurately. Unfortunately, if the wire guide is shown by radiological examination to be improperly situated, one or more additional hooked wires must be inserted into the cancerous tissue and subsequently verified under radiological control as being in the proper localized site. Once inserted, accurately or inaccurately, it is usually the surgeon who will remove the wire markers at the time of the tumor resection because the hooked end of the wire is embedded in the cancerous tissue and cannot easily be withdrawn without injuring surrounding healthy tissue regions.

When a percutaneous needle biopsy or a surgical intervention is to be executed, the surgeon's aim is to treat the patient with a one-stage surgical procedure. From this perspective, wire-guided excision of non-palpable breast cancer is a troublesome procedure as it often results in tumor resections with inadequate margins. Adequate resection of a non-palpable breast cancer is dependent both on the accuracy of wire placement by the radiologist and on the experience and three-dimensional imagination of the surgeon. Even when the diagnosis of breast cancer is known before surgery, wire-guided excision is often inadequate, and the patient has to undergo a second surgical intervention in significant

amount of all cases. Re-excision for positive margins is indicated because an increase in the local recurrence rate is clearly related to tumors resected with involved margins. Other disadvantages of hook wire placement are that the patient has to undergo an extra intervention before surgery and that hook wire placement is an unpleasant procedure which increases the patient's anxiety related to the surgical intervention. Therefore, image-guided needle biopsies for the guiding the surgeon to excise non-palpable malignancies under direct vision have been further developed so as to obtain resections with adequate surgical margins. In this context, however, it is to be noted that image-guided surgery and histological biopsies taken with a needle under image guidance or with a simple hook wire for guiding a surgeon to a cancerous tissue to be excised involves two significant drawbacks: 1. X-ray, CT, MRI and hybrid radiography/MR imaging methods (without use of adequate contrast agents specifically attaching to cancerous tissue) do not provide any information which allows the physician to differentiate between benign and malignant tissue, and 2. the length and angle of an anchoring hook wire used for marking the position of a cancerous tissue region of interest provide only a rough idea of the actual, exact tumor location.

WO 99/51143 describes a localization hook wire which is equipped with a light source attached to it. Thereby, said light source is used to better localize the tumor and to help the surgeon to easier find the center of the tumor. A method described in WO 99/51143 comprises the steps of percutaneously introducing an illumination source for localizing a target site in solid tissue to be examined and detecting the emitted illumination transmitted through the tissue to mark the target site therein.

US 6,261,240 B1 relates to an improved sentinel lymph node localization hook wire for use in breast cancer patients undergoing nodal staging, wherein said hook wire comprises an anchoring hook at a distal end which is inserted into a patient's breast tissue through a loading needle. The anchoring hook, through spring action upon release from the loading needle, is thereby embedded in the breast tissue near the location of cancerous cells. The loading needle is then removed, whereupon radioactive material may be injected into the tissue through perforations in the localization hook wire without leaving the needle in the patient or without reinserting the needle. A syringe attachment may be affixed to the proximal end of the hollow wire exterior of the patient's body to facilitate the injection of radioactive material and blue dye for localizing the sentinel lymph node.

US 5,031,634 describes a unique adjustable biopsy needle-guide device which allows it to be inserted accurately at a selected anatomic site; to be secured in an engaged position; to be disengaged on-demand into a moveable form; and to be repositioned at will.

The guide device comprises a cannula with multiple wires and sliding member elements as a preassembled unit which can be sterilized and conveniently stored until required for use by the physician. The needle-guide serves as a guide-post for the surgeon to remove small or deep seated lesions or for precise placement of biopsy needles at the target site.

Another needle biopsy system for marking a target site which will become standard in clinical practice is described in US 2006 / 0111646 A1. It comprises a sampling portion locatable inside a patient's body, wherein said sampling portion includes a stylet having a sampling region and a cannula, said stylet and cannula being relatively moveable along the stylet axis to position the cannula over the sampling region. Moreover, a sample marker is provided which is locatable in and releasable from the sampling portion.

SUMMARY OF THE INVENTION

During surgical removal of cancerous tissue under image-guided percutaneous intervention, it is thus of great importance not to cut through the tumor. As described above, needles are presently in use to guide a surgeon to impalpable lesions. Whereas the difficulty of lymph nodes resectioning from its surrounding fatty tissue is notorious, it is also well known that lymph nodes are comparatively easily stained. If stained with an appropriate fluorescent contrast agent (i.e., a targeted contrast agent fluorescent in the visible spectrum of light) and illuminated by one or more photonic needles, a surgeon will be able to see cancerous tissue regions shimmering through surrounding non-pathological tissue.

In view of the above-stated facts, it can thus be concluded that there are three problems with the current workflow for treating cancer by surgery: 1. to find the position of invisible and impalpable tumors, 2. to find the boundaries of a tumor, thus yielding information about the shape and size of said tumor, and 3. to prevent pre-metastasic cells within given tumor resection boundaries to become cancerous.

It may thus be desirable to provide for a reduced recurrence rate of resected tumors and lesions by improving tumor localization for a subsequent histological and surgical resection of cancerous and other pathological tissue anomalies.

According to an exemplary embodiment of the present invention a light guiding hookwire for localizing a region of interest is provided, the hookwire comprising a light guiding device for guiding beams of an input light to a distal end of the hookwire for illuminating the region of interest, and a liquid guiding device for providing a liquid the region of interest.

According to another exemplary embodiment of the present invention, a surgical or biopsy needle is provided for excising non-palpable cancerous tissue regions indicative of breast or prostate cancer or other diagnosed types of pathological tissue anomalies, benign tumors (such as e.g. small non-palpable fibroadenomas in the breast of a female patient) and malignant, metastasic carcinomas, sarcomas or lymphomas in the interior of a patient's body under X-ray, CT, MR, sonography, PET/CT, optical imaging, eleastography, impedence tomography, thermography or hybrid radiography/MR imaging guidance after being percutaneously introduced into this tissue. Said needle thereby comprises a liquid guiding cannula with a substantially tubular wall and an internal lumen having an open distal end similar to the needle of a hypodermal syringe for providing a liquid given by a targeted contrast agent – such as e.g. 5-amino-4-oxo-pentanoic acid ($C_5H_9NO_3$), commonly referred to as D-aminolevulinic acid (δ-ALA) – or dye fluorescent in the visible or near-infrared spectrum of light to a tumor site or other pathological tissue anomaly at the tip of the needle. This helps a surgeon to find the boundaries of the lesion and obtain information about the tumor shape and size. When waiting for some time and then illuminating the cancerous tissue via the light guiding means, said tissue will produce fluorescence light, thus helping the surgeon to decide on the best resection margin.

According to another exemplary embodiment of the present invention, the light guiding device is adapted as a hollow shaft longitudinally extending within the interior of the hookwire with an inserted light guiding means (LGM, LGHW) for guiding the beams of the input light emitted by an external light source (LA_1) from a proximal end exterior of a patient's body on which the input light is incident to a distal end placed within the region of interest.

Furthermore, according to another exemplary embodiment of the present invention, the liquid guiding device is adapted as a liquid guiding cannula (CA) with a substantially tubular wall and an internal lumen having an open distal end similar to the needle of a hypodermal syringe for providing a liquid given by a targeted contrast agent or dye fluorescent in the visible or near-infrared spectrum of light to the tip of the hookwire.

According to another exemplary embodiment of the present invention, the region of interest is selected from the group comprising non-palpable cancerous tissue regions indicative of breast or prostate cancer or other diagnosed types of pathological tissue anomalies, benign tumors and malignant, metastasic carcinomas, sarcomas or lymphomas in the interior of a patient's body.

