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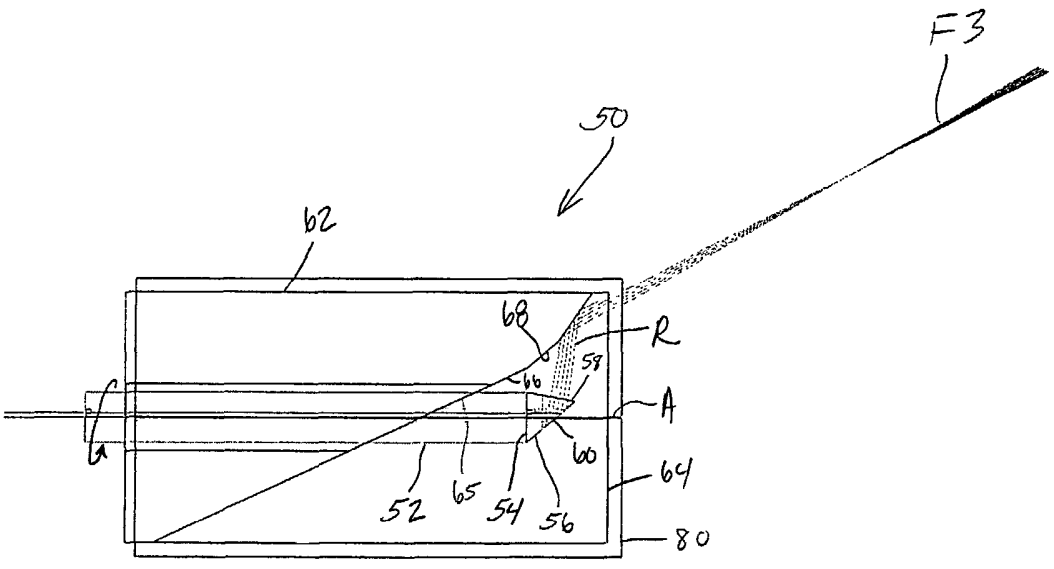

(57) Abstract: The present invention relates to the use of optical coherence tomography (OCT) for procedure- oriented applications such as precise image-guided placement of instruments and hardware in the body. The invention also relates to a thin forward- and radial-scanning OCT probe and an OCT-epiduroscopy instrument for use in such applications. In particular, the methods and apparatus of the present invention are ideally suited for real-time, high resolution imaging of the spinal epidural space, which is useful in connection with epidural regional analgesia, lysis of epidural adhesions, and high resolution diagnostic imaging of, for example, small free disc or bone fragments causing radiculopathy. The methods and apparatus are also ideally suited for real-time, hight resolution imaging within the intrathecal space, which is useful for example, for the early diagnosis of metastatic cancer within the intrathecal sac.

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OPTICAL COHERENCE TOMOGRAPHY PROBE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims priority under 35 U.S.C. §119 to U.S. Provisional Application Serial No. 60/409,774, filed September 11, 2002, which is incorporated herein in its entirety for all purposes.

TECHNICAL FIELD OF THE INVENTION

[0002] The present invention relates generally to methods of diagnosis and imaging using optical coherence tomography (OCT). More specifically, the invention relates to imaging of the spine, abdominal or pelvic organs, and the use of that imaging for diagnosis of various conditions, as well as for identifying placement of surgical instruments or needles. The invention also relates to apparati for use in those methods.

BACKGROUND OF THE INVENTION

[0003] There are a number of imaging modalities that can potentially be utilized for guidance in therapeutic interventions. CT, MRI, and ultrasound are proven technologies that have established clinical niches.

Background on OCT imaging

[0004] Optical coherence tomography (OCT) is a relatively new technology and is still in the process of identifying its niche. There are clinical needs which are uniquely suited for OCT, one of which is imaging the spinal epidural space. Therapeutic interventions within the epidural space have high impact for society, and image guidance can benefit them significantly.

[0005] Optical coherence tomography (OCT) is a fundamentally novel optical imaging technology invented in 1991 by Professor James Fujimoto of MIT (Huang et al, *Science* 1991). In a simplistic sense, OCT is analogous to ultrasound or radar, except that infrared

light is used as the excitation signal rather than sound or radio waves. In each of these three technologies, an image is constructed by measuring two parameters, namely, the strength of a reflected signal and the distance to the reflecting structure. OCT is essentially an optical ranging technology (the determination of distance to a target). In the catheter-based design, the light originates from a spinning optical fiber placed within a thin clear stationary outer catheter.

[0006] OCT utilizes an interferometry strategy to measure distances in the micron to mm range. In classic interferometry, a high coherence light source is used to produce interference over a wide range of distance (illustrated in the top right corner of Fig. 2). OCT is a form of interferometry that utilizes low coherence light in which case interference occurs only over a very short distance (illustrated in the lower right corner of Fig. 2). Interference is observed when the distance to the sample is equal the distance to the reference mirror. Thus, optical ranging can be achieved indirectly by moving the reference mirror and plotting the amplitude of the interference signal as a function of the reference mirror position. In the optical fiber implementation of OCT, the beam splitter mirror is replaced by a fiber splitter and light is guided by single mode optical fibers rather than traveling in free space.

[0007] A process known as 'coherence gating' underlies the ability of OCT to "see" through tissue. As photons in a focused beam propagate through a soft tissue such as the brain, they are scattered multiple times by inhomogeneities in the refractive index. As the scattered photons spread in space, they also disperse in time. The heterodyne detection scheme employed in OCT ensures that only those photons that experience the minimal temporal delay (less than the coherence time of the source) are amplified. Those photons that are delayed as a result of scattering (usually the overwhelming majority) form no coherent interference signal and are effectively rejected. As a result, OCT images show the pattern of minimally scattered photons that have been backscattered only a single time from microstructures in the focal zone of the lens at the tip of the fiber-optic probe.

[0008] The light source in OCT is a major determinant of the quality of the OCT images. Increasing the bandwidth of the light source results in higher resolution and decreased

speckling. Increasing the intensity of the light results in greater tissue penetration and improved signal strength relative to the background noise. The current generation of OCT engines from LightLab Imaging uses the output of SLDs with a wavelength centered at 1320 nm and a bandwidth of 35-45 nm. This corresponds to a coherence length of 10-15 microns ("dz" in Fig. 2) in tissue. The introduction of femto-second lasers in recent years has pushed the axial resolution of OCT down to 1-2 microns.

Diagnostic and therapeutic procedures which in the past suffered from imaging limitations

Epidural anesthesia

[0009] Epidural anesthesia is an intervention with high societal impact. It is often better to provide regional anesthesia rather than general anesthesia. Regional anesthesia can avoid a host of serious physiological perturbations associated with general anesthesia. Epidural is the most frequently used form of regional anesthesia. It is achieved by the placement of anesthetic solution within a local region of the spinal epidural space. This results in block of electrical signaling in spinal sensory and sympathetic nerves over a segmental region of the neural axis with relative sparing of motor fiber function.

[0010] In this country, 4.6 million babies are delivered each year. A majority of the birth mothers received epidural analgesia. Epidurals balance the need for analgesia with the desire to maintain full cognitive awareness and motor function. A comparable number of Americans receive epidurals for other surgical procedures each year. For example, drug infusion epidural catheters are routinely placed in the thoracic spine as an integral part of thoracic surgery to provide postoperative analgesia. Regional anesthesia may also permit lesser degree of general anesthesia, thereby decreasing its more serious potential complications. Aside from acute surgical pain management, analgesia from epidural drug infusion catheters has become an indispensable tool in the management of severe chronic pain. In cancer patients with painful metastasis to the ribs, regional block with a chronic epidural catheter is often better tolerated than generalized sedation by the patient. Thus, epidural anesthesia is one of the most frequently performed interventions in medicine that affect a spectrum of healthy and seriously ill Americans.

[0011] Epidurals are also routinely utilized in veterinary surgery. The need for image guidance in small animal veterinary medicine is perhaps greater than for humans. In the non-academic veterinary medicine setting epidurals are often performed by the surgeon rather than an anesthesiologist. There is considerable variability in the spine anatomy between different animals. And the dimensions of the epidural space are smaller for dogs and cats. Technology developed for epidurals in humans can be translated easily to veterinary medicine.

[0012] Complications can arise from uncertainties in the position of the epidural needle and catheter. Placement of epidural needles and catheters is essentially a 'blind' procedure that relies largely on tactile sensation and little if any visual guidance. In such blind procedures there will be a certain degree of additional uncertainty that contributes to potential complications. One set of complications arise from uncertainty in the position of the tip of the epidural needle relative to the dura and bone. Another set of complications arise from uncertainty in the position of the catheter tip relative to blood vessels, and pockets of loculated space.

[0013] A second major limitation of current epiduroscopy is the amount of fluid that needs to be injected to complete one procedure. Endoscopy is effective only if there is wide free space in front of the target. Since the epidural space is normally collapsed, injection of saline would open only transiently before collapsing again. When saline >150 to 200 cc are infused, serious complications such as retinal detachment can result. If there is an imaging method that depends less on large open space (i.e., OCT), procedures may be completed more carefully, and safely.

OCT evaluation of peritoneal nodularity

[0014] The peritoneum is an extremely valuable source of information about various gynecologic conditions affecting reproductive organs in both benign and neoplastic conditions. As examples, endometriosis is an epithelial disorder which features prominently in infertility, pelvic pain, and as a major source of repetitive surgical investigation and treatment. Current diagnostic methodologies include laparoscopy, but biopsies are often

compounded by inadequate sample due to overlying inflammatory tissue, degenerating hematomas, longstanding hemosiderin and other deposits, rather than the specific hemorrhagic/endometrial lesions of endometriosis. Especially when surface lesions are present on the Fallopian tubes, biopsy and definitive diagnosis are often precluded by the risk of damaging critical structures by the biopsy process.

[0015] Parallel issues accrue in the ongoing evaluation and treatment of advanced stages of ovarian cancer. Peritoneal nodules are not removed during ovarian cancer surgery, and their eradication is entrusted to post-operative chemotherapy. There is no imaging system available to monitor peritoneal nodules, which may account for up to 15% of overall tumor mass, and may be 100% of residual tumor following surgery. Repetitive laparoscopy carries significant morbidity, increases the risk of tumor spreading along the invasive tracks, and after repetitive surgeries becomes technically impossible. Even when nodules are visualized laparoscopically, differentiating active neoplastic lesions from inflammatory changes, burned out nodules, or old non-neoplastic peritoneal responses (e.g., remnants of previous endometriosis) is very difficult. Thus many gynecologic oncologists continue to rely on a combination of laparoscopic and open "second look" operations to determine cure rates and responses to secondary chemotherapy.

Luteal phase assessment of endometrium using OCT

[0016] Luteal phase deficiency involves premature senescence of the menstrual cycle, with inadequate preparation of the endometrium following ovulation. Because of rapid decay in ovarian production of hormones, there is inadequate build-up of nutritional uterine lining to support the initial phases of implantation and development of the primordial placenta. The diagnosis is based on the presence of irregular menses, repetitive early pregnancy wastage (spontaneous abortion before eight weeks), and otherwise negative infertility work-up. Diagnosis is by endometrial biopsy at approximately day 24 of the cycle, which typically will demonstrate very poor development of the luteal phase endometrium, inadequate nutritional storage to support implantation, and is followed shortly by spontaneous menses.

[0017] Current management includes repetitive recording of menstrual cycles, ovulation induction, hormone manipulation, and support of the early pregnancy with progesterone. This problem accounts for up to 10% of infertility investigations, and may be very difficult to diagnose if the patient does not ovulate regularly, or infrequently. Since the diagnosis is made primarily by endometrial biopsy (it correlates poorly with measured blood hormone levels), it is associated with the usual pitfalls of that technique – inadequate samples, tissue showing primarily necrosis and no apparent glandular/luteal structures, tissue of insufficient depth, traumatic sampling (including myometrium from sampling too deep). The technique is moderately invasive, causes cramping and bleeding, and is not suitable for repetition in the same menstrual cycle, hence evaluation may be required in several successive cycles.

Treatment of fetal cardiac outlet obstruction

[0018] Fetal cardiac outflow tract obstruction in the early phases of fetal development leads to irreversible changes usually associated with neonatal death. While the prototype of these abnormalities is critical aortic stenosis, which results in hypoplastic left heart (HLH) syndrome, the same would apply to the right side of the heart, in pulmonary stenosis. Developmentally, an inadequate caliber of aortic outflow results in progressive hypertrophy of the left ventricle with subsequent muscle failure, initial dilatation (reversible), damage and death of the myocardium, endocardial fibroelastosis, irreversible dilatation, accelerated EFE, and ultimately complete shrinkage of the ventricle, resulting in upstream damage to the mitral valve due to obstructed outflow, and eventually resulting in shrinkage of the left atrium as well.

[0019] The HLH syndrome requires urgent palliation (the ventricle is irreversibly damaged, so "treatment" is not possible). HLH after birth, is frequently associated with fetal and/or neonatal demise, and requires multiple surgical procedures for palliation, each of which carries its own risk of surgical death, or cerebral infarction due to complications of cardiopulmonary bypass during the operations. Because effective management, before the ventricle undergoes terminal scarification, is not available, many families choose pregnancy termination, and in many cases the surgical rescue which converts the heart into a single-

ventricle pump, is unsuccessful. While early diagnosis may be suspected as soon as 12-14 weeks, observation and definitive diagnosis of the full-blown HLH syndrome, usually takes an additional 6-10 weeks to be finalized. During this interval, a functional left ventricle is progressively damaged, leading to the near-futile consequences.

[0020] To date, a handful of attempts at intrauterine treatment have been made. A needle can be directed relatively easily under ultrasound guidance through the maternal abdomen, the uterus, membranes, and into the fetal chest, to reside within the left ventricular cavity. Visualization of the tiny aortic outflow opening, however, and passage of a balloon-tipped catheter, have proved very difficult. No direct visualization has previously been available, dye injection is not applicable to this situation, and ultrasound contrast media are not licensed for fetal use. Thus, although expertise in early diagnosis, expertise in fetal cardiac cannulation, and a high level of understanding about the disease process itself, all exist, the ultimate intrauterine surgical approach is thwarted by lack of visualization.

Diagnosis of fetal tumors

[0021] While some fetal tumors (such as cystic hygroma and sacrococcygeal teratomas) have characteristic ultrasound appearance in the mid-trimester, their early diagnosis is not so straightforward. First trimester ultrasound using intravaginal ultrasound placed only 1 or 2 mm from the fetus, is increasingly able to visualize fetal abnormalities. At this early stage, even these relatively classical types of fetal tumors may not appear in typical form. Even more likely, many of the types of fetal tumors do have diagnostic ultrasound characteristics and are not precisely diagnosed until after delivery. This delay may allow progression in the tumor resulting in a child incapable of survival (but destined to long suffering), or in a tumor that has complicated other adjacent structures, a tumor that may have been amenable to intrauterine management outgrowing potential therapy, and so on. Although these lesions are rare, definitive tissue diagnosis at the earliest possible time (and therefore meaning the least possible amount of invasion into the uterine cavity) would be a critically important advancement.

Placental evaluation associated with IUGR

[0022] Severe IUGR remains one of the greatest challenges of modern perinatal medicine. While genetic causes, fetal infection, and chromosome abnormalities all must be excluded diagnostically, the majority of cases of IUGR are due to placental failure. To understand the basis of IUGR evaluation, testing, and management, basic concepts of placentation are essential.

[0023] Schematically, human placentation takes place in three separate waves. During the first, implantation, the primordial placenta develops, there is surface erosion of the maternal (uterine) layers, and initial penetration of columns of placental cells into the superficial (decidual) circulation of the mother. This is completed in the first eight weeks of pregnancy. Over the next month, the second wave, of more differentiated cells, organized in columns, penetrates throughout the decidua (originally the endometrium), and establishes broadly-based contact between these columns of cells and free-flowing maternal vascular spaces. In the third phase of invasion, generally complete by 14-18 weeks, deep penetration through basal layers into the myometrium, up the courses of uterine vessels, and even to the extrauterine portions of the uterine circulation, establishes the true extent of placentation. Under normal circumstances, this third wave of invasion turns maternal arterial structures into high-capacitance vessels with virtually no tone, directly comparable to veins. Muscle is removed, reactivity is lost, there is no vascular tone remaining in these thin-walled wide-open vessels. Thus, the placental bed receives provision through a pressure-passive, unregulated continuous blood supply.

[0024] Failure of this process, the placental failure which results in IUGR by malnutrition, starts early with deficiencies in the second wave, and very poor invasion during the third wave, of placentation. In other words, the basis for IUGR is well established by mid-trimester. However, the fetus is usually able to grow normally and develop normally, during this gestational time – placental limitations will not have a profound effect until the demands of the fetus exceed supplies, usually as the third trimester begins. Clinically, there is significant delay between poor invasion of the placenta, and the ultimate impacts on fetal function.

[0025] These impacts follow a predictable course. First is the sacrifice in growth of non-essential organs, with preservation of central functions such as cardiac and cerebral growth and development – disproportion between head and somatic growth becomes apparent. Secondly, sacrifices are made in oxygen utilization, and metabolic priorities are established which include increased use of anaerobic metabolism, lack of nutrient storage, and biochemical evidence of malnutrition. During this phase, there is extensive cardiovascular redistribution, and apparent imprinting of the uterine condition, producing life-long impact on the individual. As fetal compromise becomes more extensive, central impairment, including heart failure, abnormal brain perfusion, and reduction of basic energy expenses such as fetal movement, are forced upon the fetus. By this stage, permanent hypoxemic and acidemic injury become significant risks.

[0026] Antenatal monitoring is designed to detect this cascade of compromises and injuries at early stages. Doppler ultrasound can demonstrate failure of the vascular changes associated with normal placentation, as early as 22-24 weeks, and fetal biometric changes, functional compromises, and behavior compensations, become apparent over the next 4-6 weeks. In the most severe cases of IUGR, this course is even more truncated, with urgent delivery for life-threatening decompensation, being required as early as 25-26 weeks. At this point, the overlay between severe IUGR and severe prematurity, becomes important. Management issues stem from the relative risk of death or damage from the consequences of pre-term delivery, contrasted with different risks for death or damage in the hostile intrauterine environment. Clearly, by the time this situation is apparent, it is far too late to impact upon placental development and function.

[0027] This lag between placental failure and the fetal consequences, means earlier detection is essential.

Monitoring of HRT with OCT

[0028] Approximately two million American women per year enter their sixth decade. For each one of them the choices for treatment of menopausal symptoms are complicated and often contradictory. Hormone replacement therapy (HRT) is a double-edged sword, carrying

therapeutic benefits and very potential negative effects. Suppression of vasomotor symptoms, maintenance of normal bone metabolism, normal cardiovascular status, normal sexual function, many cosmetic and body-image issues, and many other every day functions become critical issues successfully addressed by HRT. On the other hand, concern about aggravation of breast cancer risk, thromboembolic disease, endometrial cancer, ovarian cancer, and so on, are clear drawbacks.

[0029] Much effort is currently being focused on the monitoring, early diagnosis, and management of problems in various organ systems (e.g. yearly mammography, serial screening of coagulation factors, stress EKGs, smoking cessation), but the endometrium remains largely occult. Women on HRT have pseudo-menses at a variable interval, and the dysfunctional bleeding which results in clinical presentation may be related to undertreatment (atrophic endometrium, simply needing a small increase in hormones) or endometrial atypia (surface abnormalities, potentially progressive to endometrial cancer, requiring definitive tissue diagnosis and appropriate therapy). Clinically, the two are virtually indistinguishable.

[0030] Further, when endometrial cancer is discovered, it is much after the fact, as there is currently no reliable advanced screening method. While abnormal endometrial cells occasionally appear on Pap smears (done primarily for evaluation of cervical atypia, but sometimes containing cells from inside the uterus), the large majority of patients present with abnormal uterine bleeding. Their evaluation includes detailed physical examination, and endometrial sampling. This can be by endometrial biopsy, using a variety of instruments, usually as an outpatient/office procedure, but often requiring follow-up with outpatient/hospital formal Dilatation and Curettage (D&C). While a D&C is usually an outpatient procedure, for women with significant other health problems, it may necessitate hospitalization, multiple consultations, and pose a significant additional health risk. An easy, widely-available, reproducible method of evaluating the endometrium without causing morbidity would be ideal for all women receiving HRT, especially those with bleeding.

[0031] Therefore, in view of the aforementioned deficiencies attendant with prior art methods of imaging and diagnosing gynecological and obstetrical conditions, as well as

imaging and diagnosis of spinal conditions and procedures, it should be apparent that there still exists a need in the art for improved imaging methods which allow for earlier detection of conditions or abnormalities, as well as improved imaging for placement purposes in surgical and anesthesiological procedures.

SUMMARY OF THE INVENTION

[0032] An object of the present invention is to provide a catheter-based optical coherence tomography probe, including:

an assembly including:

a single mode optical fiber having a tip, the optical fiber emitting light;

a gradient index lens attached to the tip of the optical fiber; and

a first body attached to the gradient index lens, the first body being transparent to the light emitted by the optical fiber and having a first mirrored surface oriented to divert light passing through the gradient index lens in a radial scanning direction; and

wherein the assembly has a longitudinal axis and is rotatable over 360° about the longitudinal axis;

a housing containing the assembly and having a tip through which light is passed; and

a second mirrored surface oriented relative to the longitudinal axis of the assembly to reflect light diverted by the first mirrored surface in a forward-scanning direction over a portion of the 360° rotation of the assembly about the longitudinal axis.

[0033] In preferred embodiments, the second mirrored surface of the optical coherence tomography probe includes a single flat surface oriented at an angle of from about 40° to about 50°, preferably about 45° relative to the longitudinal axis of the assembly.

[0034] In another preferred embodiment, the second mirror surface of the optical coherence tomography is substantially flat and made of a metallic or dielectric material.

[0035] In another embodiment, the second mirrored surface is on a second body, the second body comprises an end face and the second mirrored surface is at the end face. A portion of the housing may be disposed within the second body.

[0036] In another embodiment, the housing may include the second mirrored surface. The second mirrored surface may include at least two facets oriented at different angles relative to the longitudinal axis of the assembly. The facets may be oriented at an angle of from about 25° to about 65° relative to the longitudinal axis of the assembly. The second mirrored surface may be curved and oriented at an angle of from about 25° to about 65° relative to the longitudinal axis of the assembly.

[0037] In still another embodiment, the OCT probe may further include a light transparent material covering the second mirrored surface. The light transparent material (i) may be secured to the second mirrored surface, or (ii) contain the second mirrored surface.

[0038] In yet another embodiment, the first body is a prism or a mirror. The optical fiber may also be movable relative to the housing along the longitudinal axis of the assembly to adjust a portion of the light that is directed in the forward-scanning direction during rotation of the assembly.

[0039] In one embodment, the radial scanning direction lies in a first plane substantially perpendicular to the longitudinal axis of the assembly, and the forward-scanning direction lies in a second plane extending forwardly of the tip of the housing.

[0040] In another embodiment, the second mirrored surface is (i) curved or (ii) includes at least two facets oriented at different angles relative to the longitudinal axis of the assembly, and the optical fiber is movable relative to the housing along the longitudinal axis to adjust the forward-scanning direction of the light during rotation of the assembly.

[0041] In another embodiment, the housing has a maximum dimension perpendicular to the longitudinal axis of from about 100 microns to about 1000 microns, preferably about 400 microns.

[0042] In another embodiment, the light has a wavelength of from about 0.4 microns to about 2.1 microns.

[0043] Another object of the invention is to provide a method for performing epidural regional analgesia, including inserting into the spinal epidural space of an animal an epidural needle comprising (a) a tip, wherein the tip comprises a beveled opening, and (b) an optical coherence tomography (OCT) probe.

[0044] In one embodiment, the needle further includes a perfusion catheter. The OCT probe may be positioned at the opening of the needle, and may generate a forward-scanning imaging beam, which exits unimpeded from the beveled opening. The OCT probe is preferably not allowed to advance beyond the bevel of the needle.

[0045] In another embodiment, the perfusion catheter is positioned within the epidural needle so as to pass saline through the needle creating pressure, such that resistance to the pressure can be monitored as the needle is advanced towards the epidural space. The needle is then pushed into the intervertebral space and the ligamentum flavum. Positive pressure may be applied to the perfusion catheter, such that entrance of the needle into the epidural space is indicated by a loss of resistance applied through the perfusion catheter. Entrance of the needle into the epidural space may also indicated by identification of structural landmarks by OCT imaging.

[0046] In another embodiment, the position of the needle tip is determined by its relative position to the dura, spinal cord, and epidural fat which are recognize by the OCT imaging.

[0047] Another object of the invention is to provide a method for performing epidural regional analgesia, including inserting into the spinal epidural space of an animal a drug infusion catheter comprising a front tip, an inner lumen and an optical coherence tomography (OCT) probe comprising a tip.

[0048] In one embodiment, the OCT probe generates a forward-scanning imaging beam. The tip of the OCT probe may be positioned slightly forward of the front tip of the drug infusion catheter so as to allow the scanning beam to clear the catheter tip.

[0049] In another embodiment, the OCT probe is a conventional radial-scanning OCT probe or a probe capable of forward- and radial-scanning.

[0050] In another embodiment, the inner lumen of the drug infusion catheter is slightly larger than an outer dimension of the OCT probe, so as to allow saline and drugs to pass through the catheter with the OCT probe positioned within the catheter. As the drug infusion catheter is advanced, OCT imaging may be used to monitor the position of the catheter relative to blood vessels, and its relative position within the epidural space.

[0051] Another object of the invention is to provide a method for performing high resolution diagnostic imaging of the spinal epidural space of an animal, including inserting into the spinal epidural space of said animal a forward- and radial-scanning OCT probe. The imaging may detect abnormalies such as small herniated disc fragments. The OCT probe may also be advanced within the epidural space towards a suspected site of nerve impingement, such as the neural foramen.

[0052] Another object of the invention is to provide a method for performing high resolution imaging of dural tears, including inserting a radial scanning OCT probe in the epidural space of an animal, parallel to the dural sac.

[0053] Another object of the invention is to provide a method for performing epiduroscopy, including inserting into the spinal epidural space of an animal an epiduroscopy instrument, wherein the epiduroscopy instrument includes an OCT probe, and releasing adhesions in the epidural space that are compressing nerve roots.

[0054] Yet another object of the invention is to provide a method for performing real-time, high resolution intrathecal imaging, including inserting into the intrathecal space of an animal an OCT probe to identify abnormal tissue, such as cancer cells.

[0055] The present invention also relates to the use of OCT to achieve resolution that is two orders of magnitude higher than that of CT and MRI.

[0056] Other objects and advantages will become apparent to those skilled in the art from a review of the ensuing description which proceeds with reference to the following illustrative drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

[0057] Fig. 1 is an OCT image of the epidural space from a real-time OCT video sequence as the OCT probe was advanced within the lumbar epidural space of a lamb *ex vivo*. The OCT probe is displayed as the circle near the middle of the image.

[0058] Fig. 2 is a schematic of the OCT principle. From J. Fujimoto, 2002.

[0059] Fig. 3 shows a probe of an OCT system in the sub-arachnoid space.

[0060] Fig. 4 shows a probe in the cauda equina.

[0061] Fig. 5 shows a probe next to the annulus fibrosus.

[0062] Fig. 6 shows a probe next to the ligamentum flavum in the human thoracic spine.

[0063] Fig. 7 shows a small sub-arachonoid arteriole in a human cadaver.

[0064] Fig. 8 shows structures surrounding the epidural space.

[0065] Fig. 9 shows the position and shape of the ligamentum flavum (from Brown, 1994).

[0066] Fig. 10 shows two designs and a stylet that fits inside the hollow needle. The front opening is oriented toward the side to allow easy penetration through the tough ligamentum flavum and then to allow the introduction of the drug infusing catheter. The far left pane shows the side view of the needle. The middle panel shows an oblique view. And the far right panel shows the catheter exiting the needle.

[0067] Fig. 11 depicts insertion of an epidural needle.

[0068] Fig. 12 shows proper position of the epidural needle.

[0069] Fig. 13 depicts dural puncture.

[0070] Fig. 14 shows an epiduroscopy catheter tip.

[0071] Fig. 15 shows an image obtainable from epiduroscopy; with a nerve root located at 4-5 O'clock; epidural fat located toward 9 O'clock; and bands of adhesions pointing to 12 O'clock and 6 O'clock.

[0072] Fig. 16 illustrates an enlarged top view of a vibrating spring OCT stylet.

[0073] Fig. 17 illustrates optical behavior of a GRIN (gradient index) lens to a scanning fiber.

[0074] Fig. 18 shows a spot diagram.

[0075] Fig. 19 illustrates optical behavior for an oscillating lens.

[0076] Fig. 20 illustrates a side view of an OCT stylet within an epidural needle.

[0077] Fig. 21 illustrates a front end view of an OCT stylet.

[0078] Fig. 22 depicts an electromagnet design.

[0079] Fig. 23 is a schematic of an OCT system.

[0080] Fig. 24 depicts the forward-scanning mode of the probe.

[0081] Fig. 25 depicts the side scanning retracted mode of the probe.

[0082] Fig. 26 depicts aberration free, flat, forward-scanning of a rotating fiber rotating scanner.

[0083] Fig. 27 is a side view of the forward scanner shown in Fig. 26.

[0084] Fig. 28 illustrates an OCT modified epiduroscopy catheter.

[0085] Figs. 29A-D show images taken from the first OCT video clip sequence of a mammalian spine *in vivo*.

[0086] Fig. 30 illustrates plaque characterization; *in vitro* studies.

[0087] Figs. 31 and 32 depict an embodiment of an OCT probe useful in the spinal epidural space. A flat annular shaped reflective surface is oriented at a 45° angle to the axis of the spinning grin lens/mirror assembly. Within one sector of its 360° rotation, the beam is reflected forward by the front tip of the inclined mirrored surface (schematics below). Over the rest of the rotation the probe operates in its normal radial scanning mode. By moving the spinning optical fiber/grin lens assembly forward, the relative amount of scanning dedicated to forward versus side scanning can be adjusted. If advanced forward enough, a full radial

scan is performed. Also note that the forward scan is linear (rays remain within a single plane) allowing for easier visual interpretation. Fig. 32 shows an embodiment of the reflective surface.

[0088] Figs. 33A, B are three-dimensional volume views of the design. When the mirror intercepts the beam A, it is in its forward sector-scanning mode. When the beam bypasses the mirror B it is in the radial scanning mode.

[0089] Fig. 34 is an exemplary embodiment of the catheter-based optical coherence tomography probe 50 showing light in a first, forward-scanning direction.

[0090] Fig. 35 is an exemplary embodiment of the catheter-based optical coherence tomography probe 50 showing light in a second, forward-scanning direction.

[0091] Fig. 36 is an exemplary embodiment of the catheter-based optical coherence tomography probe 50 showing light in a third, forward-scanning direction.

[0092] Fig. 37 shows another exemplary embodiment of the OCT probe.

DETAILED DESCRIPTION

[0093] Prior art methods of *in vivo* imaging, including gynecological and obstetrical conditions, had the drawbacks of poor resolution and the inability to diagnose abnormalities at an early stage. While each imaging modality has its unique strengths and limitations that determine its clinical niche, the advantages of OCT are numerous, including, high axial resolution, real-time imaging capability, compact size of the imaging probes, and relatively low cost. Moreover, OCT is not known to have been described for epidural applications.

[0094] To better understand the origin of complications in providing epidermal anesthesia, it is best to briefly review the anatomy of the epidural space and current procedures.

[0095] The inner border of the epidural space is the dural sac. Its outer border consists of the ligamentum flavum posteriorly, the lamina laterally, and the posterior longitudinal ligament anteriorly. The ligamentum flavum is the structure that the epidural needle goes through immediately prior to entering the epidural space. As the needle is advanced through this tough tissue, the anesthesiologist will feel a distinctive tactile change which provides the

most critical clue to the position of the epidural needle. The ligamentum flavum is composed of two leaves that meet in the midline at 90 degrees to form a tent-like roof (see Figs. 6 and 9). This characteristic shape can be a useful landmark for OCT guidance. The distance between the ligamentum flavum and the dura varies considerably. It is widest at the mid lumber level and is narrowest at the cervical level. Thus, lumbar epidurals are most forgiving in terms of avoiding unintended dural puncture.

[0096] The principal tissues within the epidural space are loose epidural fat and an extensive plexus of veins. The fat tissue and the venous plexus are not tightly adhered to either the dura or the outer boundary of this space. Thus, when saline or air are infused into this space for procedures such as epiduroscopy, tissue are pushed apart and an open space can be transiently created. Passing through this space are the spinal nerve roots that exit the spinal canal via the neural foramens. Herniated discs press on the nerve roots in this space to produce low back pain and sciatica. Epidural anesthesia is achieved by blocking action potential propagation in this segment of the nerve roots that passes through the epidural space. In the lumbar region the epidural venous plexus is called Batson's plexus. It is through this plexus of valve-less veins that the vast majority of metastases from prostate cancer passes to seed adjacent structures and spread systemically. During pregnancy, this venous plexus within the epidural space can become markedly dilated increasing the likelihood of vascular complications during epidural catheter placement.

[0097] Special needles are used for epidurals. The upper panel of Fig. 10 shows two common designs and a stylet that fits inside the hollow needle. The front opening is oriented toward the side to allow easy penetration through the tough ligamentum flavum and then to allow the introduction of the drug infusing catheter. The far left panel shows the side view of the needle. The middle panel shows an oblique view. The far right panel shows the catheter exiting the needle.

[0098] The most common method for needle placement is the 'loss of resistance' method. A water or air filled syringe is attached to the hub of the epidural needle. The needle and syringe are advanced with positive pressure being applied to the syringe (see Figs. 11 and

12). The anesthesiologist carefully pays attention to detect two critical events, a distinctive pop as the needle breaks through the tough ligamentum flavum and a sudden drop in resistance in the pressure applied through the syringe. In experienced hands and when carried out in young patients with normal anatomy there should be negligible complications (<2%).

[0099] If the patient is obese, it can be hard to gauge whether the needle has been advanced far enough to have gone through the ligamentum flavum. There are also tissue planes other than the epidural space that can also give rise to a "loss of resistance" in syringe pressure. Consequently, attempts to pass the catheter will be frustrating for the physician and anxiety provoking for the patient. In obese patients and in patients with spine deformities, the needle may fail to enter the window between the vertebrae and end up impaling and scrapping the sensitive periostium of the lamina. This frequent complication can be a very painful experience for the patient. Many obstetrical patients blame (probably erroneously) this complication for persistent low back pain which occurs with frequency up to 20-30%.

[00100] The more serious complication associated with needle placement is unintentional dural puncture. See Fig. 13. Multiple circumstances contribute to this complication. The physician may fail to detect the 'pop' associated with breaking through the ligamentum flavum. The patient may be agitated and moving at the wrong time. And the needle may not be aligned near the midline. The ligamentum flavum is thinner more laterally. In addition, the epidural needle may become plugged as it is advanced thereby eliminating the 'loss of resistance' in syringe pressure. If the physician is unaware of the dural puncture, anesthetics may be applied to the subarachnoid space resulting in motor paralysis that makes labor difficult. Epidural doses of anesthetic in the subarachoid space may also make it difficult to treat hypotension due to complete autonomic nervous system depression. Even if the physician becomes aware of the dural puncture (i.e., upon withdrawal of curbio-spinal fluid (CSF) through the needle), the patient may still develop a spinal headache due to persistent leakage of CSF. Unlike the thin spinal needle, the larger epidural needle can leave a much larger tear. The mothers are generally very upset because they will not be able to take care of

their newborn for a period of time that may last days to weeks. The rate of dural puncture in academic medical centers is 2-3% (Brown, 1994). When epidurals are performed in the thoracic and cervical level where the epidural space is thinner or when performed in patients with asymptomatic spinal stenosis, the incidence of dural puncture may be higher.

[00101] These complications may be minimized if the anesthesiologist can visualize in real time the position of the needle tip relative to the bone and dura. The physician will still rely on tactile information from his/her finger tips to provide an indispensable piece of positional information. The present methods of using OCT to obtain visual information will help minimize the uncertainties, especially in the difficult patient and less experienced physicians. Such an image-guidance system is especially useful for the training of young doctors or where health care manpower is scarce.

[00102] There are a number of reasons why OCT is ideally and uniquely suited for imaging needs in the abdominal, pelvic and particularly the epidural space.

[00103] OCT has the resolution to detect and identify the fine structures in the epidural space that cannot be detected by any other clinical imaging technology. The OCT probe is small enough to pass through an epidural needle or the middle of a epidural drug infusion catheter. Imaging can be in real-time. And a depth-of-field of several millimeters is adequate for most procedures within the epidural space.

[00104] OCT is also particularly well suited for detecting small irregularities located on thin smooth membranes. Combined with ultrasound guidance, OCT provides the sensitivity and resolution to identify pathological seeding on the peritoneum and other tissue surfaces. It may be used to guidance for tissue biopsy. As an intraoperative adjunct to laparoscopy, precise biopsy techniques are directed by OCT, to avoid pitfalls of inadequate sampling, and enhance the ability of laparoscopy to deal with such follow-up examinations, to the exclusion of open laparotomy.