In addition to that, the hookwire or the needle comprises a hollow shaft longitudinally extending within the interior of the hookwire/needle with an inserted light guiding means (such as e.g. an optical fiber) for transferring a beam of input light emitted by an external light source from a proximal end exterior of said patient's body on which said input light is incident to a distal end placed within a tissue region to be excised around the tip of the hookwire or the needle, thereby providing an output light assignable to the intensity of the input light for illuminating said tissue region. Said needle may thus also be referred to as a "photonic needle". The position of a tumor or lesion can then e.g. be found by means of an optical modality (e.g. a mini-camera) coupled to the distal end of the hollow shaft which provides a surgeon with image information needed to probe the dignity of the tissue at the tip of the hookwire or the needle. This allows to guide the hookwire/needle until a pathological tissue anomaly featuring cancerous optical properties has been found.

Instead of providing a surgical or biopsy needle or a hookwire being specially provided with a liquid guiding cannula as described above, the residual free internal lumen of the hollow shaft which is not occupied by the volume of said light guiding means may serve for providing the contrast agent to the tip of said needle or hookwire.

According to another exemplary embodiment, the hookwire may be equipped with a fixation means for holding the tip of the hookwire in a fixed position within the pathological tissue region to be examined during surgical removal of cancerous tissue under image-guided percutaneous intervention using said hookwire. Said fixation means may e.g. be given by a hook portion of a flexible hook wire initially housed within the hollow shaft of the hookwire, said hook portion being inserted into a detected tissue lesion via the lumen of the hollow shaft for marking and localizing the exact position of said lesion as needed for a subsequent image-guided percutaneous needle biopsy. In this case, said light guiding means may be attached to the flexible hook wire such that the distal end of said light guiding means is placed near to the position of said hook portion.

Instead of providing a surgical or biopsy needle or hookwire which comprises two separate components constituting said light guiding means and said fixation means, respectively, an alternative surgical or biopsy needle or hookwire may be provided which comprises a flexible light guiding hook wire that combines in itself all the properties of this light guiding means and the flexible hook wire.

According to another exemplary embodiment, an integrated light source disposed in an internal lumen of the hollow shaft near to the tip of the hookwire may be

provided instead of or in addition to said light guiding means. This integrated light source may e.g. be realized by a light emitting diode or semiconductor laser.

A further exemplary embodiment of the present invention refers to an X-ray, CT, MR, sonography, PET/CT, optical imaging, eleastography, impedence tomography, thermography or hybrid radiography/MR imaging guided method for excising non-palpable cancerous tissue regions indicative of breast or prostate cancer or other diagnosed types of pathological tissue anomalies, benign tumors and malignant, metastasic carcinomas, sarcomas or lymphomas in the interior of a patient's body by means of a surgical or biopsy needle percutaneously introduced a into this tissue. Said method thereby comprises the steps of providing a liquid given by a targeted contrast agent or dye fluorescent in the visible or near-infrared spectrum of light to the tip of the hookwire via a liquid guiding device which may have a substantially tubular wall and an internal lumen having an open distal end similar to a needle of a hypodermal syringe, said a liquid guiding device being comprised within the interior of the hookwire, and transferring beams of an input light to a distal end of the hookwire for illuminating the region of interest.

According to another exemplary embodiment of the present invention, the input light may be emitted by an external light source from a proximal end exterior of said patient's body on which said input light is incident to a distal end placed within a tissue region to be excised around the tip of said needle and excising the pathological tissue by means of said needle. Thereby, an output light is provided assignable to the intensity of the input light by means of light guiding means inserted into a hollow shaft longitudinally extending within the interior of the needle.

According to another exemplary embodiment, said method may comprise the steps of protruding said needle or hookwire into a pathological tissue region to be excised and measuring the intensity of the backscattered light portion received at the proximal end of said light guiding means after having placed its distal end in the pathological tissue.

Instead of or in addition to transferring beams of input light emitted by an external light source via the light guiding means for illuminating a tissue region to be excised, said tissue region being marked by the fluorescent contrast agent, this tissue region may be illuminated with light emitted from an integrated light source disposed in an internal lumen near to the tip of said needle or hookwire.

It may further be provided that the targeted contrast agent or dye fluorescent in the visible or near-infrared spectrum of light which is fed through the internal lumen and the open distal end of the cannula in the interior of said needle or hookwire or via the hollow

shaft to the tip of the needle or of the hookwire and thus to the tissue region to be excised and to which the output light supplied at the distal end of the light guiding means and/or the light emitted by the integrated light source is applied acts as a photosensitizer, thus being applicable for photodynamic therapy (PDT) performed prior to taking a histological biopt or beginning with a surgical resection of said tissue region. Applying a PDT agent via the liquid guiding cannula or via the hollow shaft of the photonic needle or of the hookwire and then illuminating a cancerous tissue covered with said PDT agent with light received via said light guiding means or with light emitted by the light source integrated in the internal lumen of the hollow shaft helps to prevent pre-metastasic cells in given tumor resection boundaries to become cancerous. Thereby, cells in the outer regions of the cancerous tissue which have not been excised will also be destroyed.

Image information needed to probe the dignity of the tissue at the tip of said hookwire or needle may be received from an optical modality constituted by a mini-camera which may be coupled to the distal end of the hollow shaft.

Furthermore, said method may also comprise the step of ablating cancerous tissue regions and other diagnosed types of pathological tissue anomalies and malignant tissue by applying high intensity laser light via said light guiding means to the tissue.

Finally, a further exemplary embodiment of the present invention is directed to using a method as described above for tumor demarcation when applying such a targeted contrast agent or dye for marking a cancerous tissue region constituting a tumor or for supporting methods for locating organs and anatomical objects, such as e.g. sentinel lymph nodes, marked by this contrast agent or dye.

BRIEF DESCRIPTION OF THE DRAWINGS

Advantageous features, aspects, and advantages of the invention will become evident from the following description, the appended claims and the accompanying drawings. Herein,

Fig. 1a shows a cross-sectional view of the Frank localizer as known from the prior art,

Fig. 1b shows a cross-sectional view of the Kopans locater as known from the prior art,

Fig. 1c shows a cross-sectional view of the Homer needle/wire localizer as known from the prior art,

Fig. 1d shows a cross-sectional view of the Sadowsky marking needle as known from the prior art,

Fig. 2 shows a schematic drawing for illustrating a sonography-guided needle biopsy taken from a patient's prostate via the rectum,

Fig. 3a+b show a photonic needle according to two alternatives of an exemplary embodiment of the present invention with and without a light guiding hook wire, respectively, wherein said needle comprises a hollow shaft longitudinally extending within the interior of the needle with an inserted light guiding means for transferring a beam of input light emitted by an external light source from a proximal end exterior of said patient's body on which said input light is incident to a distal end placed within a tissue region to be excised around the tip of said needle, thereby providing an output light assignable to the intensity of the input light for illuminating said tissue region,

Fig. 3c shows a photonic needle according to a further alternative of this exemplary embodiment, whereupon, instead of or in addition to said light guiding means, an integrated light source disposed in an internal lumen of the hollow shaft near to the tip of said needle is provided, and

Fig. 3d shows a schematic drawing of a light guiding hookwire according to an exemplary embodiment of the present invention,

Fig. 4 shows a flow chart consisting of two parts for describing the proposed X-ray, CT, MR, sonography, PET/CT, optical imaging, eleastography, impedence tomography, thermography or hybrid radiography/MR imaging guided method for excising non-palpable cancerous tissue regions indicative of breast or prostate cancer or other diagnosed types of pathological tissue anomalies, benign tumors and malignant, metastasic carcinomas, sarcomas or lymphomas in the interior of a patient's body by means of a surgical or biopsy needle percutaneously introduced a into this tissue according to the present invention.

DETAILED DESCRIPTION OF THE PRESENT INVENTION

In the following sections, the claimed biopsy needle and method for using such a biopsy needle will be explained in more detail with respect to special embodiments referring to the accompanying drawings and in comparison to the prior art. It should be understood, however, that the drawings and detailed description are not intended to limit the invention to the particular form disclosed, but, on the contrary, the intention is to cover all

modifications, equivalents and alternatives falling within the spirit and scope of the present invention as defined by the appended claims.