[00105] OCT can also be used for the precise identification of the cycle stage of the endometrium using non-biopsy methods, including tissue thickness, reflectance characteristics, cell density (endometrium accumulates glycogen as the cycle progresses).

OCT can be used for virtually daily evaluation of the endometrium all in the same cycle, allowing the diagnosis to be made immediately, and facilitating biopsy as indicated. Abnormalities of the uterine cavity, which may predispose to repetitive early pregnancy loss, are also diagnosed during this examination.

[00106] OCT can be used for the correlation between abnormal development and ultimate placental failure. OCT can also be used to visualize the visible characteristics of villous tissue, which can provide a key for early detection, and a platform for successful intervention. Minimally invasive techniques to image early invasive villi, to define their extent and depth of penetration, and to define their relationship with the maternal microvasculature, none of which are possible with current imaging techniques, are realistically possible with OCT. These relationships, which define the essence of placentation, offer a genuine opportunity to influence the course of IUGR.

[00107] Some of the advantages of the present invention include reduced frequency of open laparotomy, improved biopsy accuracy, fewer total biopsies, shorter operating times, and reduced anesthetic and recovery requirements.

[00108] OCT allows certain structures to be recognized by their characteristic optical signatures. For example, epidural fat (see Fig. 4) has a speckled appearance of varying intensity. This is presumably due to the back scattering properties of round globules of fat. The annulus fibrosus that surround the nucleus pulposus of the intervetebral disc can be recognized by its coarse linear striations separated slightly from each other. Often they may take on a weaved straw basket appearance with thick bundles that are oriented at slightly different angle. The spinal cord has a very smooth homogenous texture that is best appreciated when it is close to the OCT probe (where the transverse resolution is best) (Fig. 3). The periostium of bone tends to have more of a 'glare' than surrounding tissue, presumably because of its high reflectivity (Fig. 1).

[00109] Other structures can be identified by their size, shape, and relative position. For example, the dura has a homogenous, dull appearance. It has smooth edges and uniform thickness (Figs. 1 and 3). The arachnoid is a thinner membrane that is located on the cord

side of the dura (Fig. 3). The pia mater can also be identified directly on the surface of the spinal cord in Figure 3. Fig. 4 illustrates the appearance of the bundle of nerve roots in the cauda equina. Ligamentum flavum is the tough fibrous tissue that forms the posterior roof of the epidural space. Its light scattering properties are similar to the dura, but it can be identified because it forms the tent-shaped roof at the posterior midline of the spinal canal (Fig. 6). Figs. 6 and 7 were obtained from the thoracic spine of a human cadaver. The OCT probe that was used in these two images had a lower NA than the probes used to obtain the other images. This results in poorer transverse resolution but better depth of field.

[00110] In *ex vivo* and post-mortem tissue small arterioles can be more easily identified than veins. This is probably because the thin-walled veins are expected to be collapsed when blood is removed. Figures 3 and 7 illustrate examples of small arterioles devoid of blood. The thick wall prevents them from collapsing.

[00111] Identification of structures is easier during real-time OCT imaging because the structures move to fluid injection and because one can appreciate the three dimensional context of continuous structures as the probe is slowly moved. For example, one can follow the path of a blood vessel or nerve root over a considerable distance.

[00112] Once the needle is in the epidural space, a stylet is used to clear the needle of debris and the drug infusion catheter is threaded through the needle. The catheter is advanced past the tip for a couple of inches. Negative pressure is applied via a syringe to make sure blood or CSF does not return. Significant blood return would indicate cannulation of the venous plexus. CSF return would indicate entrance into the subarachoid space. The most common and serious complication associated with epidurals are tied to the blind placement of the drug infusion catheter.

[00113] In pregnancy there is a massive dilatation of the venous plexus in the lumbar epidural space. This is due in part to the overall increase in blood volume and in part due to pressure on the inferior vena cava from increased abdominal pressure. Thus, the reported incidence of laceration of venous plexus during catheter placement is 18% (Verniquet, 1980). The reported incidence of aspirated blood from the catheter, indicating venous cannulation, is

10% (McBeill and Thorburn, 1988). When blood is aspirated, the catheter is repositioned. But it is possible for a tissue flap to be placed against the catheter opening acting as an one-way valve causing a false negative response. With the use of side port catheters, the catheter tip may be within a vein but the side ports can be initially outside the vein. Over time, the catheter can migrate further into the vein. If significant anesthetic were to be infused into the venous system, the mother would develop local anesthetic toxicity such as serious convulsions (Dunne and Kox, 1991). In such cases the child would most likely die or develop permanent handicaps. This complication is the single most common cause of major malpractice suits against obstetrical anesthesiologists (Sorely, 2000).

[00114] The anesthesiologist has some, but not complete, control over this situation. First, since the venous plexus is most dense toward the lateral aspect of the epidural space, by keeping the catheter close to the midline and by avoiding the distance the catheter is advanced, it is possible to decrease venous cannulation at a minimum. The anesthesiologist can also limit the rate and amount of anesthetic at a minimum. Despite these precautions, this remains a serious current unsolved problem for epidural anesthesia. It is a problem which is solved by catheter-based OCT.

[00115] Another common problem with epidurals is incomplete or asymmetric analgesia (Webb and Kantor, 1992). This occurs when the tip of the catheter is trapped in a loculated pocket. An example in a human cadaver is shown in Fig. 6. It can also occur if the catheter tip is wedged in the lateral recess resulting in hemi-anesthesia which does not serve the patient well in surgery. Currently, the solution is to increase the amount of anesthetic that is infused which lead to its own set of problems. OCT imaging easily solves this problem as well.

[00116] Chronic low back pain is one of the most common ailments in modern medicine. Lumbar discectomy is the surgery performed to remove herniated lumbar disc causing painful radiculopathy and sciatica. Lumbar discectomy is, in fact, the most common neurosurgical procedure in the US with nearly 300,000 procedures performed each year (Koebbe et al, 2002). The financial burden of this problem on society exceeds $50 billion

annually. Contributing to this burden is the high frequency of the 'failed back syndrome' in which pain persists or worsens after surgery. Estimations show that 5% to 40% of lumbar surgies results in this syndrome (Fritsch et al., 1996; Manchikanti and Singh, 2002). Post-operative adhesion/fibrosis is increasingly recognized as an important contributor to this worsening pain, especially in those patients without spine instability or retained herniated disc fragments. Postsurgical adhesions can form tight bands that compress nerve roots. These fibrosis bands progressively tighten over time. One high estimate has epidural fibrosis being responsible for as much as 25% of all 'failed back' syndrome (Gasinski et al., 2000). The true incidence of symptomatic epidural fibrosis is difficult to establish because fibrosis develops in every patient to varying extent. The only means to establish the incidence of symptomatic fibrosis is if its removal relieves the pain. Open surgery for fibrolysis is frowned on by surgeons because of increased risk of dural tear in scarred tissue and because it may induce further fibrosis. The alternative is to use blunt dissection during epiduroscopy. Current epiduroscopy procedures have serious limitations (to be discussed in the following paragraphs). Nevertheless, a significant fraction of patients who have undergone fibrolysis by epiduroscopy report immediate pain relief. Because current limitations of epiduroscopy can be solved with OCT, the true frequency of symptomatic epidural fibrosis may be determined and chronic pain may be relieved for large number of patients.

[00117] Epiduroscopy is endoscopy within the spinal epidural space. In one commercially available device (Myelotec), there is a 3 mm diameter flexible catheter that can be introduced through the caudal approach. This catheter has two ports, each with a 1.3 mm opening. One port is used for a endoscope connected to a video camera. The other port can either be used for fluid perfusion or a thin surgical instrument. The fluid infusion port is used to open up the normally collapsed epidural space. It is also used to determine whether tissue is mobile or fixed. The catheter can be rotated and steered from the outside. A catheter tip is shown in Fig. 14.

[00118] Currently, the use of epiduroscopy to treat postsurgical adhesions faces two serious limitations. The video endoscopic images provide insufficient information to identify

structure with high degree of confidence. See Fig. 15. The fundamental problem is that endoscopic images provide a surface or 'en face' view only. Color and real-time images of the mobility of structure are of considerable help. But distinguishing tough thick adhesions from nerve roots and dura can still be difficult. Thus, cutting instruments are avoided in epiduroscopy to avoid catastrophic complications. Fibrolysis is accomplished solely by blunt dissection with the tip of the catheter. Thus, tough adhesions that press tightly around nerve roots can not be released. These are the lesions that are expected to cause the greatest problems. Because surface imaging can be complemented by high resolution tomographic imaging, tissue identification will be greatly improved. For example, OCT imaging of dura, fat, periostium, annulus fibrosis, and blood vessels have unique optical signatures that are independent of their surface appearances. Combining these two sets of information greatly improves tissue identification. It is possible to introduce finer instruments to more effectively release troublesome adhesion while improving safety.

[00119] In order to maximize the efficiency of an imaging technology *in vivo,* one preferably seeks to have both adequate resolution and maximum contrast. Molecular contrast provided by OCT can be enhanced using pump-probe techniques. Metallic nanoshells are also useful as OCT contrast agents (Drezek, West, Halas, in press).

Epidural regional analgesia

[00120] The present invention solves many of the insufficiencies associated with prior art methods of imaging. In one embodiment of the invention, a thin forward-scanning OCT probe/needle is provided. Such a probe is useful for a number of procedure-oriented applications such as imaged-guided biopsies and precise placement of instrument and hardware in the body.

[00121] Fujimoto et al. had developed a handheld forward-scanning probe using a piezoelectric cantilever strategy (Boppart et al., 1997). Another design used a galvanometer strategy in conjunction with a Hopkins lens relay (Li et al., 1999). The smallest forward-scanning probe was a Russian designed endoscopic microprobe (Sergeev et al., 1997).

However, none of these probes were small enough to be fit within a needle or catheter. The major contributing factor to the large size of current forward-scanning probes is that the actuator for the scanning movement (i.e., piezoelectric material or galvanometer) is placed within the probe shaft. If the actuator for generating the scanning movement is located not within the shaft of the probe, but the movement is propagated to the front of the probe, one can produce thinner probes.

[00122] Two preferred embodiments of the present invention which solve the problem associated with probe size are the"vibrating spring fixed GRIN lens" and the "oscillating lens microfluidics". In both cases, the OCT probe is built in the dimensions of the stylet that normally fits within the epidural needle. This allows one to continue to use current disposable epidural needles. Also, if the operator does not feel comfortable with the imaged guided procedure, he/she can simply remove the OCT insert and proceed with current procedures without any hassles.

[00123] "Vibrating spring" strategy Referring to Fig. 16, the optical fiber is fixed to a thin flexure spring made of stainless steel. By choosing a thin plate shape, it is possible to limit the vibration to a single plane. This spring/fiber assembly is placed within a thin-walled hollow tube. In a preferred embodiment, the tube is 1.3 mm o.d. (dimensions stylet for a thin-walled 16 Gauge epidural needle). In a preferred embodiment, the tube is~120 mm in length.

[00124] The fiber/spring assembly is fixed at 2 or more points in positions to allow for the establishment of a standing wave at a harmonic frequency preferably of about ~20 Hz. The swinging scanning end of the fiber is placed slightly behind a GRIN lens. A electromagnetic device is used to drive the oscillation. When inserted into the needle, the electromagnet is located proximal to the hub of the needle. A special property of a GRIN lens enables it to carry out sector scanning with a tapered front.

[00125] GRIN (gradient index) lens are particularly well suited for this application. In Fig. 17, the optical behavior of a GRIN lens made from NSG's SLW 1.0 GRIN material was modeled for a scanning fiber single element design. Note that as the end of the fiber is used

to scan different positions, the beam for each respective position exits the front of the lens in the same small region at the center. This is ideally suited for forward-scanning needle probes because a tapered front lens can then be used. For a lateral movement of 0.45 mm the beam is steered by 19 degrees. The spot diagram for the three positions shown in Fig. 18 illustrates that there are few noticeable aberrations. Stronger GRIN material allows for greater scan angles using a thinner lens. It is preferable to achieve the same degree of scanning with a lens <1 mm in diameter.

[00126] In another preferred embodiment, a microfluidics-driven oscillating lens is provided. Lateral movement of a small lens in front of a stationary fiber can also implement forward sector scanning. Lateral movement may be driven by a microliter-volume of fluid through thin fused silica tubing (PolyMicroTechnology). This design has the advantage that it can be completely free of electrical power and free of metallic components. This can have some advantage for patient safety and MRI compatibility issues. Microfluidics is generally more robust than mechanical designs with moving parts. The moving lens is confined to a fluid filled micro chamber. One embodiment of this strategy is to use a small air bubble (< 1 mm) to deflect the beam. Surface tension at these small dimensions is a powerful force that maintains a well behaved shape. Low frequency sound waves (i.e., 10-20 Hz) are generally sufficient to drive the air bubble.

[00127] In both of the above strategies, a syringe can no longer be attached to the hub of the epidural needle to monitor the "loss of resistance". To retain the useful "loss of resistance" cue, an automated pressure/impedence monitoring system is preferably built into the stylet. A thin tubing is placed on the bottom of the OCT stylet, below the vibration plane of the vibrating fiber (see Figs. 20 and 21). The lower section of the GRIN lens is removed since the scanning beam does not pass through this region. A hole is also created through the GRIN lens to allow the tubing to pass through it and then sealed. In this way it is still possible to monitor the "loss of resistance". An additional improvement of this design is that it will be less likely for hard tissue to become forcibly wedged into the epidural needle as is the case with current open needles.

[00128] The tubing is connected to a pressure/impedance transducer whose readings are displayed, for example, as an analogue signal on a portable 4 x 4 inch LCD monitor on which the OCT image is also be displayed. Sudden drops in impedance indicating the "loss of resistance" as the needle breaks through the ligamentum flavum triggers a warning light. An automated impedance detection capability frees up the hand that previously was required to apply pressure to the syringe. This makes it easier to hold, stabilize, and advance the epidural needle, especially in an agitated patient. The height of the clear aperture at the front of the GRIN lens is designed to be at least twice the size of the beam diameter. Its width is determined by the width of the needle bevel. As is shown in Fig. 17, the scanning beam does not change its exit position.

[00129] In an exemplary embodiment, a permanent magnet (e.g., a NdFeB permanent magnet) is preferably mounted in the middle of a non-magnetic flexure (410 series stainless steel, heat treated to spring temper). A moving magnet, preferably about one-gram, is mounted in the middle of a 10 cm span is made to resonate over a distance of 0.25 – 1 mm, and most preferably about 0.5 mm, at 1-30 Hz, and most preferably 10 to 30 Hz, about 250 mV, and about 200 milliamp applied to the pair of coils. At resonant frequency, the power required to sustain the vibration is small. The minimum required voltage and current are empirically determined.

[00130] The magnet structure is composed of a 3 mm outer diameter magnet with poles at either end. It is magnetized axially (marked "N" and "S" in Fig. 22). The poles are used to focus the flux so that it radiates out through the coil and into the shell. The magnet moves concentrically within a stationary shell, preferably about 8 mm, and the two excitation coils. The proposed reaction mass is symmetrically positioned on the flexure to take full advantage of the aligning influence of the two coil system and alignment/tuning springs at either end of the magnet structure to most efficiently confine the motion along one direction. The springs also provide design stroke limits. Small holes are made in the shell to allow for the movement of the flexure. Redundant steps are taken to insure electrical isolation to the

epidural needle. The focus is on the coils. A non-metallic thin-walled tubing can also be used (Fig. 22).

[00131] A schematic of an OCT system is illustrated in Fig. 23. The OCT light source is located within the engine. A single-mode optical fiber is used to transmit the broadband light from the engine to and from a scan head. Electrical connections transmit power and control information between the OCT system components. The system can include two galvanometer-driven scan mirrors. Preferably, the needle probe uses only one galvanometer. The galvanometer has a feedback circuit that facilitates precise positioning. The MIU (microscope interface unit) controls the galvanometer with a digitally-synthesized alternating current waveform. The waveform can take any shape and is adjustable in frequency, phase, amplitude and offset via software.

[00132] To facilitate phase locking of the fiber with the OCT engine, a small stationary mirror is preferably placed in the tip of the probe and reflects the OCT beam when the fiber is at a limit of its swing. A personal computer (PC) having software detects the strong signal resulting from the reflection and adjusts for phase discrepancies by digitally phase shifting the waveform output of the MIU. Programmability is a preferable feature of the MIU. However, should logic modifications be desired, the programmable logic resources within the MIU are ample and can be easily expanded. Analog electronics to drive the needle coil are preferably added. The drive electronics preferably are in the form of a single integrated circuit.

[00133] During operation, the reflected light signal is received by the OCT engine where it is mixed with a reference beam, converted to an electronic signal, digitized, and then processed to extract desired information.

[00134] The engine preferably employs a microcontroller to coordinate overall control of the engine and manage communications with the PC. The microcontroller software controls some aspects of the MIU's operation, thus microcontroller software modifications are preferable with the addition of the phase-locking scheme. These are straightforward and the microcontroller has ample resources for the addition.

[00135] The PC constructs a desired image from the digital OCT data from the engine. This process is referred to as "scan conversion." OCT data is converted from the coordinate system of the scanner to a Cartesian system suitable for display on the PC's monitor. The needle scanner operates in a polar coordinate system with its scan angle being a sinusoidal function of time. Thus, the needle scan converter uses basic trigonometric functions to derive the Cartesian data points.

[00136] Software is used to display a geometrically correct needle scanner image. The scan converter can employ Pentium MMX instruction set and is carefully coded to allow accurate and timely processing. The software is preferably adaptable to variable scanner configurations (e.g., fiber length, scan amplitude, optical magnification, and the like).

[00137] The PC software also provides the user interface, overall control of the OCT system, and recording capability. The engine and software are sufficient for prototyping the needle scanner and gauging its performance. The software provides for adjusting many of the system's parameters, facilitating operation with experimental components. The software modifications described above are obviate manual adjustments and provide a user-friendly and comprehensive needle scanner system.

[00138] The following examples are presented in order to more fully illustrate the preferred embodiments of the invention. They should in no way be construed, however, as limiting the broad scope of the invention.

EXAMPLES

EXAMPLE 1: Long-Term Monitoring of Hormone Replacement Therapy With Volemetric OCT Endometrial Surveillance

[00139] The radial-viewing optical coherence tomography (OCT) catheter with a light emitting and receiving window located near its tip is introduced into the uterus. It is advanced to the top of the uterus. The catheter may, but not necessarily, be introduced within a blunt-tipped hollow guide. Once the OCT probe/introducer is properly situated, the tip of the OCT probe is exposed for imaging if used with an introducer. The position of the OCT probe

along with the cross-sectional tomographic images is recorded as the probe/introducer is smoothly withdrawn. Each optical section (tomographic image) is co-registered with the axial position of the probe. The stack of images and their respective axial positions are stored digitally. The border separating the endometrium and the underlying stroma and myometrium is identified using image segmentation software. The area comprising the endometrium in each tomographic image is measured by integrating the endometrium segmented region (automated software). The volume comprising the endometrium from the top of the uterus to its opening is calculated by summing the product of the segmented region and the distance between each tomographic image. The stack of images may also be stored and be subsequently three dimensionally rendered for qualitative evaluation. This evaluation may include, for example, examination for cystic glandular hyperplasia, areas of atypical hyperplasia, endometrial polyps, and loss of definition between tissue layers.

[00140] Optical contrast agents introduced either by IV, PO, or by intra-uterine infusion may be used to enhance contrast between different tissue components. Another means to enhance tissue contrast is to use different wavelengths of light. For example, by using light wavelengths close to 1700nm versus 1500 nm it may be possible to differentiate light attenuation by fat versus water. The different wavelengths may scan the tissue either in a multiplex manner or sequentially after the completion with each wavelength.

[00141] Approximately thirty million women currently are or have taken HRT. The gradual increase in average age of the American population will further increase this number, and tax current resources to deal with the estimated 25% of these women who require definitive evaluation of abnormal uterine bleeding sometime in their postmenopausal HRT experience.

[00142] Patients with surface abnormalities of the endometrium and OCT-directed endometrial biopsy, are able to be screened rapidly for definitive gynecologic investigation and/or hysterectomy with appropriate oncology follow-up. In patients having diagnostic and/or therapeutic D&C, OCT provides a reliable means of ongoing follow-up, as opposed to the current practice of repetitive D&C.

[00143] Non-invasive monitoring of the endometrial cavity and OCT-directed endometrial biopsy supplants random endometrial sampling and/or D&C as the primary investigation for dysfunctional bleeding, and provides reliable ongoing endometrial monitoring (currently not done by any method) for all women on HRT. The methodology provides serial estimates of endometrial volume to become part of the routine annual evaluation for all post-menopausal women on HRT. Improved rates of early or pre-malignant endometrial atypia, lower frequency of invasive sampling procedures, and precise adjustment of HRT dosage to produce ideal endometrial support, are obtained.

[00144] The endometrial volume determined by this method is used to better manage postmenopausal women on HRT and with vaginal bleeding. Normal values are based on multiple factors including individual uterine size, thickness, interval since menopause began, type and duration of HRT, last menses/D&C, etc. Even more preferable are serial measurements of endometrial volume, carried out yearly (more frequently in high risk patients, or on demand for symptomatic patients) to evaluate responses to changes in therapy, and in patients on stable therapy to detect increases in endometrial volume premonitory of endometrial atypia. In patients with abnormal or increasing endometrial volume, specific surface rendering illustrates areas of atypia, and provides precise direction for immediate endometrial biopsy. (It should be emphasized that the current technique of endometrial biopsy is random, extremely imprecise, and provides representative samples of all quadrants of endometrium in a small minority of cases sampled.) Qualitative evaluation may be used to screen for early evidence of endometrial cancer.

EXAMPLE 2: Minimally-Invasive Evaluation of Benign and Neoplastic Peritoneal Nodularity

[00145] A number of OCT probes capable of scanning surfaces can be used. A radial scanning probe would be most efficient for the inspection of Fallopian tube. For large, flatter surfaces, a linear scanning mechanism (optical fiber sensor that moves axially within a rigid transparent outer catheter) may also be used. Two different methods of insertion and

guidance would be appropriate. Ultrasound direction of the probe, inserted through a freestanding needle into the peritoneal cavity, would be appropriate for tissue inspection of Fallopian tubes and the anterior peritoneal cavity, appropriate to post-treatment cases of endometriosis. In the second method, passage of the probe down the operating port of any standard laparoscope would be used to facilitate proper tissue discrimination for detailed small volume peritoneal biopsies. Because of this precision, it is expected that the caliber of introducing instruments can be reduced from the 5-8 mm laparoscopes currently in use, down to 1-2 mm mini-scopes, with very significant reduction in operative morbidity. In fact, procedures performed with this mini equipment are usually done without anesthesiology coverage or techniques, under local anesthetic with minimal patient sedation.

[00146] To enhance image contrast, decrease background noise, and increase depth of field, air or clear fluid may be locally infused to form a continuous contact with the membrane surface.

EXAMPLE 3: <u>OCT in Luteal Phase Assessment of Pre-Implantation Endometrium</u>

[00147] Infertility patients with appropriate symptomatology and/or undiagnosed reproductive failure are at risk.

[00148] Referral to a reproductive endocrinology specialist will assure optimized hormone support, timing of ovulation induction, timing of insemination and early-pregnancy ultrasound surveillance, timed relative to endometrial maturation.

[00149] The radial-viewing OCT catheter is introduced into the uterus and advanced to the top of the uterus. This is preferably, but not exclusively introduced using a hollow blunt tipped guide introducer. The OCT probe is withdrawn smoothly while the axial position of the probe position is registered with each tomographic image. Parameters of endometrial growth are established on a daily basis to correspond with current biopsy standards, for correlation to timing of ovulation, duration of cycle, and efficacy of supportive hormone manipulation. If indicated, withdrawal of the catheter can be halted at the level of any

suspicious endometrial lesion, the exterior sheath re-introduced to facilitate OCT-directed biopsy.

[00150] In addition to applying primarily to the group of women with luteal phase insufficiency, as success develops, application to the larger group of women undergoing assisted reproductive technologies (ART) is also appropriate. In the case of IVF, precise timing of embryo transfer relative to endometrial development may further enhance successful implantation and successful pregnancy rates. Because the technique does not require disruption of the endometrium to ascertain ideal histologic development, it is ideally suited to allow evaluation of the endometrium as a determinant for embryo transfer rather than the current random situation.

EXAMPLE 4: Intrauterine Diagnosis And Surgical Treatment Of Fetal Cardiac Outlet Obstruction

[00151] The frequency of HLH in a high risk center is approximately one per two hundred births, recognizing a state-wide referral pattern. Should effective intrauterine surgery result, at least double that number would become available, representing about 50% or more of families who currently elect pregnancy termination because of the severe consequences of this problem. This is a national issue of major concern.

[00152] Development of a viable intrauterine procedure for correction of HLH before its final irreversible step, will markedly decrease the mortality of this procedure (currently as high as 70%, based on mid-trimester antenatal diagnosis), decrease the number of full Norwood procedures (the operation that reduces the heart to a single ventricle), and reduce morbidity among surgical survivors due to pump accidents, intraoperative complications, and prematurity.

[00153] Under local anesthetic and continuous ultrasound guidance, a 20 gauge spinal needle is introduced through the maternal abdomen and uterine layers, to rest against the fetal chest at the sixth intercostal space. Depending on fetal position and activity, fetal paralysis may be induced using a 22 gauge spinal needle at a separate site, guided with continuous

ultrasound to the umbilical vein at its insertion on the surface of the placenta. Paralysis is then induced with pancuronium 0.3 mg intravenously. In this case, paralysis is virtually immediate, and will be sustained for approximately two hours, depending on dosage and gestational age. The procedure is then carried out with no risk of sudden severe fetal activity causing dislodgment of the needle or intracardiac perforation. Through this needle the end-firing OCT unit is inserted, and using ultrasound guidance the probe is positioned adjacent to the aortic orifice. Direct visualization of the gap between leaflets of the aortic valve will permit navigation into the aortic root, where the OCT probe will function as a guide wire for insertion of the balloon catheter. The smallest sizes of standard vascular balloon catheters (the type used for coronary artery angioplasty) will be appropriate for the diameter of the aortic root at these gestations. The balloon is inflated in the aortic root, and then vigorously drawn back into the ventricle, producing an aortic valvulotomy. Once an adequate diameter of outflow tract has been created, the hypertrophied left ventricle will maintain flow, and ongoing tissue modeling of the aorta will result in maintenance of the orifice, and growth of the ascending aortic arch. Ongoing functional monitoring and long-term evaluation of cardiovascular status would not require further invasive techniques, but can be accomplished with current state of the art prenatal and neonatal ultrasound.

EXAMPLE 5: Minimally Invasive Diagnosis Of Fetal Tumors

[00154] Fetal tumors are rare complications but each one requires meticulous work-up and almost always at least one intrauterine procedure.

[00155] In some cases the diagnosis of lethal fetal tumors will be made, and pregnancy options will be able to be considered in full light of a histologic diagnosis. In many other cases, however, reassurance of a normal prognosis, organization of surgical attendance at the time of delivery, including changing the venue from suburban hospitals to University-based centers is made possible.

[00156] OCT provides improved precision and more accurate biopsies where currently, biopsies are unavailable or unsatisfactory technically.

[00157] Depending on the location and consistency of the tumor, either the end-firing or radial-firing OCT transducer can be utilized. Via minimally invasive spinal needle inserted under direct ultrasound guidance into the amniotic cavity, the OCT probe is directed to the area of the fetal body where the tumor was visualized. In the case of subcutaneous tumor (muscle tumors, hemangiomas, other soft tissue tumors) direct needling of the tumor itself may not be necessary, due to the attenuation of the overlying skin, and the precise definition of tissue layers. Otherwise, the introducing needle is inserted in the tumor itself, the trocar removed, and the imaging probe inserted down the needle. Direct tissue contact of the probe is achieved by gradual withdrawal of the exterior needle, until the probe lies by itself within the tumor mass. Precise definition of tumor cellular characteristics, connective tissue and other stromal layers, in relation to adjacent structures, is then determined by direct imaging. Finally, using combined ultrasound and OCT imaging (coordinated on the same screen using standard dual-projection integrated video system), precisely located fetal biopsies are obtained. (Currently, such fetal biopsies are usually directed by ultrasound, but are blind to the actual tissue planes, these being too subtle for reliable interpretation by ultrasound in most cases.) The OCT probe is then withdrawn, and the needle withdrawn out of the fetus, available for appropriate fetal blood sampling and/or fetal amniotic fluid sampling before removal from the mother.

EXAMPLE 6: <u>In Vivo Placental Evaluation In Pregnancies At Risk</u>

[00158] About 16% of all pregnancies (more common in women in their first pregnancy) have complications related to deficient placentation, manifest in the fetus as IUGR, and in the mother as pre-eclampsia.

[00159] Placental abnormalities depicted this early in gestation may be amenable to intrauterine therapy with anticoagulants (heparin), central manipulation of maternal blood pressure, agents to enhance uterine artery blood flow, or antiplatelet agents. A major role in directing monitoring, centralized care, and clinical investigation will also be served by the early identification of at risk pregnancies.

[00160] The ability to influence placental development at an earlier stage than currently clinically possible, will be manifest in longer gestations, healthier newborns, and reduced pregnancy wastage. The ultimate impact, as illustrated by the Barker hypothesis of fetal disorders producing adult medical illnesses, may be much larger.

[00161] The OCT probe is introduced transcutaneously under direct ultrasound guidance. The placental bed is readily visualized using real time ultrasound, supplemented by color Doppler flow mapping, to allow placement of the probe in an ideal location where actively-dividing villi can be identified. Because the hemochorial placenta is basically a hydroponic model (solid villi suspended in fluid [blood] filled maternal spaces), the visualizing interface will be appropriate to the OCT, allowing detailed evaluation of the tissue structure of individual villi. Correlating this *in vitro* placental damage with our in vivo pathology data will provide an index for evaluating successful placentation. Damaged villi are fewer in number, are blunted, have far fewer branches, and have reduced central flow (these vessels are just three cell layers from the surface so they are also available for imaging). The frequency and severity of placental damage, will precede Doppler changes, growth disturbances and the cascade of more serious consequences, by many weeks.

EXAMPLE 7: <u>OCT Guidance For Epidural Anesthesia</u>

[00162] The introduction of anesthetics into the spinal epidural space is a very common and important method for inducing regional anesthesia. It is most commonly employed in the lumbar sacral region for labor and delivery. It can also be used at higher levels (i.e., the thoracic spine) in conjunction with general anesthesia for major thorathic surgery. Even though in experienced hands the complication rate for epidural space is quite low, complications such as the injection of anesthesia into the subdural space or into the epidural venus plexus can occur. This may result in complications that range from an unpleasant labor and delivery to death due to massive drop in blood pressure. The catheter tip may also be wedged in a confined epidural space toward one side of the spine resulting in only hemianesthesia. More commonly the introducer can puncture the dura without necessarily

injection of anesthesia into the subdural space. This may induce a significant CSF leak and result in a spinal headache. The fundamental reason for these complications is that the procedure is blind and relies on the "feel" of the needle going through the ligament flavum of the spine and the experience of knowing when to stop advancing the needle before reaching the dura. OCT can make the procedure easier and more reliable by providing real time visual feedback on the position of the needle tip relative to the dura, nerve roots, and blood vessels within the spinal canal. OCT can also provide documentation of the precise position of the epidural catheter relative to the dura, nerve roots, and blood vessels during drug infusion. This will protect the physician against the large numbers of malpractice suits associated with epidural anesthesia that are justified or unjustified.

[00163] OCT is well suited for imaging within the epidural space because it can unequivocally distinguish between CSF, dura, and epidural fat. By injecting fluid through the needle, the operator can observe the movement of the different structures to further confirm their identity and to increase the depth of view.

[00164] The use of OCT guidance in epidural anesthesia may be even more useful in veterinary medicine where there is wide variability in the anatomy of the spinal canal and where surgery are done without the help of anesthesiologists.

[00165] A radial-scanning OCT probe can be either built into the epidural needle, into the drug infusing catheter, or as an independent probe that fits inside of the epidural needle. In the latter case the probe is placed within a hollow slightly bent-tipped epidural needle. The front of the OCT probe is flush with the tip of the needle. The two are advanced through the ligament flavum of the spine in the usual manner. As soon as the needle is through the ligament, the OCT probe can be used to determine the distance to the dura and the location of nerve roots and blood vessels. If still not sure of the position, the probe, not the needle, is then advanced forward while the surrounding structures are image. Important landmarks include epidural fat, dura, blood vessels, and CSF. Small amounts of saline can be infused to observe the movement of the tissue surrounding the tip of the OCT catheter probe.

[00166] The same basic procedure may be used to guide the placement of hardware in the epidural space such as electrical stimulators and chronic drug infusion catheters.

EXAMPLE 8: OCT in the treatment of chronic pain

A. Removal of epidural adhesions

[00167] Chronic low back pain following spine surgical procedures (or "failed backs") is a major medical and societal problem without a satisfactory solution. One important cause of the chronic pain in "failed backs" is the development of adhesion near the site of the spinal surgery. These adhesions gradually impinge on nerve roots. Further surgery would only compound the problem. Currently, fiber optic endoscopes are placed in the epidural space to visualize and to break the adhesions. Problems include poor resolution, small viewing angle, and the need to infuse large amounts of fluids in order to open up the epidural space for endoscopic viewing. Because the small dimensions of the OCT catheter, its high resolution, higher viewing angles, and ability to see through thin tissue, OCT is better suited for imaging in the confined epidural space.

[00168] A forward-viewing OCT probe is introduced into the epidural space in a manner similar to current methods for introducing fiber optic endoscopes. The OCT probe is placed within a larger semi-rigid introducer. A retractable probe for cutting the adhesion may, but not necessarily, also be included in the introducer. Small amounts of saline are also infused to open up the epidural space and to look for the movements different tissues. A much smaller amount of fluid will be used compared to current methods.

B. Guidance for the direct placement of long acting drugs on nerve roots

[00169] An evolving strategy for the treatment of chronic pain is to place long acting drugs directly on to nerve roots. This may achieve greater pain relieve while minimizing systemic toxicity. The ideal drug is one that is not water-soluble but which has to be directly applied. Once applied it should adhere to the nerve strongly. This requires high precision imaging in tight space. OCT provides these capabilities.

[00170] A forward-viewing or a partially forward-viewing OCT probe is placed along with the drug application catheter within a semi-rigid introducer. The OCT/introducer is placed in the epidural space as in section A (above). Small amounts of saline or air are infused to open up the epidural space. The appropriate nerve root will be identified. The soft tipped drup application is brought directly in contact with the nerve root and the long acting drug painted onto the nerve. The drug application catheter has a suction capability to remove any free floating or loosely adhering drug.

C. Guidance for nerve block outside the spine

[00171] Effective nerve block whether for short term anesthesia or long term would work best if the anesthetic is placed close to the intended target. Nerve trunks are highly reflective and therefore appear sharply on OCT.

[00172] A thin forward-viewing or partially forward-viewing OCT probe is placed within the needle used to infuse the anesthesia. The needle retains the ability to infuse the medication. The OCT images will help identify the correct target by the size, shape, and reflective properties of the nerve. The OCT probe is also used to avoid blood vessels on the way to the target.

EXAMPLE 9: Evaluation of OCT guided needle placement

[00173] The most basic mechanical performance of the OCT stylet is tested in *ex vivo* lamb spine. Lamb spine is readily obtained from a local slaughter house immediately after slaughter. The dimensions of the cord and epidural space approximates that of man. Once the prototype OCT stylet has been constructed, it is mounted within the epidural needle and subjected to tests of its mechanical integrity.

[00174] It is less likely that the impedance/pressure monitor opening will become plugged with the OCT stylet in place than with the standard open epidural needle because there will no longer be any direct path into the needle. A direct comparison is conducted to determine whether there is significant difference in needle blockage. The automated impedance

monitor is more sensitive to the 'loss of resistance' when the needle breaks through the ligamentum flavum. Because of the decrease in the rate of needle blockage and because pressure transducers' accuracy is less sensitive to movement, the OCT stylet is equal to, if not more sensitive than the current syringe method. A direct comparison is easily carried out in the lamb spine. False positives are detected by the inability to pass a catheter through the open epidural needle. False negatives (and degree of insensitivity) are assessed by measuring the distance the needle has traveled past the ligamentum flavum.

[00175] One of the reasons for using OCT in epidural anesthesia is to supplement the 'loss of resistance' cue with optical cues. There are several unequivocal optical cues. The first is the smooth high contrast CSF- ligamentum flavum border (Fig. 6). Next is the characteristic globular appearance of epidural fat (Fig. 4). And finally, there is the distinctive homogenously thick and smooth edged dura (Fig. 13).

[00176] With the present apparatus and method, there is a significant decrease in the incidence of unintended dural puncture.