As already mentioned above, biopsies are conventionally taken for correct preoperative diagnosis of various cancer diseases. This can either be via a lumen of an endoscope or via needle biopsies. A wide variety of different wire guides and needle devices have been developed to aid the surgeon in the biopsy procedure and are in routine use today. From the prior art, four basic types of conventionally available wire guide devices as depicted in Figs. 1a-d that are typically used for marking and localizing the position of a cancerous tissue region of interest to be excised are known and to be distinguished: the Frank localizer, the Kopans locater, the Homer needle/wire localizer and the Sadowsky needle marking system.

The Frank localizer, which is shown in Fig. 1a in a longitudinal cross-sectional view, typically consists of a hook wire HW_1 with a total length of 12 cm and a hook or spur H_1 having a length of 5 mm at the tissue insertion end. The hook wire HW_1 is typically carried by a 20-gauge syringe needle N_1 having a length of about 9 cm. While the length of hook wire HW_1 is inserted into the bore of needle N_1, hook H_1 remains outside the needle tip during its introduction into a patient's body tissue at the preselected site of insertion. Unfortunately, once hook wire HW_1 and needle N_1 have been inserted at a chosen site, the needle can only be advanced deeper into the tissue; it cannot be withdrawn even slightly without releasing hook wire HW_1 into the tissue. The hook wire itself cannot be repositioned at any time, even if it is not situated close enough to the target lesion. Furthermore, hook wire HW_1 is extremely thin, difficult to palpate, and may be accidentally cut during the surgery.

Another frequently used wire guide device is the Kopans locater, which is depicted in Fig. 1b in a longitudinal cross-sectional view. As designed, the entire length of the hereby applied hook wire HW_2 and its hooked end H_2 are intended to remain within the bore of a needle N_2 during insertion into a tissue region in the interior of a patient's body. Once positioned, the beveled needle tip is checked radiologically for proximity to the target area. If incorrectly situated, needle N_2 can be adjusted if necessary. Once believed to be in the correct target area, wire hook H_2 within the bore of needle N_2 is extended and thereby released into the surrounding tissue. The hollow needle is then typically removed, thus leaving hook wire HW_2 in the extended position within the tissue. There are, however, some deficiencies in the Kopans system. The tip of needle N_2 is not completely secure in the tissue after insertion and prior to release of the wire hook H_2; for example, it may become displaced by involuntary movement of the subject between the time the needle position is

radiologically checked and wire hook H_2 is finally extended. Furthermore, the entire wire length may be drawn into the tissue during a position verification procedure. Accordingly, either the tissue, such as a breast, must be kept in constant compression or an external screw clamp must be utilized to prevent the length of hook wire HW_2 from being drawn into the tissue and lost. The hook wire within the needle bore typically has a thickened segment along its length to assist surgical palpation, but may become broken or accidentally cut above or below this segment. Since the needle lumen must accommodate both hook H_2 and the shaft of said hook wire HW_2, the wire diameter can be no more than half the diameter of the lumen or one quarter of its cross-sectional area. This necessitates a larger bore needle for any required wire thickness.

In Fig. 1c, a Homer needle/wire localizer is shown in a longitudinal cross-sectional view. Typically, the device comes in either long or short length formats. A beveled syringe needle N_3 is utilized into which a J-shaped hook wire HW_3 is inserted, said hook wire being formed from a metal with strong spring recovery which can be temporarily straightened as it is drawn into the bore of needle N_3. Typically, a wire screw clamp SC_3 is attached to hook wire HW_3 at its proximal end to indicate the orientation of the J-shaped hook H_3 and to provide some indication of the depth of hook wire HW_3 in the needle and tissue. During insertion of needle N_3 into the tissue, J-shaped hook H_3 remains within the bore of needle N_3. Once the tip of needle SN_3 is found to be in the desired area of the target lesion, hook wire HW_3 is extended through the needle bore and J-shaped hook H_3 pushes out into the surrounding tissue in a sweeping curve. Needle N_3 is optionally left in place within the tissue along with hook wire HW_3 during the biopsy. However, needle N_3 is difficult to control during insertion such that J-shaped hook H_3 may be delivered at an unintended location. Withdrawing needle N_3 can result in a cutting sweep of tissue by J-shaped hook H_3 as it is retracted into the bore of needle N_3. Finally, while the clamp SC_3 at the proximal end of hook wire HW_3 is meant to indicate the orientation of J-shaped hook H_3, it is common for the hook wire to become twisted or disoriented with relation to screw clamp SC_3.

Another wire guide device known from the prior art is the Sadowsky marking system as shown in Fig. 1d in a longitudinal cross-sectional view. The Sadowsky needle and wire guide is similar to the Kopans device previously described herein. A hook wire HW_4 with a V-shaped hook H_4 is intended to remain within the bore of a beveled edge needle N_4 during insertion of the device into the tissue. A screw clamp SC_4 is typically mounted on the outside of the needle to a preset needle depth which is believed to be appropriate for the target lesion. Hook wire HW_4 usually has individual markings along its length to identify its

depth as well. Once needle N_4 is inserted into the tissue and verified as to be correctly positioned, while hook wire HW_4 is advanced out of the needle bore into the tissue substantially as shown. Once advanced into the tissue, hook wire HW_4 cannot be withdrawn or repositioned. The other deficiencies of the Sadowsky system are similar to those previously enumerated for the Kopans system.

An example for a conventional image-guided needle biopsy is shown in Fig. 2, where a needle biopsy is taken under image control from a patient's prostate P via the rectum. In order to find the correct position to take the biopsy, various imaging modalities and methods may be used, such as e.g. X-ray, CT, MR, sonography or hybrid radiography/MR imaging. In case of prostate cancer, a needle biopsy is usually guided by a sonography, which in case of sonography requires an ultrasound probe UP (cf. Fig. 2). Although helpful, these methods of guidance are far from being optimal. On the one hand, resolution is limited, and in most cases these imaging modalities are not able to discriminate between benign and malignant tissue. As a result, a surgeon does not know for certain that a biopsy is taken from the correct part of a tissue region to be examined. Hence, biopsies are taken almost blind and even if after inspection of the tissue no cancerous cells are detected, the surgeon does not know for certain that he/she did not simply miss the right spot to take the biopsy.

If the biopt taken appears to be cancerous, this cancerous tissue will typically be removed by surgery (especially when the tumor is well localized). Here another problem arises due to the fact that the surgeon can only use his/her eyes and hands (palpation) to find the tumor. If the tumor is large enough and if the center of the tumor is more compact than the surrounding tissue, it can be localized by palpation during surgery. Tissue can removed with an apparently sufficient margin around it. However, in a considerable number of cases the tumor is still soft and very difficult to feel or distinguish by eye. To help the surgeon, a wire is inserted into the respective tissue region, e.g. under X-ray, CT, MR, sonography or hybrid radiography/MR imaging guidance, with the end point of the wire located at the center of the tumor.

As described above, it is particularly difficult to find the boundaries of the tumor, in fact it is virtually impossible. The surgeon therefore removes a significant amount of tissue around the tumor center to be sure that all of the tumor is removed. Although removing an additional amount of tissue around the tumor will indeed lead in most cases to complete removal, the surgeon can never be sure. The number of recurrences of the cancer after removal is significant, which already shows that not enough tissue has been removed.

One could of course increase the amount of tissue to be removed, but in several cases this turned out to be very difficult. In some cases, vital structures are present in the tissue (such as e.g. nerves, important blood vessels, brain tissue, etc.). The surgeon has then to decide whether the resulting disability of the patient due to the additional tissue outweighs the risk of not completely removing the tissue. It is important to note that when resection is not complete, the surgeon has, in fact, cut through the tumor and as a result has caused the tumor to spread. A second operation to repair these damages is very invasive and leads to severe side effects such mutilation and loss of function of body and/or mind.

A third problem with the current way of removing tumors by surgery is that although a resection was complete according to the diagnosis of the current methods of pathology, the tumor boundaries may still contain pre-metastasic cells. These cells, which are still not so far developed that they can be diagnosed as being cancerous, may develop in cancer soon, thus being again the cause of tumor recurrence.