EXAMPLE 10: <u>OCT guidance of epidural catheter placement</u>

[00177] As was discussed above, cannulation and infusion of anesthetic into the venous plexus is one of the most troubling problems in obstetrical anesthesiology. The consequences are devastating and current steps to prevent it are not foolproof. One means to minimize this complication is to be able "look around" the tip of the catheter as it is being advanced. OCT can readily detect blood vessels 1-3 mm away from the probe. The thin OCT probe can be threaded through the drug infusion catheter to its tip where it can monitor the position of the catheter tip. Once its position is satisfactory, the OCT probe will be removed and standard drug infusion procedures are then instituted. A side-scanning OCT catheter is adequate (LightLabs), but not ideal, for this purpose. Indeed, it can be easily passed to the tip of the epidural catheter. It can determine whether the catheter is staying in the midline based on the distinctive tent-shaped roof of the ligamentum flavum. Blood vessels are most congested toward the lateral recess. It can also determine if a vessel is pressed against the probe

laterally. However, more preferable is a thin OCT probe that can switch between a side scanning mode and a forward-scanning mode. Such a device may be of the 'cylindrical mirror' and the 'parallel mirror' design.

[00178] Cylindrical mirror strategy. A relatively simple modification of a side-scanning probe is made to the tip of the drug infusion epidural catheter. A low index plastic cylinder is fabricated with an inner diameter slightly larger than the outer diameter of the OCT probe. The beveled lower surface of the cylinder is mirrored. The angle of the bevel is designed to align the reflected beam parallel to the axis of the catheter. The front surface is angled slightly to prevent direct back reflection. This cylinder is firmly placed at the tip of the drug infusion catheter. A reversible locking mechanism can stabilize the OCT probe position within the drug infusion catheter. It is locked in a position that allows the side scanning rotating beam to intersect the cylindrical mirror. In this manner the radial scanning beam is converted to a forward cylindrical scanning beam. Images from a cylindrical scan are a little more difficult to interpret, but should be adequate for detecting blood vessels. It is possible to retract the spinning inner fiber while the outer catheter is kept stationary. In the retracted mode, scanning returns to the radial direction. Empiric testing is used to determine the width of the gap between the OCT probe and the cylinder. It may be necessary to flush blood from the front of the catheter. There may be enough space to force solution through a small gap. Alternatively, the OCT probe can be retracted slightly past the cylinder. Since the inner diameter of the drug infusion is typically much larger than the OCT probe, sufficient solution can be forced past the front to flush the the tip of the catheter.

[00179] To partially solve the cylindrical scanning problem, one can bevel the front surface of the cylinder to different angles depending on the rotational position of the scanning beam. The beveling serves as a prism that bends the beam. The goal is to convert a cylindrical scan to a flattened oval shaped scan. For example, at 12 and 6 O'clock of rotation, the beam will be directed straight ahead. But at 3 and 9 O'clock the beam will be directed toward the side by 20 degrees. Astigmatism may be introduced which may degrade the resolution. A separate but related limitation is the astigmatism which may be introduced by the curved

inner surface of the cylinder. To solve this problem one chooses low index material. The curved mirror surface may also contribute some aberration. However, because the NA of the beam is relatively small compared to the radii of curvatures, the amount of aberrations should be acceptable.

[00180] Parallel flat mirrors' strategy. Flat, forward-scanning with minimal aberrations can be achieved from a rotating side scanning beam by using a novel 'parallel flat mirror' strategy. A catheter OCT (LightLabs) achieves radial scanning by rotating a fiber with a side deflecting front prism. The beam is actually oriented slightly forward from the side. If a short flat mirror is placed in the path of the beam which deflects the beam again to a second flat mirror that reorients the beam forward, the rotational motion of the beam is transformed to a flat side to side flat scanning motion. This scanning motion can only be achieved for a portion of the rotation (i.e., between 11 and 1 o'clock in Fig. 26). Note that if a second set of mirrors is placed on the other side of the rotation, flat scanning can be achieved between 5 and 7 o'clock of the fiber rotation. Instead of scanning the same plane, it may be preferable to scan a second parallel plane .2 to .5 mm apart. There are three significant advantages to this design. Firstly, it introduces no additional aberrations. One can think of it as analogous to the two scanning mirrors within a scanning confocal microscope. The beam spot does not change size or shape at different angles of orientation. Secondly, the beam will be scanning at the same rotational rate. Thirdly, when the beam is not in the forward-scanning sector, it will be providing side scanning. Thus, maximal amount of useful non-redundant information can be acquired. Display software is written to place the three separate images on the same monitor.

[00181] It is preferable to fabricate the two mirrors as two mirrored surfaces of a monolithic prism. The minimum dimensions that can be realistically achieved are determined. It is possible to achieve a tip diameter between 0.5 and 1 mm using monolithic prisms, but if the side mirror is placed on the drug infusion catheter instead, probes with outer diameter <0.5 mm are possible. A method for precise mirror alignment is required.

EXAMPLE 11: Evaluate OCT guided catheter placement

[00182] The ability to detect epidural blood vessels is tested in living animals. Anesthetized dogs that have been used for other studies and are about to be sacrificed can be used to avoid the use of any extra animals and avoid subjecting the animals to any pain. It is possible to introduce epidural catheters at all levels in the dog spine. Because the L7 interspace is typically the easier to enter, one preferably begins there.

[00183] The frequency of venous cannulation is the primary parameter for comparison. Cannulation is defined as the aspiration of blood through the catheter. The rate of cannulation in obstetrics is 10% (McBeill and Thorburn, 1988). If one assumes that the rate in non-pregnant dog is half as frequent, it would take 20 catheterization to obtain a single incidence of cannulation. To compensate for this low rate, epidural catheterization is carried out at multiple levels. If five catheterizations are performed in each dog, cannulation is observed on average for every four dogs studied. Because OCT is able to keep the catheter within the midline and because blood vessels can be readily detected by OCT, statistical significance is achieved very rapidly.

EXAMPLE 12: Develop a combined OCT-epiduroscopy instrument

[00184] OCT imaging capability is added to the current epiduroscopy instrument in order to improve the reliability for identifying the various structures within the epidural space while using the least amount of saline perfusion. Visionary BioMedical's steerable Myelotec epiduroscopy catheter is the preferable platform for this instrument. This catheter has two open ports 40,42 (Fig. 14). Port 42 is used for the fiber-optic endoscope 44. The other is used to house the forward-scanning OCT imaging probe described above. The inner diameter of the second port (1.3 mm) accommodates the OCT 'stylet' design. The scanning plane of OCT probe is oriented orthogonal to the center of the catheter.

[00185] Modifications can be made to the needle 'stylet' design. Because the length of the epiduroscopy catheter is ~12 inches, the vibrating spring mechanism will have to use 3-4 'stops' to sustain and control the standing wave vibration. A second modification may be the

addition of a retractable blunt tipped side-cutting/dissecting probe. Perfusion solution can be delivered through two or more thin-walled catheters. If a non-steerable epiduroscopy catheter with less space constraints is used as the basic platform, it is possible to build a thin push-pull mechanism to pivot the cutting probe. The pivoting movement is parallel to the plane of the OCT scanning (Visionary BioMedical, Inc., Roswell, GA).

EXAMPLE 13: Evaluation of the performance of OCT guided epiduroscopy in cadavers

[00186] Those with a history of lumbar discectomy and persistent radicular pain involving one root, yet without obvious reasons on MRI (i.e., spine instability, large retained disc fragments, and significant arthritis) have a high incidence of epidural fibrosis. Epiduroscopy is performed. The first objective is to determine whether the tomographic imaging property of OCT assists the surface-only imaging of conventional endoscopy. One first identifies structures by endoscopy only. They are provided OCT cross-sectional images of the same structures, along with the endoscopy images. Differences in the structures identified are noted. Verification of the true identify of the structure is accomplished, in part, by cutting of the structure with the cutting probe, and, in part by open dissection of the spine at the end of the procedure.

[00187] OCT can help accurately identify structures with a minimum of perfusion saline because OCT can see through tissue and more easily view through slits of openings. The same procedures are performed but with the condition that only 100 cc of saline is used. The number of accurate structures identified by endoscopy only and with the additional help of OCT are compared.

[00188] Fibrolysis can be accomplished more effectively and safely with the addition of OCT guidance and the addition of a dissecting/cutting probe. The probe has a round blunt tip to avoid unintentional puncture. The cutting edge is aligned parallel to the OCT imaging plane so that the section to be cut can be visualized. Cadavers found to have extensive epidural fibrosis are divided into two random groups. One receives fibrolysis by endoscopy only and the other using the novel instrument. The addition of the dissecting/cutting probe

greatly improves the effectiveness of fibrolysis. Adhesion tightly surrounding a nerve root or which are too strong to be broken by the endoscope itself can now be precisely cut.

EXAMPLE 14: High resolution diagnostic imaging

[00189] CT and MRI imaging technologies have revolutionized clinical imaging. But there are still situations where they do not have the resolution to detect the pathology within the epidural space. Because the resolution of OCT can be two orders of magnitude better than CT and MRI, OCT may fill these more demanding imaging needs. Two such needs are the detection of dural tears and the identification of small symptomatic disc fragments. Even though they are not encountered nearly as often as epidural anesthesia or post-surgical epidural adhesions, they are real problems without any good solution.

[00190] One of the suspected causes of the 'failed back' syndrome is a retained disc or bone fragment wedged within the neural foramen. If the fragment is <1 mm, CT and MRI will not be able to detect it. Yet it may still cause in nerve irritation in the confines of the neural foramen. This is the suspected reason for the continued pain following discectomy for Baltimore Oriole legend, Cal Ripken, and which lead to his high profile retirement from baseball. It is a frustrating diagnosis because a definitive positive imaging diagnosis is not possible. OCT, in contrast, has the sensitivity to detect such small structures.

[00191] Those with a history of lumbar discectomy with persistent radicular pain involving one root, yet without obvious reasons on MRI (i.e., spine instability, large retained disc fragments, and significant arthritis) are selected for evaluation. Indeed, the OCT-epiduroscopy device and the forward-scanning catheter based OCT probe can be evaluated on the same patients. There has previously been no definitive study to determine the relative contribution of retained disc fragment versus epidural fibrosis for the 'failed back' syndrome.

[00192] The thin forward-scanning OCT probe is threaded through a steerable epidural catheter whose front tip can maintain a small degree of curvature. By rotating the steering catheter, it is possible to guide the OCT probe toward the lateral recess and the neural foramen. Alternatively, one may use a portable fluoroscope with which to guide the catheter.

One determines whether free fragments can be found in the affected foramen. The OCT criteria are small structures that are not smoothly meshed with the nerve root sleeve, the periostium, or the annulus fibrosus. If such structures are detected, the spinal canal is carefully dissected.

Dural tears

[00193] Dural tears are typically iatrogenic. They frequently follow spinal taps, placement of epidural stimulating electrodes, and spinal surgery. A small number may also arise following traumatic cord injury. The patient presents with symptoms of headache associated with sitting or standing which is relieved by laying down. Management dilemma arises when the cause of postural headaches and the location of the leak is unknown. In such cases, it is helpful to have a diagnostic procedure to identify or rule out dural tears. If spinal headaches do not resolve spontaneously, but the site of the leak is known, the standard protocol is to inject 20 cc of whole blood into the epidural space near the suspected site of tear. But blood patches do not always work. Image guided application of neurosurgical fibrin clots may seal the CSF leak.

[00194] OCT is ideally suited to detect iatrogenic dural tears. Epidural needles are used to create a dura lacerations of variable sizes. The thin OCT probe is then introduced at another spinal level through a catheter that can be steered. The OCT probe is advanced slowly for a few centimeters, withdrawn, steered to a slightly different angle and advanced again to cover systematically a predetermined area. The objective is to determine the frequency with which laceration of different dimensions can be detected. Follow-up may include sealing lacerations with neurosurgical fibrin glue using a OCT-epiduroscopy catheter whose retractable, pivoting, dissecting probe will be replaced with a injection needle.

[00195] The present invention can provide more effective pain relief for hundreds of thousands of Americans each year.

EXAMPLE 15: *In vivo* real-time, high resolution imaging of the epidural space

[00196] We recently received institutional approval to proceed with imaging of the epidural space in anaesthesized dogs. The images in Figs. 29A-D were taken from the first OCT video clip sequence of a mammalian spine *in vivo*. There were no problems with performing epidurals in the live dog. The OCT probe can be moved easily up and down the spinal canal for imaging. Anatomic structures can be readily identified. Because the CSF is under a modest pressure within the intact dura sac in a living animal, there is a uniform CSF gap separating the cord from the dura. This results in clear identification of the dura and cord. Thin-walled veins are not collapsed in the living animal and therefore are easier to identify. Epidural veins are expected to be significantly bigger in the pregnant mother than shown here for this small dog. Fat cells appear to 'sparkle' more *in vivo* than *ex vivo* and, therefore, much easier to identify. This may be due either to the effect of temperature on the optical properties of oil droplets stored within the fat cells or to the collapse of the round shape of the oil droplets post-mortem.

[00197] OCT is thus ideally suited for real-time, high resolution imaging of the spinal epidural space. No other imaging modality can achieve comparable performance in live subjects.

EXAMPLE 16: Spectral and birefringence OCT of the epidural space

[00198] Spectral OCT exploits the differential absorption of light of different wavelength of a specific tissue. Water and fat have sharp absorption peaks in the 1300-1600 nm wavelength range. By using 2 or more SLDs of different central wavelengths and ratiometrically comparing their backscattering intensities it is possible to differentiate between subsets of tissues. Birefringence OCT exploits the non-random polarization produced by certain tissues. For example, one would expect nerve roots containing thousands of parallel fibers to produce high birefringence. Spectral and birefringence imaging capabilities will be particularly helpful for lysis of epidural adhesions. The ability to distinguish between nerve root, adhesions, and blood vessels with high confidence is critical for such a procedure. This degree of confidence may be achieved by combining such three

complementary set of OCT acquired information. The data can be acquired simultaneously. Fig. 30 demonstrates the ability to image plaques on the coronary artery wall.

EXAMPLE 17: Improving resolution and tissue penetration

[00199] The use of ultra-high bandwidth laser light sources (i.e., from Menlo Systems, Munich, Germany) is used to improve resolution and decrease speckling by ~1 order of magnitude. A novel class of high power, higher bandwidth multi-quantum well SLD light sources is used to improve tissue penetration.

EXAMPLE 18: OCT probe for use in the spinal epidural space

[00200] Forward imaging ability is desirable for any image-guided intervention that involves insertion of a probe into tissue. Currently, such a thin forward-scanning OCT probe does not exist. Thus, considerable effort was devoted to such a development. A flat mirror is used to intercept a sector of the radial scanning beam, and the intercepted beam is used for linear forward-scanning.

[00201] At least one probe construction can be used with the epidural needle as well as the drug infusion epidural catheter. This is preferred construction because of its simplicity, compact size, ruggedness, and feasibility in fabrication. Preliminary data on its performance in a prototype model has been obtained.

[00202] This Example describes fabrication procedures and modifications that render it more rugged during clinical use. A flat annular-shaped reflective surface is oriented at a 45° angle to the axis of the spinning GRIN lens/mirror assembly. Within one sector of its 360° rotation, the beam is reflected forward by the front tip of the inclined mirrored surface (Fig. 31A). Over the rest of the rotation the probe operates in its normal radial scanning mode. If the spinning optical fiber/grin lens assembly is moved forward, the relative amount of scanning dedicated to forward versus side scanning can be adjusted. If the assembly is advanced forward enough, it will perform a full radial scan. The forward scan is linear (rays remain within a single plane) allowing for easier visual interpretation.

[00203] Figs. 32A,B provide a 3D volume rendering of the design. When the mirror intercepts the beam A it is in its forward sector-scanning mode. And when the beam bypasses the mirror (B) it is in the radial scanning mode.

[00204] In an exemplary embodiment, the mirrored surface of the assembly is fabricated out of a thin cylinder having an outer diameter of about 300 μm and an inner diameter that is slightly larger than the outer diameter of the GRIN lens/mirror assembly. One end of the brass cylinder is polished to an angle of from about 40°-40°, preferably about 45°, to form a λ/4 surface and then coated with a metallic film, such as a gold film.

[00205] To protect the inclined mirrored surface as the probe is pushed into tissue, it is preferably covered by a clear hard surface. In an embodiment, a clear thin cap may be placed over the cylinder. Alternatively, a solid, clear plastic cylinder can be attached to the inclined cylinder. To ease passage through tissue, the front of this cap can be rounded (not shown) except for the region through which the beam passes.

[00206] The narrow dimensions of this probe easily allow it to be placed within the lumen of the epidural needle. A stylet may need to be built to hold the thin OCT stable within the needle and orient the forward-scanning region of the probe to the upper opening of the epidural needle (see Fig. 10). The narrow dimensions of this probe also allow it to be directly threaded through the drug infusion epidural catheter.

EXAMPLE 19: Alternative OCT probe for use in the spinal epidural space

[00207] As illustrated in Figures 34-37, the OCT probe 50 comprises an assembly including a single-mode optical fiber 52 having a tip 54. The optical fiber 52 can be selected to emit light having a wavelength that can range from about 0.4 microns to about 2.1 microns. The light is passed to a gradient index (GRIN) lens 56 attached to the tip 54 of the optical fiber 52. A body 58, such as a prism or a lens, is attached to the gradient index lens 56. The body 58 is transparent to the light emitted by the optical fiber 52. The

body 58 has a first mirrored surface 60 oriented to divert light in a radial scanning direction R, which is substantially perpendicular to the longitudinal axis A of the assembly.

[00208] A housing 62, such as a sleeve having a cylindrical or other suitable shape, contains the assembly. The housing 62 is stationary and has a tip 64 through which light is passed. The housing 62 preferably has a maximum dimension perpendicular to the longitudinal axis A (e.g., a diameter) of from about 100 microns to about 1000 microns, and more preferably less than about 400 microns.

[00209] The assembly is rotatable over 360° about the longitudinal axis A. The assembly can be operatively connected to a motor, which is operable to rotate the assembly at a desired speed. The OCT probe 50 comprises a second mirrored surface, which is oriented relative to the longitudinal axis A of the assembly to reflect light diverted by the first mirrored surface 60 in a forward-scanning direction over a portion of the 360° rotation of the assembly about the longitudinal axis A. The second mirrored surface can be provided on a face 65 of the housing 62. The second mirrored surface can include one flat surface 64 as in the embodiment shown in Fig. 37. The surface 64 is preferably oriented at an angle of from about 40° to about 50°, and more preferably about 45, relative to the longitudinal axis A. Alternatively, the second mirrored surface includes two or more flat facets, such as the facets 66, 68, and 70, as shown in Figs. 34, 35 and 36. The facets 66, 68, and 70 are oriented at different angles relative to the longitudinal axis A. The angles of the facets preferably can range from about 25° to about 65°.