Associated with tumors and tumor removal is the spreading of cancerous cells into a patient's lymph nodes. Nowadays, the lymphatic system can be stained by using methylene blue injected at the site of the tumor, and in this way the sentinel node can be located. It is then removed and pathologically investigated. In a significant amount of all cases the node is affected by the tumor, and all neighboring lymph nodes are removed as well. It should be noted that lymph nodes are embedded in fatty tissue, which has the same pale yellowish color, and cannot be found by eye unless they are stained. Resection of suspicious lymph nodes is radical: All nodes are removed including the surrounding fatty tissue. It should be noted that the surgeon and the patient would be helped enormously if only those lymph nodes could be identified that actually need to be removed because they host cancerous cells.

In the following, the exemplary embodiments as proposed by the present invention and refinements of these embodiments will be described in more detail with reference to the diagrams depicted in Figs. 3a-d and the flow chart shown in Fig. 4. The reference signs in brackets beginning with the capital letter "S" thereby refer to the particular steps of the herein illustrated method.

As will now be explained with reference to the simplest exemplary embodiment of the present invention, a surgical or biopsy needle N is proposed which comprises a combined light guiding and fixation means such as e.g. a light guiding hook wire LGHW as a way to find a tumor center and as a way to mark the distance of the needle from the center of the tumor (see Fig. 3a). Having a surgical or biopsy needle that is equipped with

such a light guiding means and fixation means results in a "photonic needle" which can advantageously be employed to support and improve demarcation and localization of cancerous tissue regions indicative of breast or prostate cancer or other diagnosed types of pathological tissue anomalies, benign tumors and malignant, metastasic carcinomas, sarcomas or lymphomas in the interior of a patient's body during an image-guided needle biopsy or surgical intervention when supplying (S3) said light guiding means LGHW with a beam of light emitted by a light source LA_1 disposed exterior to said patient's body. Tumor demarcation and localization is thereby done as follows: First, the light guiding hook wire LGHW is placed at or near to the center of the tumor, which may be accomplished in the same way as with a conventional hook wire under X-ray, CT, MR, sonography, PET/CT, optical imaging, eleastography, impedence tomography, thermography or hybrid radiography/MR imaging guidance. Once the light guiding hook wire LGHW is at its place, said light source LA_1 can be attached to its proximal end such that the tip of hook wire LGHW at its distal hooked end LGH illuminates the tumor from inside. To find the tumor, a surgeon just has to find the location with the highest light intensity. This gives a much easier guidance than just guessing based on the length of the hook wire LGHW its angle at which it penetrates the tissue. Furthermore, this light intensity can be used to better estimate the size of a cancerous tissue region to be excised. Cutting just at the place where the intensity has dropped below a certain level will lead to remove tissue within a spherical region around the center of the tumor. This guidance will reduce errors in cutting by the surgeon that can have severe consequences with regard to tumor recurrence. In addition thereto, this method helps to minimize the amount of tissue to be removed since in case of no guidance the surgeon just removes more tissue to be extra safe.

Furthermore, the light guiding and fixation means LGHW may comprise a liquid guiding means (not depicted in Fig. 3a), as described in more detail with respect to Fig. 3d.

As will now be discussed with reference to a further refinement of the exemplary embodiment referring to said needle, tumor localization and lesion boundary demarcation can be further improved when providing such a "photonic needle" with a liquid guiding cannula CA for providing (S1) a targeted contrast agent or dye fluorescent in the visible or near-infrared spectrum of light to the tip of needle N. Thereby, a fluorescent contrast agent is chosen which specifically binds to or accumulates at the tumor. Illumination of the contrast agent can then occur via a usual light guiding means LGM, such as e.g. an optical fiber integrated in the needle N (see Fig. 3b), or via the above-described light guiding

hook wire LGHW (see Fig. 3a), and the tumor tissue can be selectively removed by cutting away (S6) those tissue parts that emit fluorescence light after having protruded (S1) said needle N (together with the hookwire) into this pathological tissue region. Since the wavelength of the fluorescence light can be selected to be different from that of the illumination wavelength of the light guide through the photonic needle, a cancerous tissue region can simply be selected based on the color of light it emits. There are various well-known ways to supply such a contrast agent to the patient. By using special goggles (containing some filter glass) or an additional camera, the differences can be made even more visible.

According to a still further refinement of the exemplary embodiment referring to said photonic needle, a light source LA_2, such as e.g. a light emitting diode (LED) or semiconductor laser (not shown), may be integrated in the needle (see Fig. 3c). A pathological tissue region to be excised (S6) is thus illuminated (S3') with light emitted from the integrated light source LA_2, wherein the latter may e.g. be disposed in an internal lumen near to the tip of said needle.

According to another refinement of the exemplary embodiment referring to the photonic needle, a surgical or biopsy needle N may be provided with a light guiding means LGM (or LGHW, respectively) which reflects light backscattered from an illuminated tissue region to the proximal end of said needle such that the intensity of the backscattered light portion received at the proximal end of said light guiding means can be measured (S4). As will be described, such a photonic needle N is capable of guiding its tip towards the tumor before being fixed to the cancerous tissue. There are various well-known ways to characterize tissue by light, for instance based on elastic backscattering and absorption (measured as a function of wavelength) or based on inelastic backscattering properties, such as e.g. fluorescence. Based on these optical tissue interactions, various optical techniques are proposed, such as e.g. diffuse reflectance spectroscopy, differential path length spectroscopy, light scattering spectroscopy, autofluorescence spectroscopy, multi-photon autofluorescence spectroscopy, Raman spectroscopy or optical coherence tomography. On the basis of these methods, it can be discriminated between differences in properties of tissue, in particular between normal and cancerous tissue regions. These signals can then be used to guide the needle tip to a tumor position. In addition or alternatively to that, the position of a tumor or lesion can also be found by wiredly or wirelessly receiving (S5) information from a mini-camera (not shown) coupled to the distal end of the hollow shaft which provides a surgeon with image information needed to probe the dignity of the tissue at the tip of said needle.

A further improvement arises when the contrast agent is not only able to produce fluorescence but also applicable for photodynamic therapy (PDT), which thus allows to combine tumor localization and lesion boundary demarcation with pre-surgical treatment as will now be explained with reference to a refinement of the exemplary embodiment referring to the proposed method. In PDT treatment (S6') a physician makes use of the fact that certain fluorescent dyes (commonly referred to as photosensitizers, which means specific chemicals that increase the photosensitivity of the organism) accumulate or are destructed at different rates in tumor tissue than in normal tissue. Such a photosensitizer is e.g. 5-amino-4-oxo-pentanoic acid ($C_5H_9NO_3$), also referred to as D-aminolevulinic acid (δ-ALA). It elicits synthesis and accumulation of fluorescent porphyrins, such as e.g. protoporphyrin IX (PpIX) in epithelia and neoplastic tissues, among them malignant gliomas, and is used to visualize cancerous tissue in neuro-surgical procedures. PpIX thereby serves as a precursor for the heam cycle. Because the transformation of protoporphyrin IX to heam is slow and differs greatly between different tissues, different amounts of PpIX will be present in the tumor cells rather than in normal cells. When being illuminated, protoporphyrin IX can produce fluorescence but can also react with oxygen, thus giving rise to very reactive oxygen radicals that can lead to necrosis, which is the basis of the photodynamic therapy. Said photosensitizer can thereby be applied in various well-known ways.

Fig. 3d shows a schematic drawing of a light guiding hookwire 300 according to an exemplary embodiment of the present invention. The hookwire 300 comprises a light guiding device 304. Light 307 is guided by the light guiding device 304 to the distal end of the hookwire. The light guiding device 304 may be adapted as a glass fiber and emits light 305 inside the region of interest 306.

Furthermore, the light guiding hookwire 300 comprises a liquid guiding device 302 for providing a liquid the region of interest 306, which may be a tumor. The liquid guiding device 302 is adapted as a liquid guiding cannula (CA) with a substantially tubular wall and an internal lumen having an open distal end for providing a liquid given by a targeted contrast agent or dye fluorescent in the visible spectrum of light to the tip 308 of the hookwire 300.

The hookwire 300 further comprises a wire-like hook device 303 forming a flexible hook at the tip 308. A hollow outer shaft 301 is provided in which the inner shaft 302 is for guiding the fluid, the light guiding device 304 and the wire 308 are at least partially arranged.

As will now be explained with reference to a further refinement of the exemplary embodiment referring to said method, the hollow shaft longitudinally extending within the interior of the photonic needle (or withing the hookwire) which contains the inserted light guiding means is used instead of said liquid guiding cannula CA to apply (S2) a contrast agent or photosensitizer to a tissue region of interest. This allows to supply the contrast agent or photosensitizer directly into the tumor, which leads to much higher concentration differences between the contrast agent or photosensitizer present in the tumor and in the surrounding tissue (simply due to diffusion properties). Thereby, non-specific sensitizers may be used as the concentration gradient can be regulated by changing the supply of contrast agent fed through the hollow shaft of the hookwire.

According to a further refinement of the exemplary embodiment referring to said method, said light guiding means LGM (in particular, the light guiding hook wire LGHW) may be used to ablate (S6'') cancerous tissue regions with laser light. The hollow shaft extending in longitudinal direction within the interior of the proposed biopsy needle can thereby be used to supply anesthesia before beginning with the ablation treatment.

APPLICATIONS OF THE INVENTION

An immediate application of the claimed biopsy needle and method consists in image-guided surgical and minimally invasive interventions, in particular in the field of percutaneous needle biopsies executed under X-ray, CT, MR, sonography or hybrid radiography/MR imaging, where a photonic needle as proposed would provide for a better tumor localization and resectioning.

While the present invention has been illustrated and described in detail in the drawings and in the foregoing description, such illustration and description are to be considered illustrative or exemplary and not restrictive, which means that the invention is not limited to the disclosed embodiments. Other variations to the disclosed embodiments can be understood and effected by those skilled in the art in practicing the claimed invention, from a study of the drawings, the disclosure and the appended claims. In the claims, the word "comprising" does not exclude other elements or steps, and the indefinite article "a" or "an" does not exclude a plurality. The mere fact that certain measures are recited in mutually different dependent claims does not indicate that a combination of these measures can not be used to advantage. Any reference signs in the claims should not be construed as limiting the scope of the invention.

CLAIMS:

1. A light guiding hookwire for localizing a region of interest, the hookwire comprising:

- a light guiding device for guiding beams of an input light to a distal end of the hookwire for illuminating the region of interest; and
- a liquid guiding device for providing a liquid the region of interest.

2. The light guiding hookwire of claim 1,

wherein the light guiding device is adapted as a hollow shaft longitudinally extending within the interior of the hookwire with an inserted light guiding means (LGM, LGHW) for guiding the beams of the input light emitted by an external light source (LA_1) from a proximal end exterior of a patient's body on which the input light is incident to a distal end placed within the region of interest; and

wherein the liquid guiding device is adapted as a liquid guiding cannula (CA) with a substantially tubular wall and an internal lumen having an open distal end similar to the needle of a hypodermal syringe for providing a liquid given by a targeted contrast agent or dye fluorescent in the visible or near-infrared spectrum of light to the tip of the hookwire.

3. The light guiding hookwire of claim 1,

wherein, instead of being specially provided with such a liquid guiding cannula (CA), the residual free internal lumen of the hollow shaft not being occupied by the volume of the light guiding means (LGM, LGHW) serves for providing the contrast agent to the tip of said needle (N).

4. The light guiding hookwire of claim 1,

comprising a fixation means (HW, LGHW) for holding the tip of the hookwire in a fixed position within the pathological tissue region to be examined during surgical removal of cancerous tissue under image-guided percutaneous intervention using said needle (N).

5. The light guiding hookwire of claim 4,
wherein the fixation means is given by a hook portion (H, LGH) of the flexible hook wire (HW, LGHW) initially housed within a hollow shaft of a needle (N), said hook portion (H, LGH) being inserted into a detected tissue lesion via the lumen of the hollow shaft for marking and localizing the exact position of said lesion as needed for a subsequent image-guided percutaneous needle biopsy.

6. The light guiding hookwire of claim 5,
wherein the light guiding means (LGM) is attached to the flexible hook wire (HW) such that the distal end of said light guiding means (LGM) is placed near to the position of said hook portion (H).

7. The light guiding hookwire of claim 6,
wherein said light guiding means (LGM, LGHW) is an optical fiber.

8. The light guiding hookwire of claim 4,
wherein, instead of or in addition to said light guiding means (LGM, LGHW), an integrated light source (LA_2) disposed in an internal lumen of the hollow shaft near to the tip of the hookwire is provided.

9. The light guiding hookwire of claim 1,
wherein an optical modality constituted by a mini-camera is coupled to the distal end of the hollow shaft which provides a surgeon with image information needed to probe the dignity of the tissue at the tip of said needle (N).

10. A surgical or biopsy needle comprising a light guiding hookwire of claim 1.

11. An X-ray, CT, MR, sonography, PET/CT, optical imaging, eleastography, impedence tomography, thermography or hybrid radiography/MR imaging guided method for excising non-palpable cancerous tissue regions indicative of breast or prostate cancer or other diagnosed types of pathological tissue anomalies, benign tumors and malignant, metastasic carcinomas, sarcomas or lymphomas in the interior of a patient's body by means of a light guiding hookwire percutaneously introduced into this tissue, said method comprising the steps of:

- providing (S2) a liquid given by a targeted contrast agent or dye fluorescent in the visible or near-infrared spectrum of light to the tip of the hookwire via a liquid guiding device;
- transferring (S3) a beam of an input light to a distal end of the hookwire for illuminating the region of interest.

12. The method according to claim 11, comprising the steps of:

protruding (S1) the hookwire into a pathological tissue region to be excised and measuring (S4) the intensity of the backscattered light portion received at the proximal end of said light guiding means (LGM, LGHW) and placing its distal end within the pathological tissue.

13. The method according to claim 12, which, instead of or in addition to transferring (S3) a beam of the input light emitted by an external light source (LA_1) via the light guiding means (LGM, LGHW) for illuminating a tissue region to be excised, said tissue region being marked by the fluorescent contrast agent, comprises the step of:

illuminating (S3') this tissue region with light emitted from an integrated light source (LA_2) disposed in an internal lumen near to the tip of said needle (N).

14. A method according to claim 13,

wherein

the targeted contrast agent or dye fluorescent in the visible or near-infrared spectrum of light which is fed through the internal lumen and the open distal end of the cannula (CA) in the interior of the hookwire or via the hollow shaft to the tip of the needle (N) and thus to the tissue region to be excised and to which the output light supplied at the distal end of the light guiding means (LGM, LGHW) and/or the light emitted by the integrated light source (LA_2) is applied acts as a photosensitizer, thus being applicable for a photodynamic therapy (PDT) performed (S6') prior to taking a histological biopt or beginning with a surgical resection of said tissue region, said therapy destroying pre-metastasic cells of a cancerous tissue covered with said agent by illuminating this tissue with light received via said light guiding means (LGM, LGHW) or with light emitted by the light source (LA_2) integrated in the internal lumen of the hollow shaft.

15. A method according to claim 14, comprising the step of:

receiving (S5) image information needed to probe the dignity of the tissue at the tip of the hookwire from an optical modality constituted by a mini-camera which is coupled to the distal end of the hollow shaft.