[00210] In another exemplary embodiment, the second mirrored surface can be curved, such as a continuously curved surface. The curved surface preferably is oriented at an angle of from about 25° to about 65° relative to the longitudinal axis A.

[00211] The second mirrored surface has a substantially flat contour. The second mirrored surface can be made of any suitable material, e.g., a metallic or dielectric material.

[00212] A cover 80, such as a light transparent cap, can be placed over a portion of the housing 62. The cover 80 protects the second mirrored surface of the OCT probe 50 when inserted into tissue. Alternatively, the second mirrored surface can be covered by a light transparent material to provide such protection. The light transparent material can be adhered to the second mirrored surface, or applied as a coating, for example.

[00213] In another exemplary embodiment, the second mirrored surface can be provided on a second body instead of on the housing 62. For example, the second body can be a cylinder, semi-cylinder, rectangle, or other suitable shape that supports the housing 62. The second body is preferably configured to receive a portion of the housing 62. The second mirrored surface can be an end face of the second body facing the housing 62. The second mirrored surface can be, for example, of a metallic or dielectric material applied on the surface.

[00214] As shown in Figs. 34-36, the optical fiber 52 is movable relative to the housing 62 along the longitudinal axis A of the assembly to adjust a portion of the light that is directed in the forward-scanning direction during rotation of the assembly. The forward-scanning direction lies in a plane oriented to extend forwardly of the tip 64 of the housing 62. In addition, the optical fiber 52 can be moved along the longitudinal axis A to change the location of the second mirrored surface at which the light diverted by the first mirrored surface 60 impinges on the second mirrored surface. For example, in the position of the optical fiber 52 shown in Fig. 34, the diverted light impinges on the facet 68, and light is directed in the forward-scanning direction F1. By moving the optical fiber 52 backwards as shown in Fig. 35, the light is caused to impinge on the facet 66, and the light is directed in forward-scanning direction F2. As shown in Fig.36, by moving the optical fiber 52 forwardly of the position shown in Fig. 34, during rotation of the assembly, the diverted light is caused to impinge on the facet 70, and the light is directed in forward-scanning direction F3. By moving the optical fiber 52 sufficiently forwardly of the position shown in Fig. 36, the light does not impinge on the second mirrored surface and is directed only

in a radial scanning direction. The light can also be directed in different forward-scanning directions by providing a curved second mirrored surface, instead of a multi-faceted surface.

[00215] While the invention has been described and illustrated herein by references to various specific material, procedures and examples, it is understood that the invention is not restricted to the particular material combinations of material, and procedures selected for that purpose. Numerous variations of such details can be implied as will be appreciated by those skilled in the art.

The following publications, which may be cited above, are hereby incorporated by reference in their entireties for all purposes:

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Li, X, Drexler W, Pitris C et al. Imaging of osteoarthritic cartilage with optical coherence tomography: Micron-structure and polarization sensitivity. In: Conference on Lasers and Electro-Optics. Baltimore, MD: Opt Soc Am. 1999, CWP5.

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Webb RJ, Kantor GS. Obstetrical epidural anaesthesia in a rural Canadian hospital. Can J Anaesth 39:390-3, 1992.

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U.S. Patent Nos. 6,564,087, 6,596,257, 5,699,795

A

WHAT IS CLAIMED IS:

1. A catheter-based optical coherence tomography probe, comprising:
an assembly including:
a single mode optical fiber having a tip, the optical fiber emitting light;
a gradient index lens attached to the tip of the optical fiber; and
a first body attached to the gradient index lens, the first body being transparent to the light emitted by the optical fiber and having a first mirrored surface oriented to divert light passing through the gradient index lens in a radial scanning direction; and
wherein the assembly has a longitudinal axis and is rotatable over 360° about the longitudinal axis;
a housing containing the assembly and having a tip through which light is passed; and
a second mirrored surface oriented relative to the longitudinal axis of the assembly to reflect light diverted by the first mirrored surface in a forward-scanning direction over a portion of the 360° rotation of the assembly about the longitudinal axis.

2. The optical coherence tomography probe of claim 1, wherein the second mirrored surface includes a single flat surface oriented at an angle of from about 40° to about 50° relative to the longitudinal axis of the assembly.

3. The optical coherence tomography probe of claim 2, wherein the angle is about 45°.

4. The optical coherence tomography probe of claim 1, wherein the second mirrored surface is substantially flat and made of a metallic or dielectric

material.

5. The optical coherence tomography probe of claim 1, wherein the second mirrored surface is on a second body.

6. The optical coherence tomography probe of claim 5, wherein the second body comprises an end face and the second mirrored surface is at the end face.

7. The optical coherence tomography probe of claim 6, wherein a portion of the housing is disposed within the second body.

8. The optical coherence tomography probe of claim 1, wherein the housing includes the second mirrored surface.

9. The optical coherence tomography probe of claim 1, wherein the second mirrored surface includes at least two facets oriented at different angles relative to the longitudinal axis of the assembly.

10. The optical coherence tomography probe of claim 9, wherein the facets are oriented at an angle of from about 25° to about 65° relative to the longitudinal axis of the assembly.

11. The optical coherence tomography probe of claim 1, wherein the second mirrored surface is curved and is oriented at an angle of from about 25° to about 65° relative to the longitudinal axis of the assembly.

12. The optical coherence tomography probe of claim 1, further comprising a light transparent material covering the second mirrored surface.

13. The optical coherence tomography probe of claim 12, wherein the light transparent material (i) is secured to the second mirrored surface, or (ii) contains the second mirrored surface.

14. The optical coherence tomography probe of claim 1, wherein the first body is a prism or a mirror.

15. The optical coherence tomography probe of claim 1, wherein the optical fiber is movable relative to the housing along the longitudinal axis of the assembly to adjust a portion of the light that is directed in the forward-scanning direction during rotation of the assembly.

16. The optical coherence tomography probe of claim 1, wherein the radial scanning direction lies in a first plane substantially perpendicular to the longitudinal axis of the assembly, and the forward-scanning direction lies in a second plane extending forwardly of the tip of the housing.

17. The optical coherence tomography probe of claim 1, wherein the second mirrored surface is (i) curved or (ii) includes at least two facets oriented at different angles relative to the longitudinal axis of the assembly, and the optical fiber is movable relative to the housing along the longitudinal axis to adjust the forward-scanning direction of the light during rotation of the assembly.

18. The optical coherence tomography probe of claim 1, wherein the housing has a maximum dimension perpendicular to the longitudinal axis of from about 100 microns to about 1000 microns.

19. The optical coherence tomography probe of claim 18, wherein the housing has a maximum dimension perpendicular to the longitudinal axis of less than about 400 microns.

20. The optical coherence tomography probe of claim 1, wherein the light has a wavelength of from about 0.4 microns to about 2.1 microns.

21. A method for performing epidural regional analgesia, comprising inserting into the spinal epidural space of an animal an epidural needle comprising (a) a tip, wherein the tip comprises a beveled opening, and (b) an optical coherence tomography (OCT) probe.

22. The method of Claim 21, wherein the needle further comprises a perfusion catheter.

23. The method of Claim 21, wherein the OCT probe is positioned at the opening of the needle.

24. The method of Claim 21, wherein the OCT probe generates a forward-scanning imaging beam.

25. The method of Claim 24, wherein the forward-scanning imaging beam exits unimpeded from the beveled opening.

26. The method of Claim 21, wherein the OCT probe is not allowed to advance beyond the beveled opening of the needle.

27. The method of Claim 22, wherein the epidural the perfusion catheter is positioned within the epidural needle so as to pass saline through the needle creating pressure, such that resistance to the pressure can be monitored as the needle is advanced towards the epidural space.

28. The method of Claim 22, wherein the needle is pushed into the intervertebral space and the ligamentum flavum.

29. The method of Claim 28, wherein positive pressure is applied to the perfusion catheter.

30. The method of Claim 29, wherein entrance of the needle into the epidural space is indicated by a loss of resistance applied through the perfusion cateter.

31. The method of Claim 29 or 30, wherein entrance of the needle into the epidural space is indicated by identification of structural landmarks by OCT imaging.

32. The method of Claim 31, wherein the position of the needle tip is determined by its relative position to the dura, spinal cord, and epidural fat which are recognize by the OCT imaging.

33. A method for performing epidural regional analgesia, comprising inserting into the spinal epidural space of an animal a drug infusion catheter comprising a front tip, an inner lumen and an optical coherence tomography (OCT) probe comprising a tip.

34. The method of Claim 33, wherein the OCT probe generates a forward-scanning imaging beam.

35. The method of Claim 34, wherein the tip of the OCT probe is positioned slightly forward of the front tip of the drug infusion catheter so as to allow the scanning beam to clear the catheter tip.

36. The method of Claim 33, wherein the OCT is a conventional radial-scanning OCT probe or a probe capable of forward- and radial-scanning.

37. The method of Claim 33, wherein the drug infusion catheter comprises an inner lumen.

38. The method of Claim 33, wherein the inner lumen of the drug infusion catheter is slightly larger than an outer dimension of the OCT probe, so as to allow saline and drugs to pass through the catheter with the OCT probe positioned within the catheter.

39. The method of Claim 33, wherein as the drug infusion catheter is advanced, OCT imaging is used to monitor the position of the catheter relative to blood vessels, and its relative position within the epidural space.

40. A method for performing high resolution diagnostic imaging of the spinal epidural space of an animal, comprising inserting into the spinal epidural space of said animal a forward- and radial-scanning OCT probe.

41. The method of Claim 40, wherein said imaging detects abnormalies.

42. The method of Claim 42, wherein said abnormalities are small herniated disc fragments.

43. The method of Claim 40, wherein the OCT probe is advanced within the epidural space towards a suspected site of nerve impingement.

44. The method of Claim 43, wherein the suspected site of nerve impingement is the neural foramen.

45. A method for performing high resolution imaging of dural tears, comprising inserting a radial scanning OCT probe in the epidural space of an animal, parallel to the dural sac.

46. A method for performing epiduroscopy, comprising inserting into the spinal epidural space of an animal an epiduroscopy instrument, wherein the epiduroscopy instrument comprises an OCT probe, and releasing adhesions in the epidural space that are compressing nerve roots.

46. A method for performing real-time, high resolution intrathecal imaging, comprising inserting into the intrathecal space of an animal an OCT probe to identify abnormal tissue.

47. The method of Claim 46, wherein the abnormal tissue comprises cancer cells

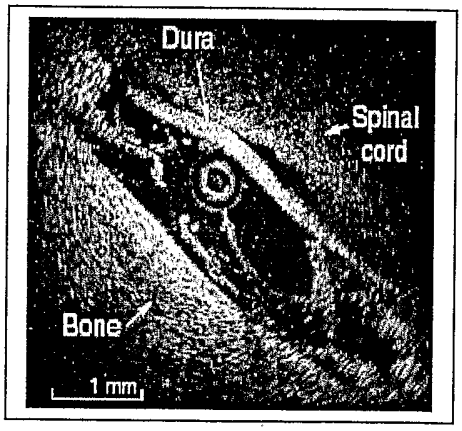
Dura
Spinal cord
Bone
1 mm

FIG. 1

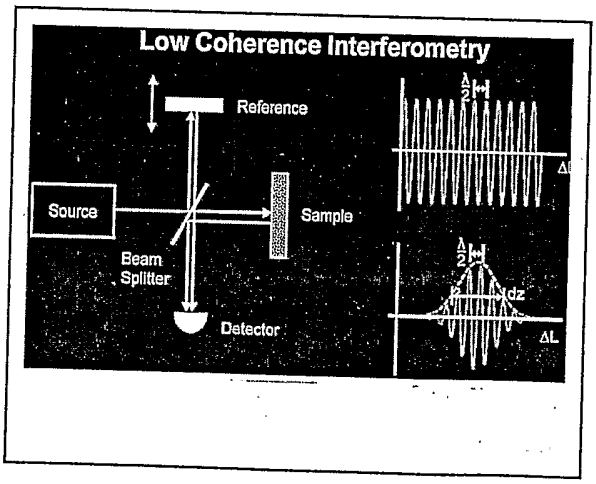
Low Coherence Interferometry
Reference
Source
Sample
Beam Splitter
Detector
dz
ΔL

FIG. 2

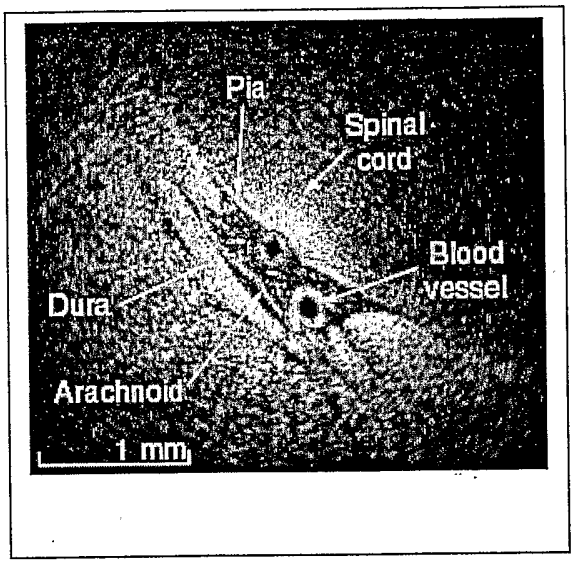

FIG. 3

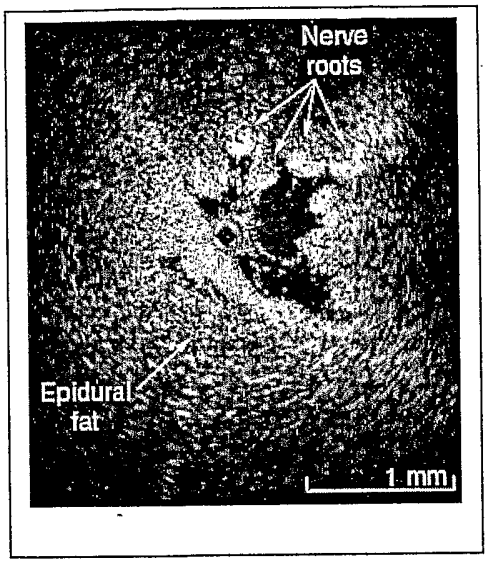

FIG. 4

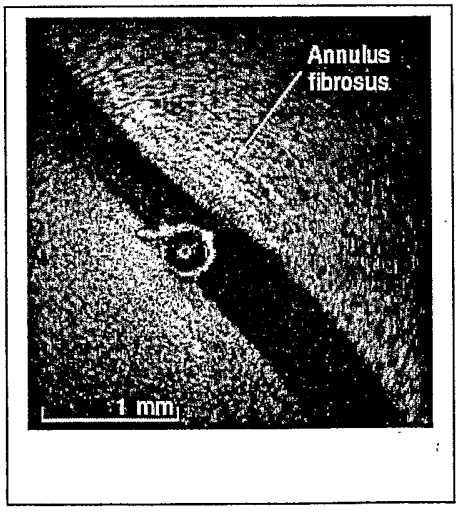

FIG. 5

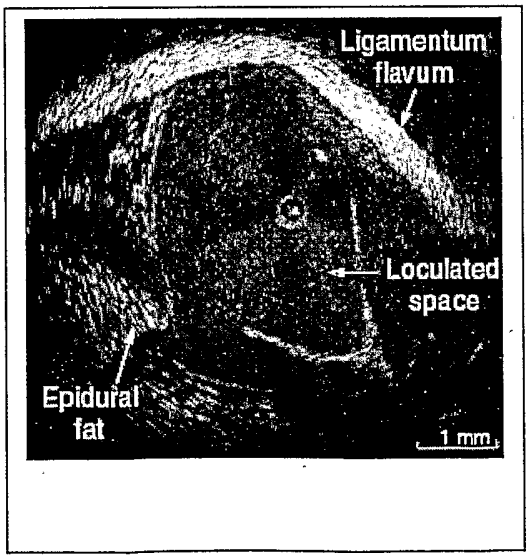

FIG. 6

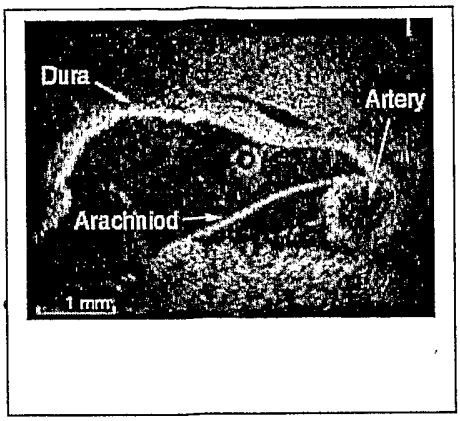

FIG. 7

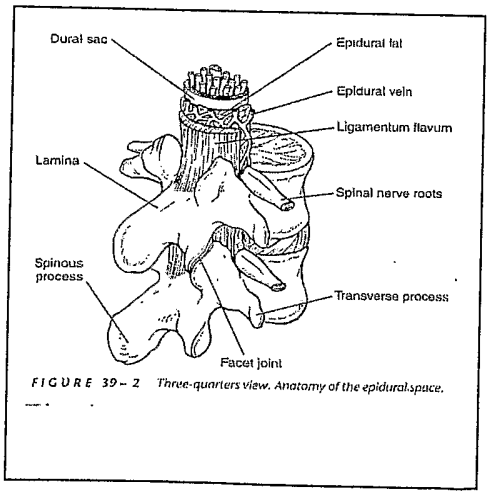

FIGURE 39–2 Three-quarters view. Anatomy of the epidural space.