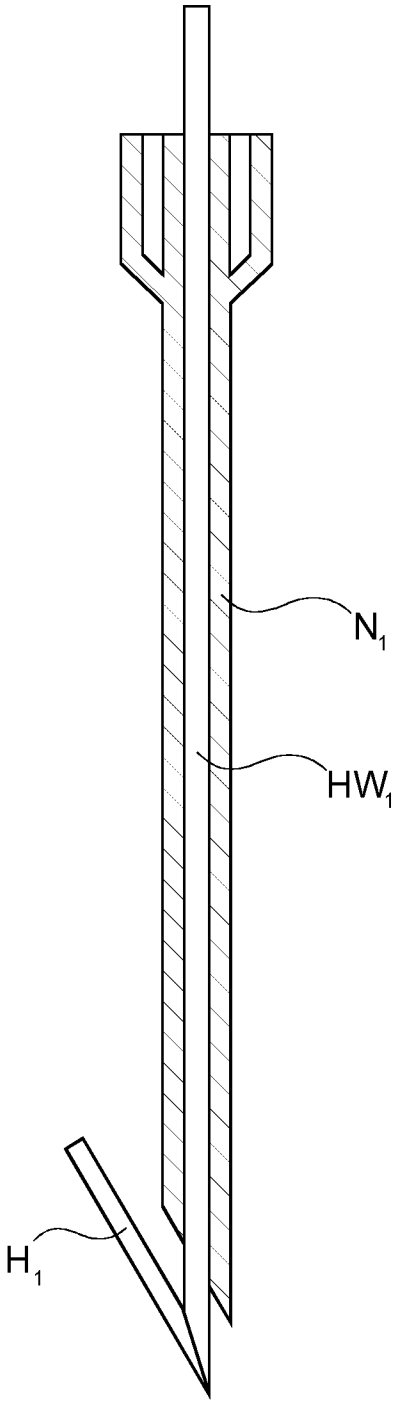

Fig. 1a
(Prior Art)

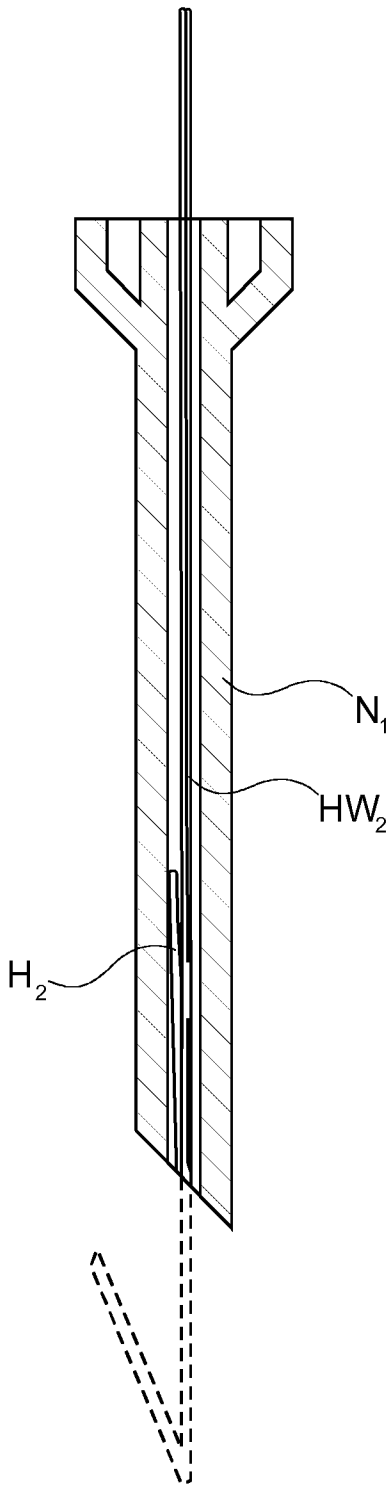

Fig. 1b
(Prior Art)

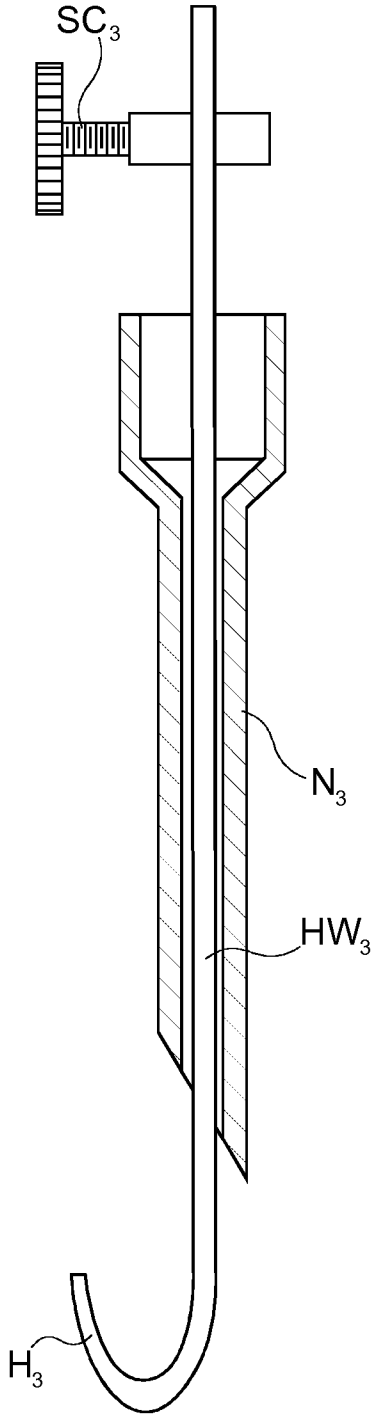

Fig. 1c
(Prior Art)

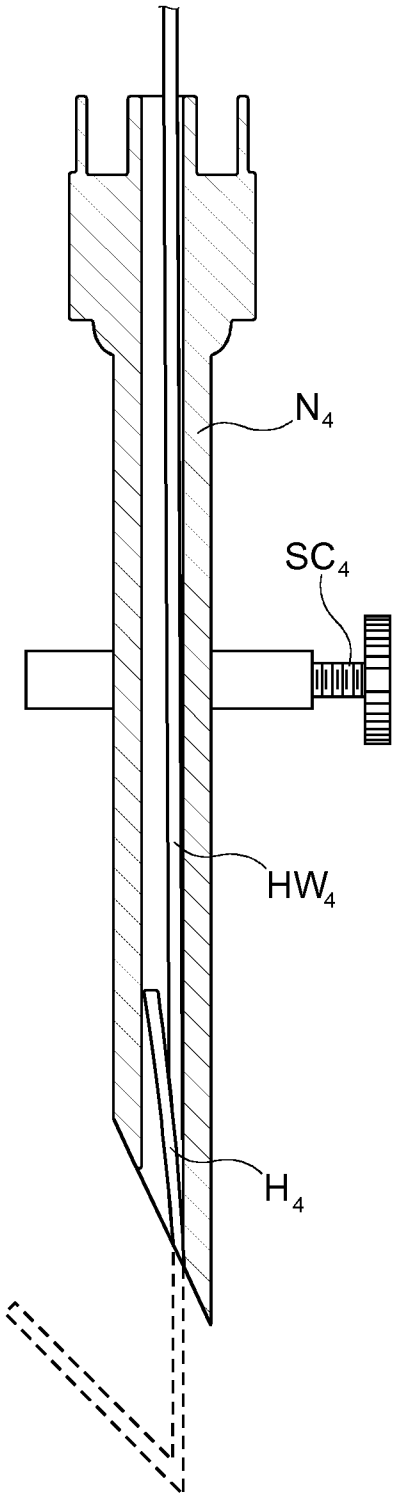

Fig. 1d
(Prior Art)

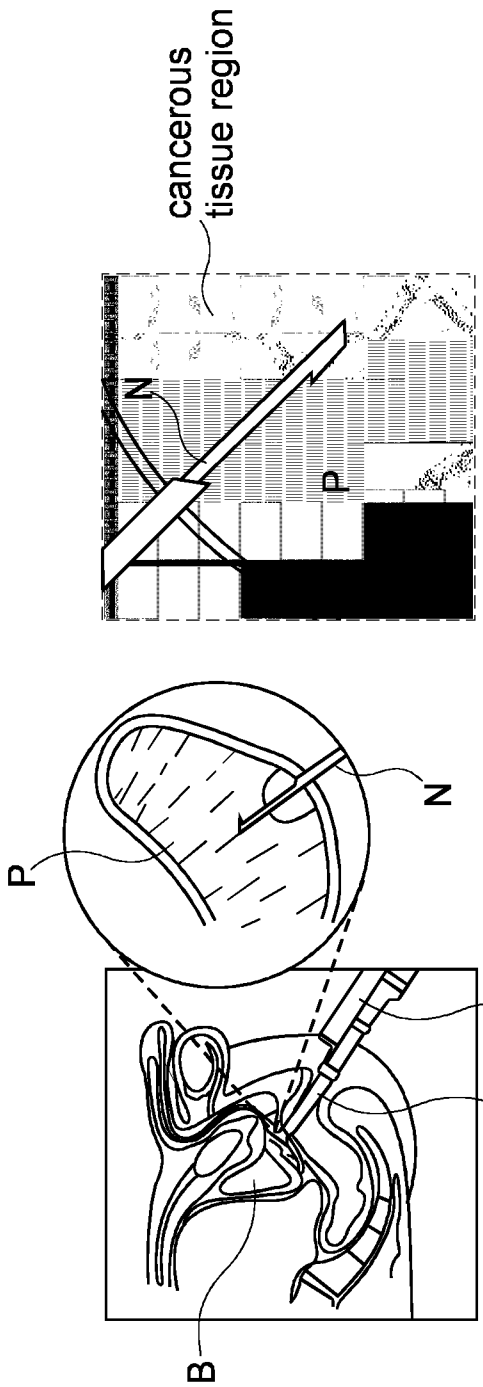
cancerous tissue region
N
P
N
P
NG
UP
B
B: bladder
N: surgical or biopsy needle
NG: needle guide
P: prostate
UP: ultrasound probe