FIG. 8

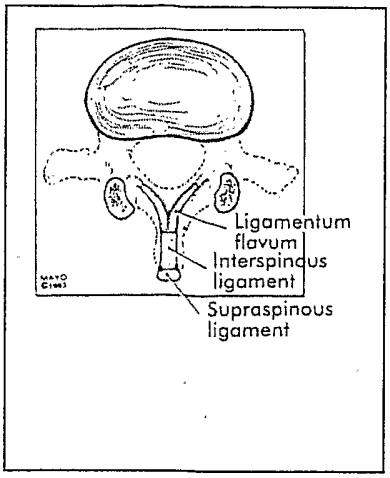
Ligamentum flavum
Interspinous ligament
Supraspinous ligament

FIG. 9

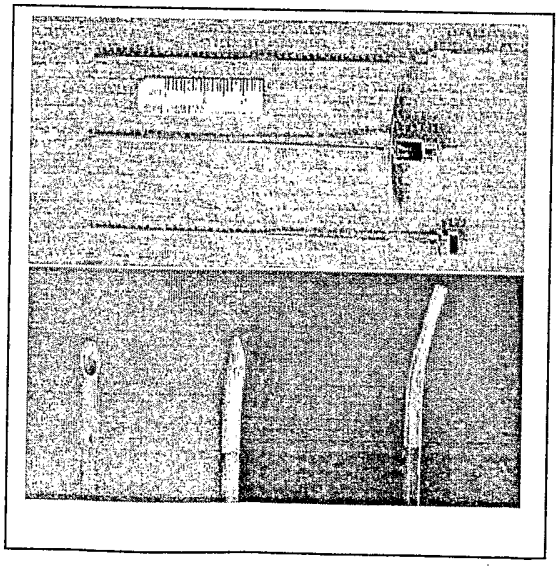

FIG. 10

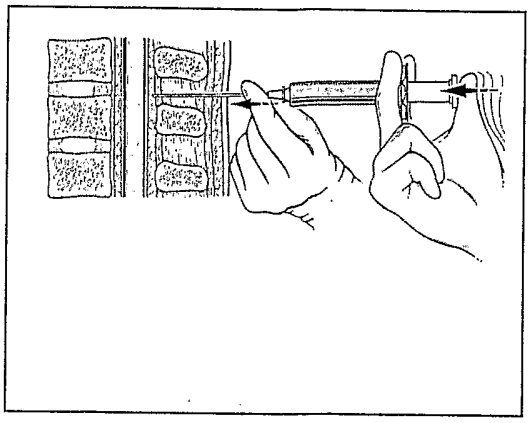

FIG. 11

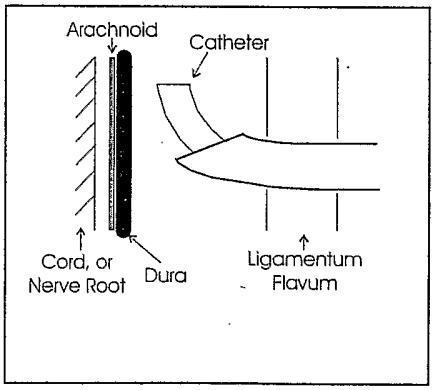
Arachnoid
Catheter
Cord, or
Nerve Root
Dura
Ligamentum
Flavum

FIG. 12

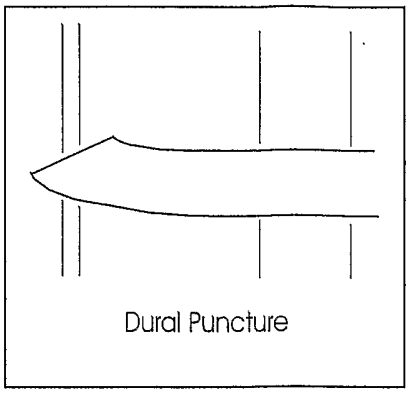

FIG. 13

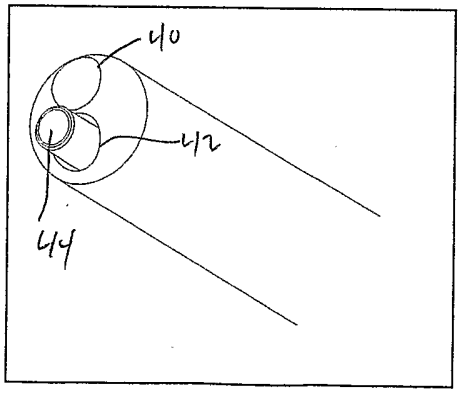

FIG. 14

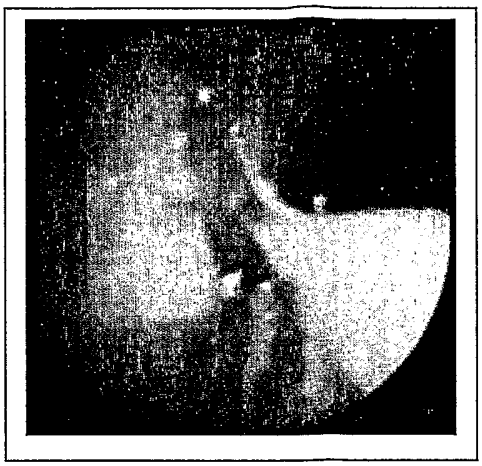

FIG. 15

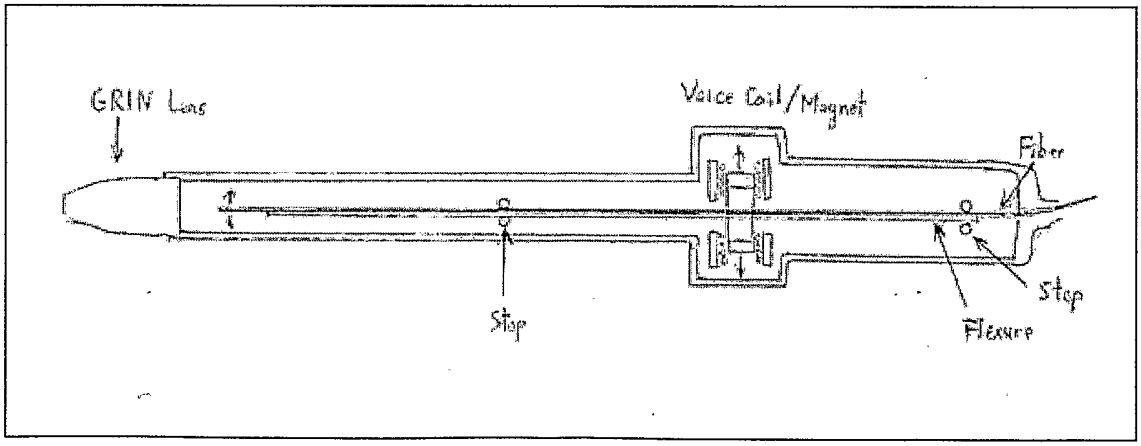

FIG. 16

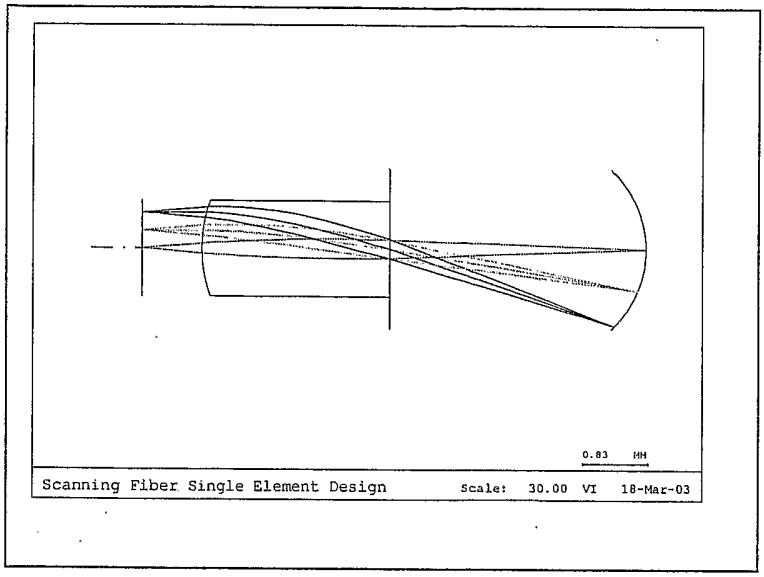
0.83 MM
Scanning Fiber Single Element Design
Scale: 30.00 VI 18-Mar-03

FIG. 17

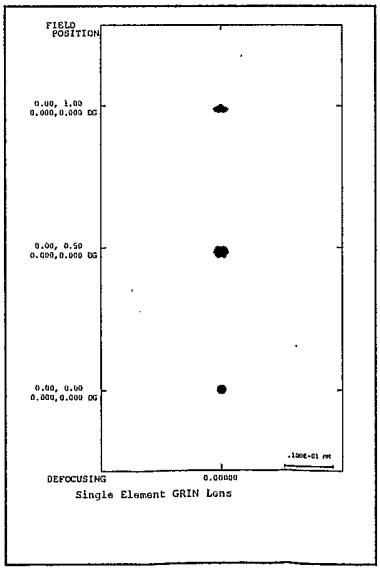
FIELD POSITION
0.00, 1.00
0.000,0.000 DG
0.00, 0.50
0.000,0.000 DG
0.00, 0.00
0.000,0.000 DG
DEFOCUSING
0.00000
Single Element GRIN Lens

FIG. 18

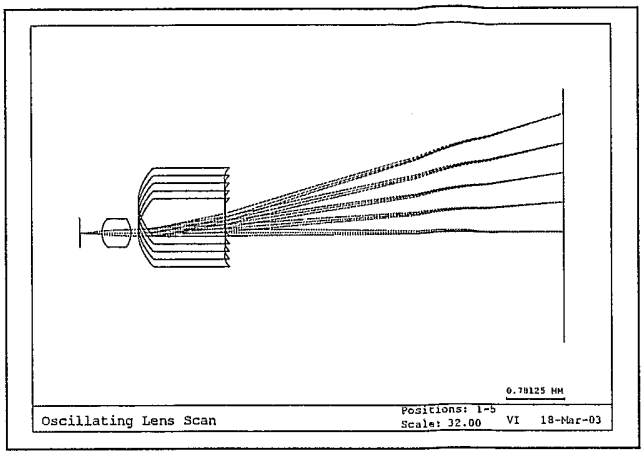
0.78125 MM
Oscillating Lens Scan
Positions: 1-5
Scale: 32.00
VI
18-Mar-03

FIG. 19

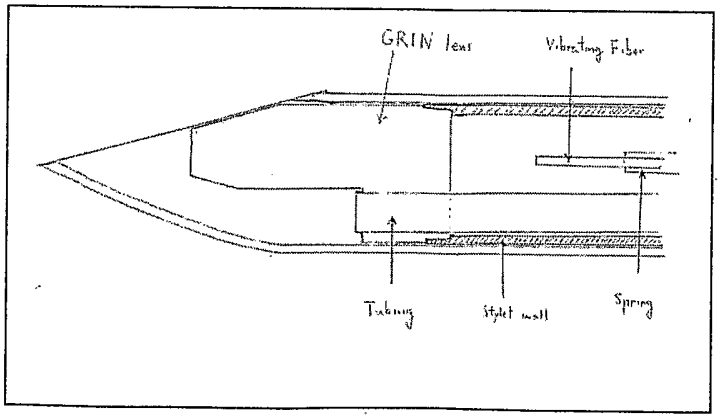
GRIN lens
Vibrating Fiber
Tubing
Stylet wall
Spring

FIG. 20

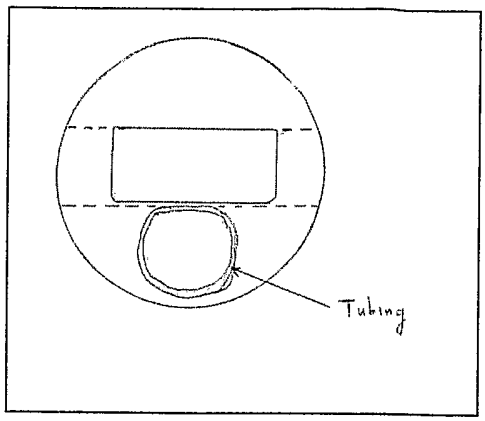
Tubing

FIG. 21

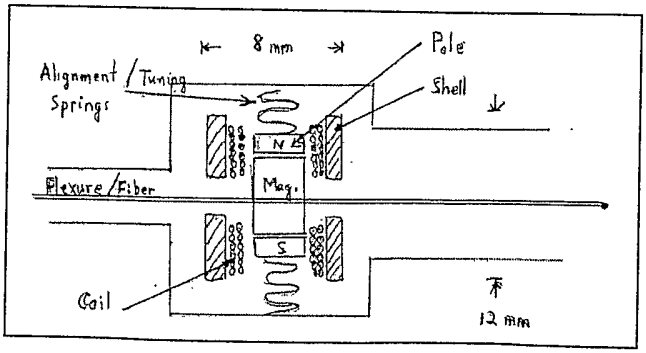
8 mm
Pole
Alignment / Tuning Springs
Shell
N
S
Mag.
Flexure / Fiber
Coil
12 mm

FIG. 22

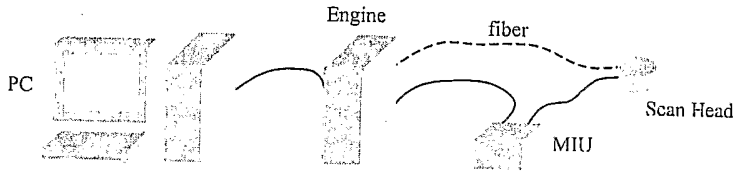

FIG. 23

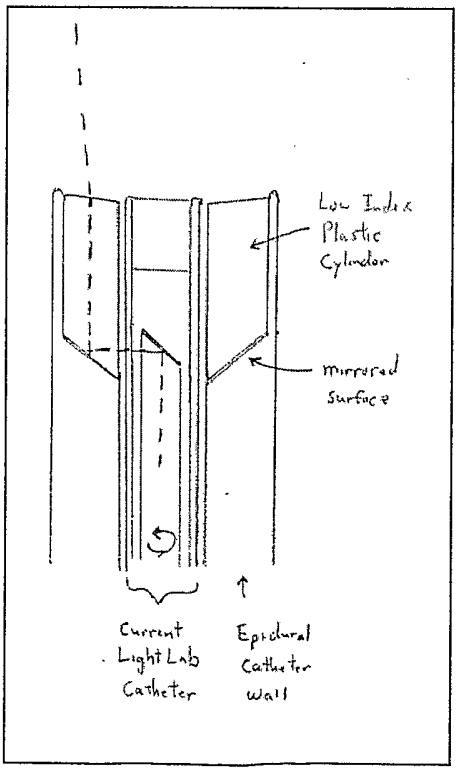

FIG. 24

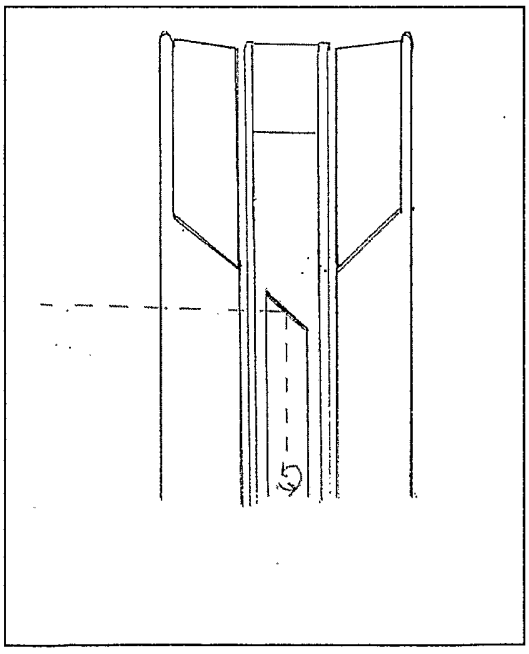

FIG. 25

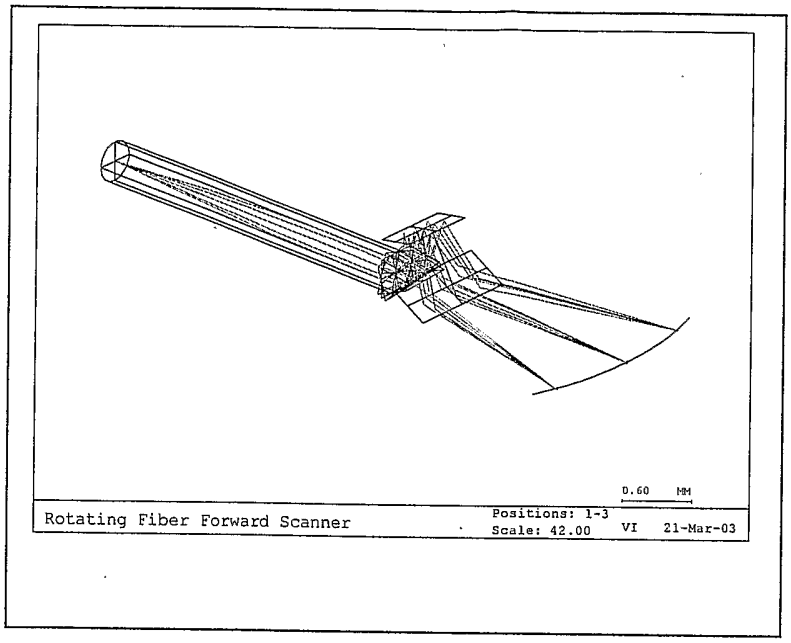
0.60 MM
Rotating Fiber Forward Scanner
Positions: 1-3
Scale: 42.00
VI 21-Mar-03

FIG. 26

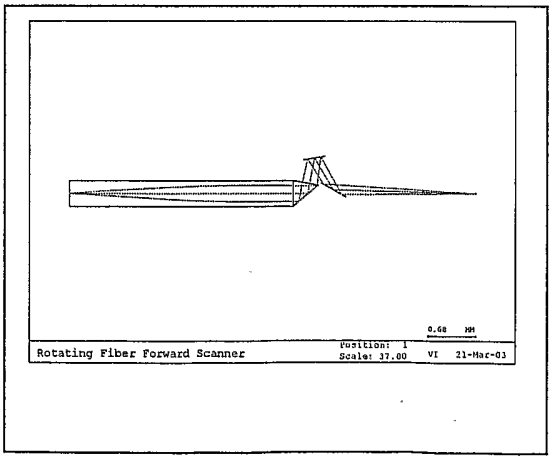
0.68 MM
Rotating Fiber Forward Scanner
Position: 1
Scale: 37.00
VI 21-Mar-03

FIG. 27

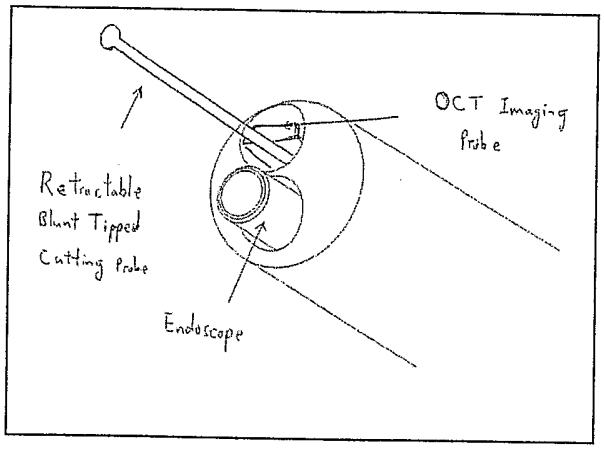
OCT Imaging
Probe
Retractable
Blunt Tipped
Cutting Probe
Endoscope

FIG. 28

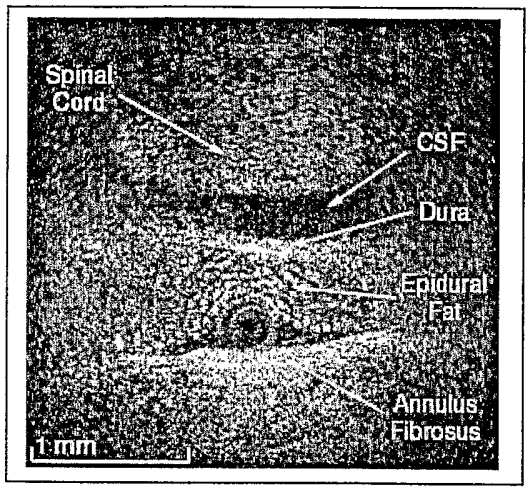

FIG. 29A

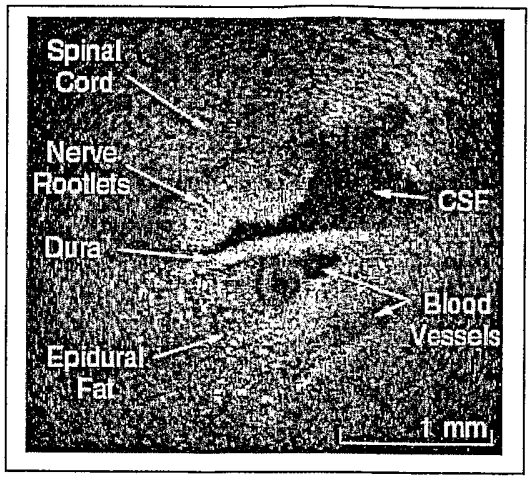

FIG. 29B

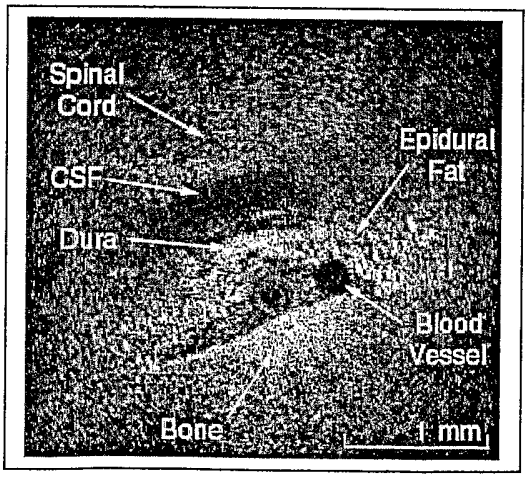

FIG. 29C

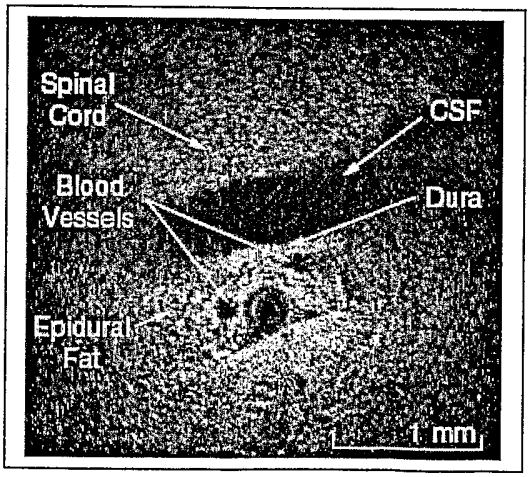

FIG. 29D

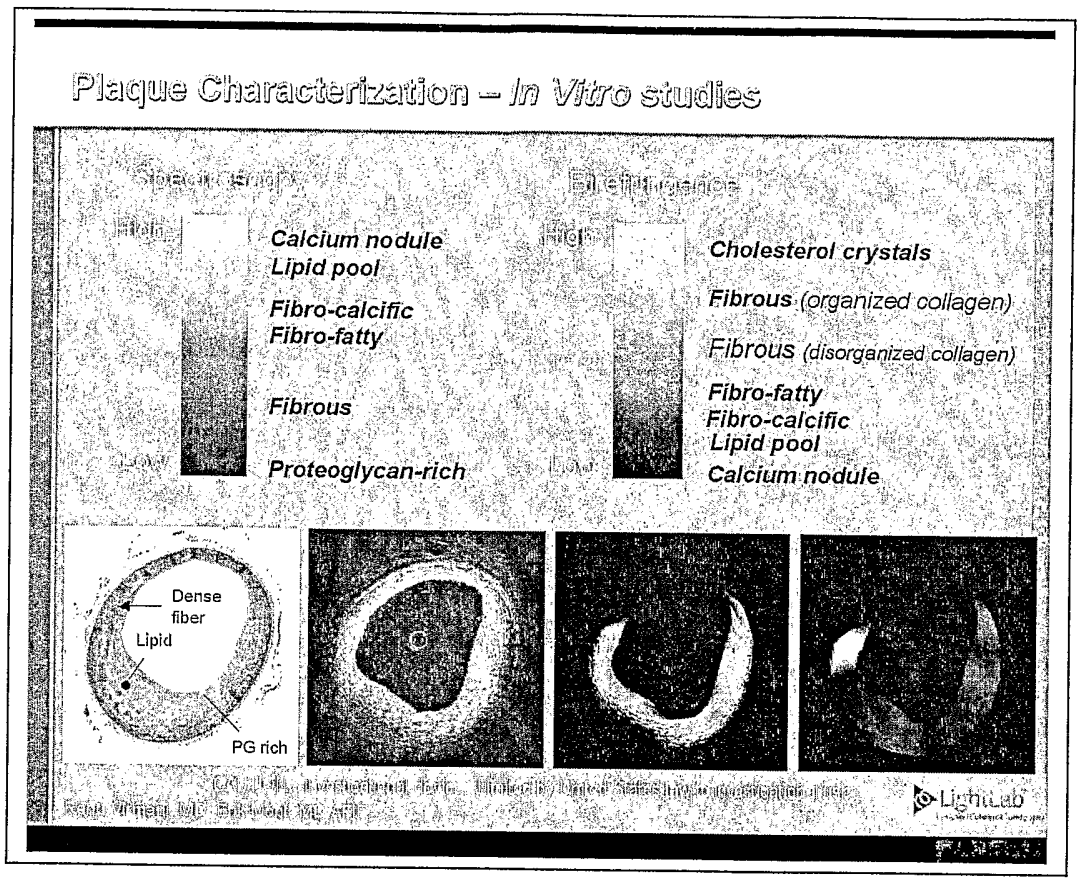
Plaque Characterization – In Vitro studies
Calcium nodule
Lipid pool
Fibro-calcific
Fibro-fatty
Fibrous
Proteoglycan-rich
Cholesterol crystals
Fibrous (organized collagen)
Fibrous (disorganized collagen)
Fibro-fatty
Fibro-calcific
Lipid pool
Calcium nodule
Dense fiber
Lipid
PG rich

FIG. 30

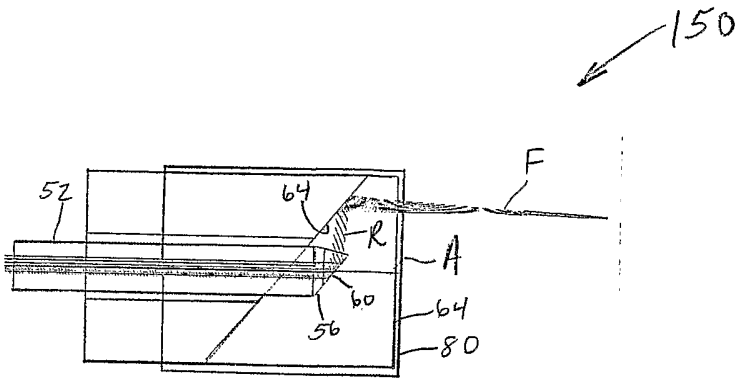
150
52
64
F
R
A
60
64
56
80

FIG. 31

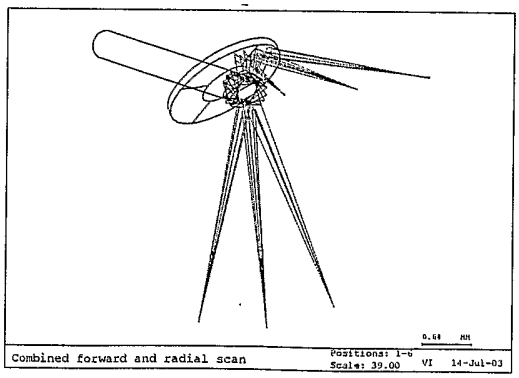
Combined forward and radial scan
Positions: 1-6
Scale: 39.00
VI
14-Jul-03

FIG. 32

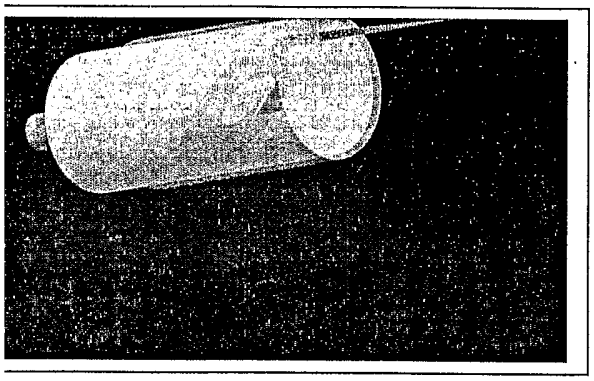

FIG. 33A

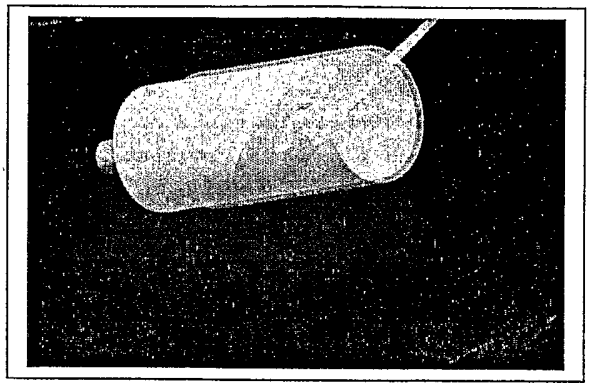

FIG. 33B

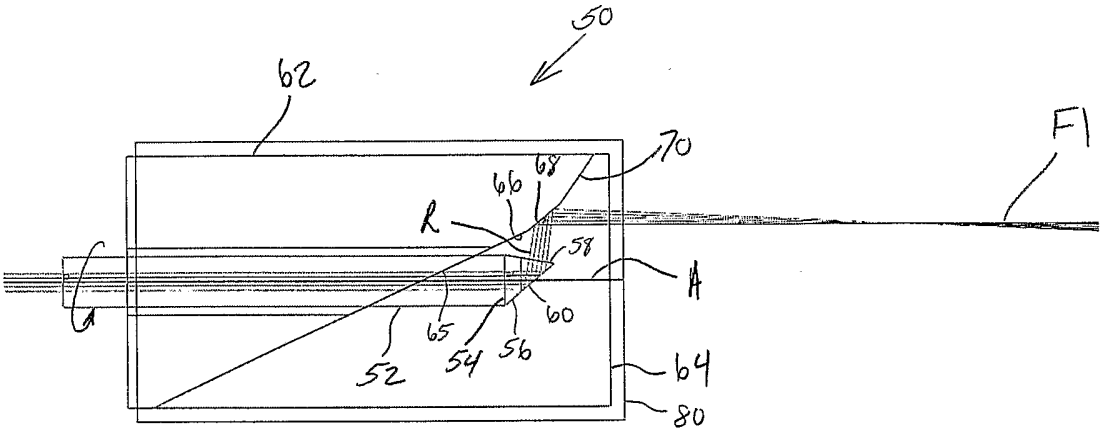
50
62
70
F1
66
68
R
58
A
65
60
52
54
56
64
80

FIG. 34

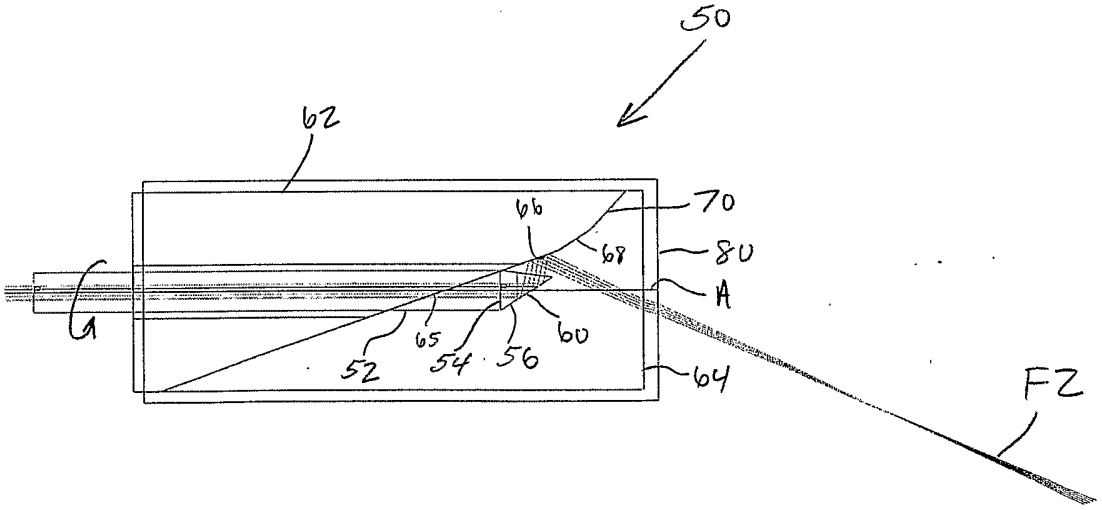
50
62
66
70
68
80
A
65
60
52
54
56
64
F2

FIG. 35

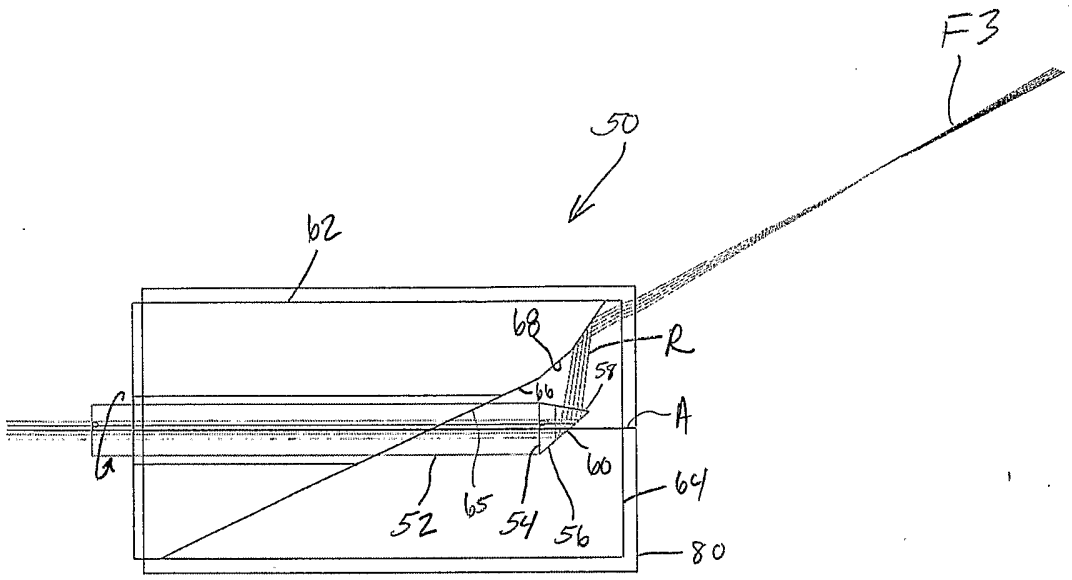

FIG. 36

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/28352

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 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)
IPC 7 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

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 134 003 A (BOPPART STEPHEN A ET AL) 17 October 2000 (2000-10-17) column 7, line 54 -column 11, line 31; figures 6-11 abstract	1-20
X	WO 98 38907 A (MASSACHUSETTS INST TECHNOLOGY) 11 September 1998 (1998-09-11) page 28; figures 6-8,12,13,18,21,23,28B	1-20

-/--

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

[X] Patent family members are listed in 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
8 December 2003	19/12/2003

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, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Rodríguez Cossío, J

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/28352

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	BOPPART S A ET AL: "FORWARD-IMAGING INSTRUMENTS FOR OPTICAL COHERENCE TOMOGRAPHY" OPTICS LETTERS, OPTICAL SOCIETY OF AMERICA, WASHINGTON, US, vol. 22, no. 21, 1 November 1997 (1997-11-01), pages 1618-1620, XP000726918 ISSN: 0146-9592 cited in the application	
A	US 5 957 941 A (REAM JOHN H) 28 September 1999 (1999-09-28)	
A	WO 00 42906 A (MASSACHUSETTS INST TECHNOLOGY) 27 July 2000 (2000-07-27)	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/28352

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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.: 21-47
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
Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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

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

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

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

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

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

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

INTERNATIONAL SEARCH REPORT

nation on patent family members

International Application No
PCT/US 03/28352

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
US 6134003	A	17-10-2000	US	5748598 A	05-05-1998
			US	5459570 A	17-10-1995
			AU	1977597 A	16-09-1997
			EP	0883793 A1	16-12-1998
			JP	2000503237 T	21-03-2000
			JP	2002214127 A	31-07-2002
			US	6485413 B1	26-11-2002
			US	6111645 A	29-08-2000
			WO	9732182 A1	04-09-1997
			US	6160826 A	12-12-2000
			US	6564087 B1	13-05-2003
			US	6501551 B1	31-12-2002
			US	6282011 B1	28-08-2001
			US	5956355 A	21-09-1999
			US	2001036002 A1	01-11-2001
			WO	9701167 A1	09-01-1997
			US	5784352 A	21-07-1998
			WO	9723870 A1	03-07-1997
			WO	9533970 A1	14-12-1995
			DE	69227902 D1	28-01-1999
			DE	69227902 T2	17-06-1999
			EP	0581871 A1	09-02-1994
			JP	6511312 T	15-12-1994
			WO	9219930 A1	12-11-1992
			US	5465147 A	07-11-1995
			US	5321501 A	14-06-1994
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			JP	2001515382 T	18-09-2001
			US	6485413 B1	26-11-2002
			WO	9838907 A1	11-09-1998
US 5957941	A	28-09-1999	WO	9812967 A1	02-04-1998
WO 0042906	A	27-07-2000	US	6564087 B1	13-05-2003
			WO	0042906 A2	27-07-2000