Fig. 2

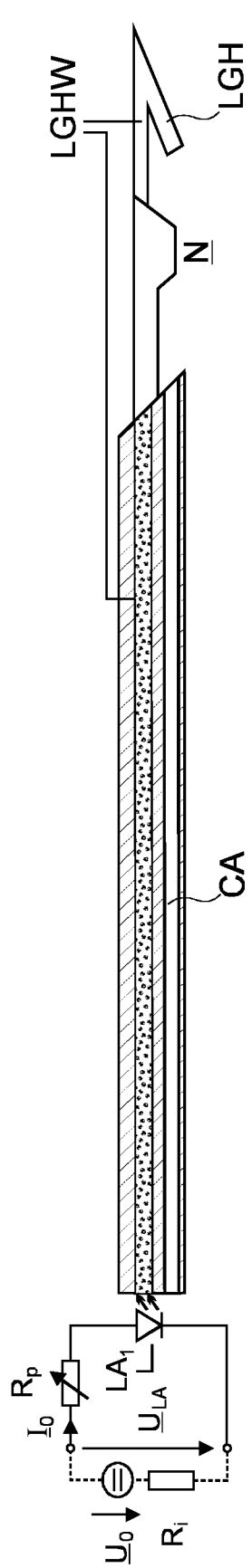

Fig. 3a

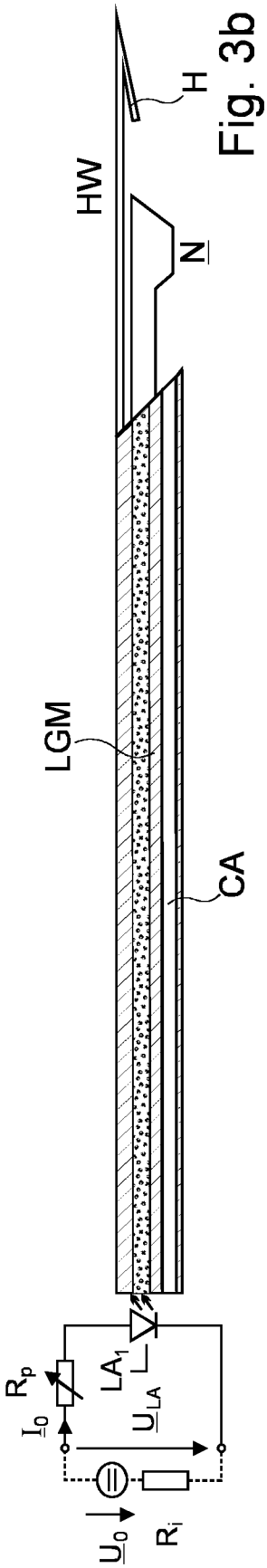

Fig. 3b

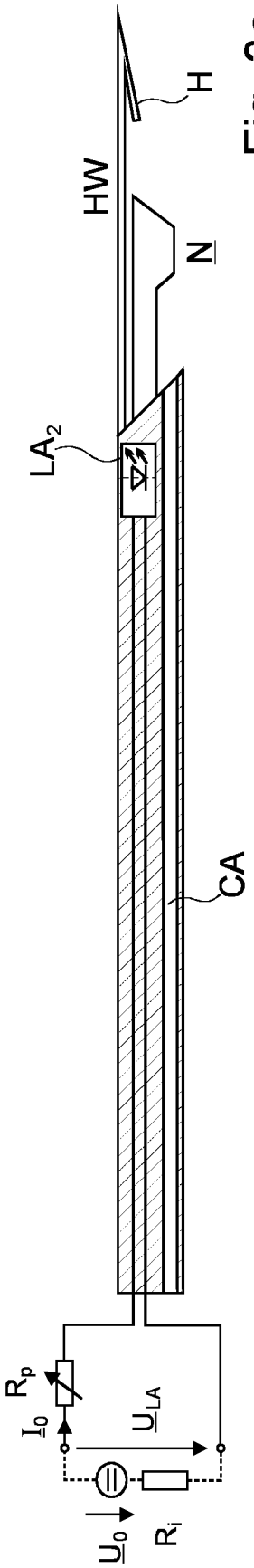

Fig. 3c

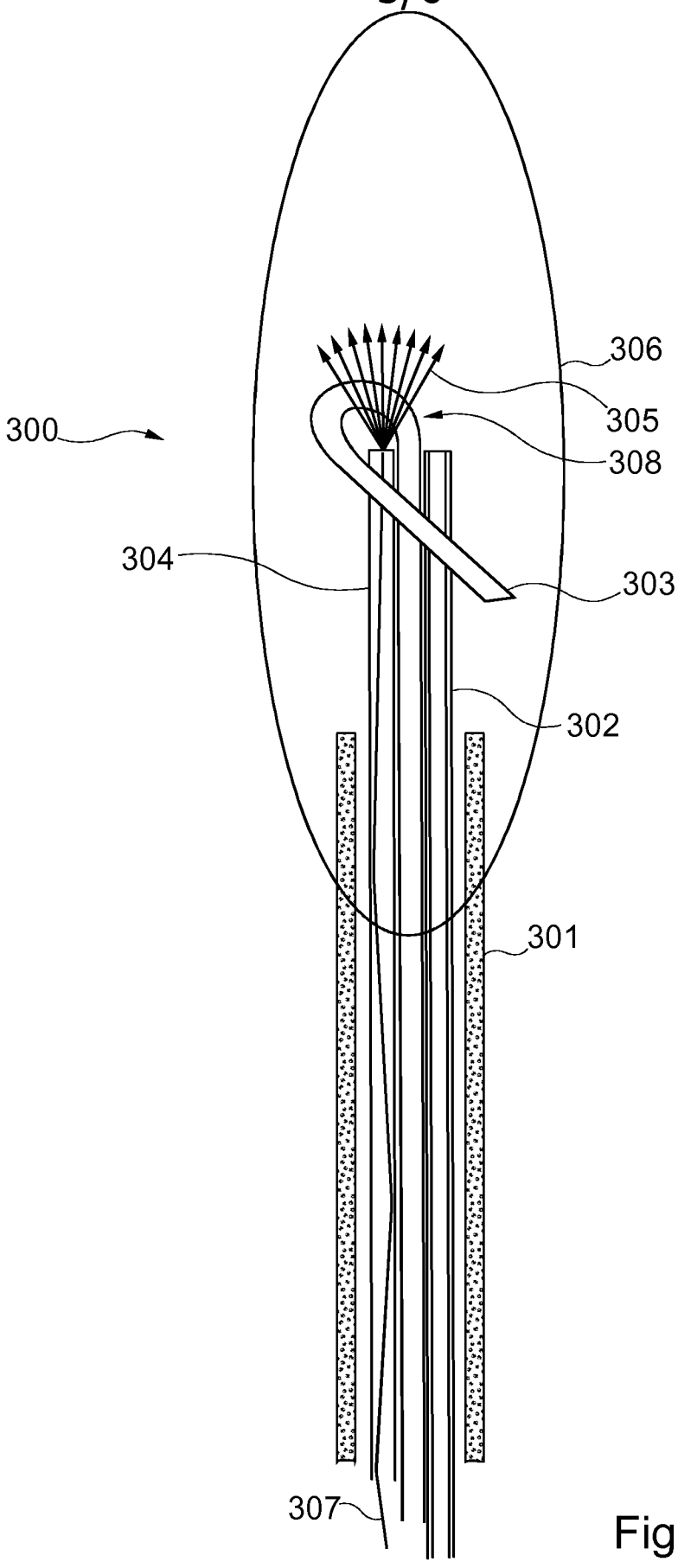

Fig. 3d

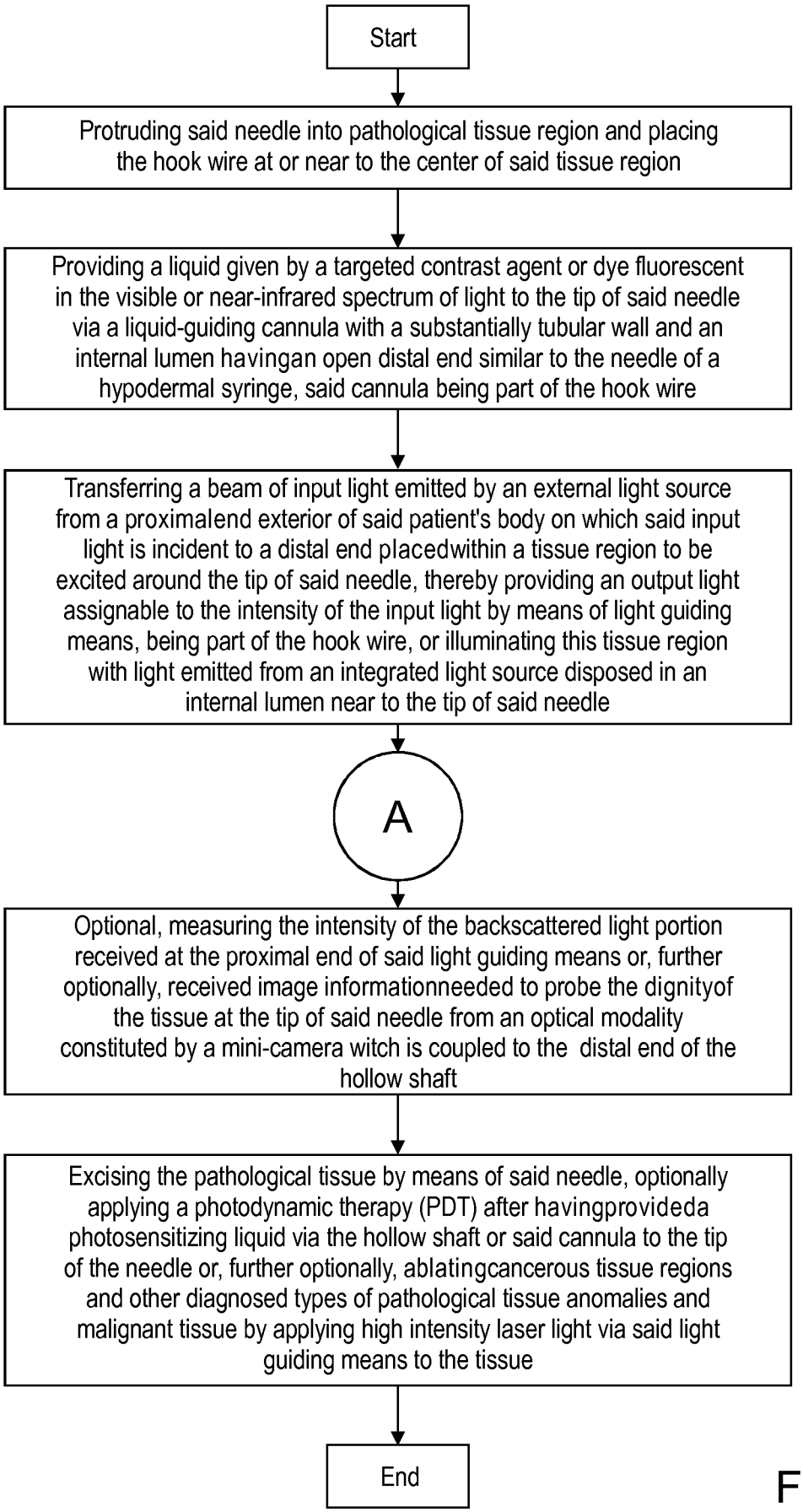
Start
Protruding said needle into pathological tissue region and placing the hook wire at or near to the center of said tissue region
S1
Providing a liquid given by a targeted contrast agent or dye fluorescent in the visible or near-infrared spectrum of light to the tip of said needle via a liquid-guiding cannula with a substantially tubular wall and an internal lumen havingan open distal end similar to the needle of a hypodermal syringe, said cannula being part of the hook wire
S2
Transferring a beam of input light emitted by an external light source from a proximalend exterior of said patient's body on which said input light is incident to a distal end placedwithin a tissue region to be excited around the tip of said needle, thereby providing an output light assignable to the intensity of the input light by means of light guiding means, being part of the hook wire, or illuminating this tissue region with light emitted from an integrated light source disposed in an internal lumen near to the tip of said needle
S3,S3'
A
Optional, measuring the intensity of the backscattered light portion received at the proximal end of said light guiding means or, further optionally, received image informationneeded to probe the dignityof the tissue at the tip of said needle from an optical modality constituted by a mini-camera witch is coupled to the distal end of the hollow shaft
S4 or S5
Excising the pathological tissue by means of said needle, optionally applying a photodynamic therapy (PDT) after havingprovideda photosensitizing liquid via the hollow shaft or said cannula to the tip of the needle or, further optionally, ablatingcancerous tissue regions and other diagnosed types of pathological tissue anomalies and malignant tissue by applying high intensity laser light via said light guiding means to the tissue
S6, S6' or S6"
End

Fig. 4

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2008/054253

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61B5/00

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 6 261 240 B1 (CARLSON KARA L [US] ET AL) 17 July 2001 (2001-07-17) cited in the application column 2, line 21 - column 3, line 14 figures 1,2	1-10
Y	US 5 782 771 A (HUSSMAN KARL L [US]) 21 July 1998 (1998-07-21) column 2, line 46 - column 3, line 31 figures 1-30	1-10
A	WO 99/51143 A (WINDY HILL TECHNOLOGY INC [US]) 14 October 1999 (1999-10-14) cited in the application page 3, line 16 - page 6, line 31 figures 1-4	1-10

-/--

[X] Further documents are listed in the continuation of Box C.

[X] 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 doubts 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.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
3 March 2009	11/03/2009

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Abraham, Volkhard

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2008/054253

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 167 297 A (BENARON DAVID A [US]) 26 December 2000 (2000-12-26) column 4, line 23 - column 7, line 46 figures 1-3	1-10
A	US 2002/115918 A1 (CROWLEY ROBERT J [US]) 22 August 2002 (2002-08-22) paragraphs [0009] - [0011] paragraphs [0028] - [0031] figure 4	1-10

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2008/054253

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

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

1. [X] Claims Nos.: 11-15
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 No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

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

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2008/054253

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6261240 B1	17-07-2001	NONE	
US 5782771 A	21-07-1998	US 6135993 A	24-10-2000
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		WO 0068665 A1	16-11-2000
		US 6246901 B1	12-06-2001
US 2002115918 A1	22-08-2002	NONE	