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(54) **SYSTEM AND METHOD FOR THERAPY AND DIAGNOSIS COMPRISING OPTICAL COMPONENTS FOR DISTRIBUTION OF RADIATION**

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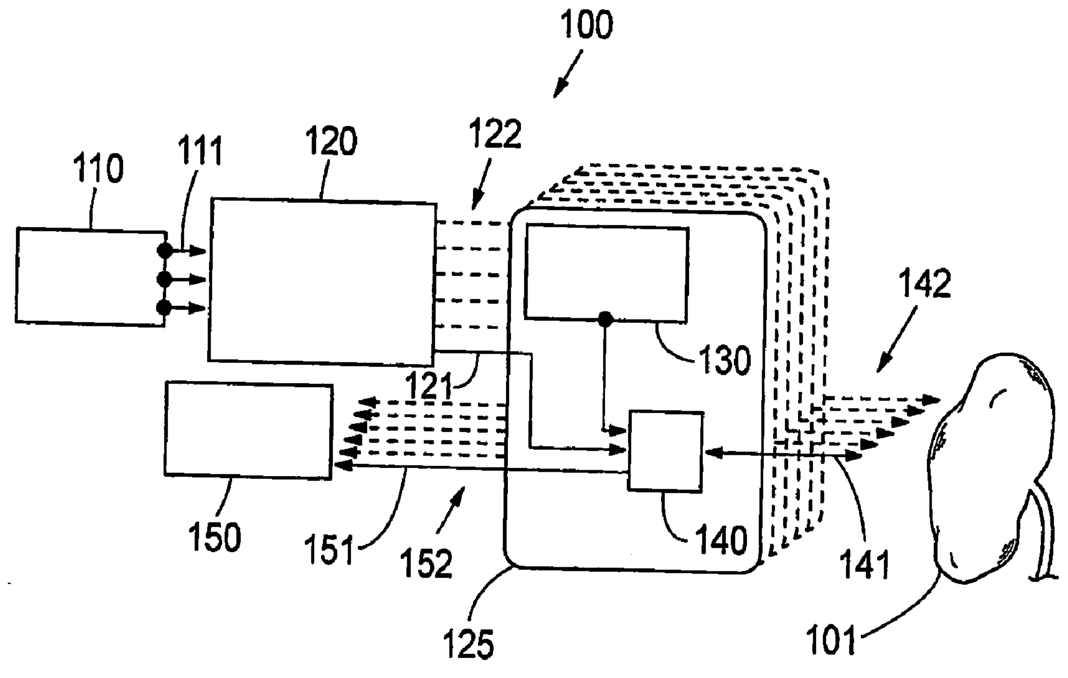
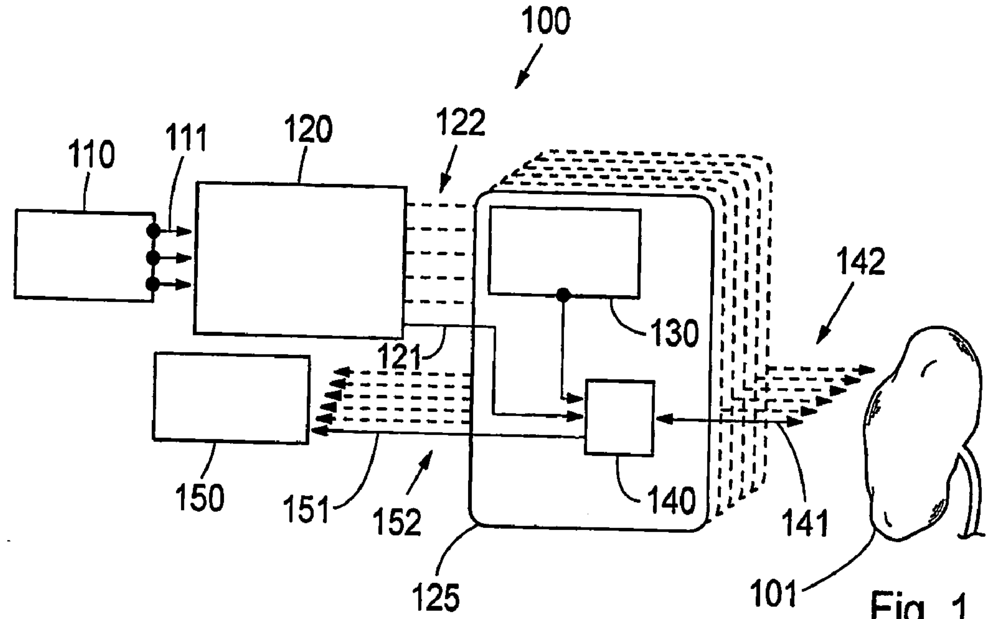
(57) **ABSTRACT**

A system and method for interactive therapy and diagnosis of a human or animal comprising at least one first radiation source for emission of a diagnostic radiation, at least one second radiation source for emission of a therapeutic radiation, and at least one radiation conductor adapted to conduct radiation to a tumour site at or in said human or animal. A non-mechanical operation mode selector directs the therapeutic radiation and/or the diagnostic radiation to the tumour site through the radiation conductors. The operation mode selector means is preferably a non-mechanical optical switch and/or an optical combiner. The system may be used for interactive interstitial photodynamic tumour therapy.




100
110
111
120
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142
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121
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125
101

Fig. 1

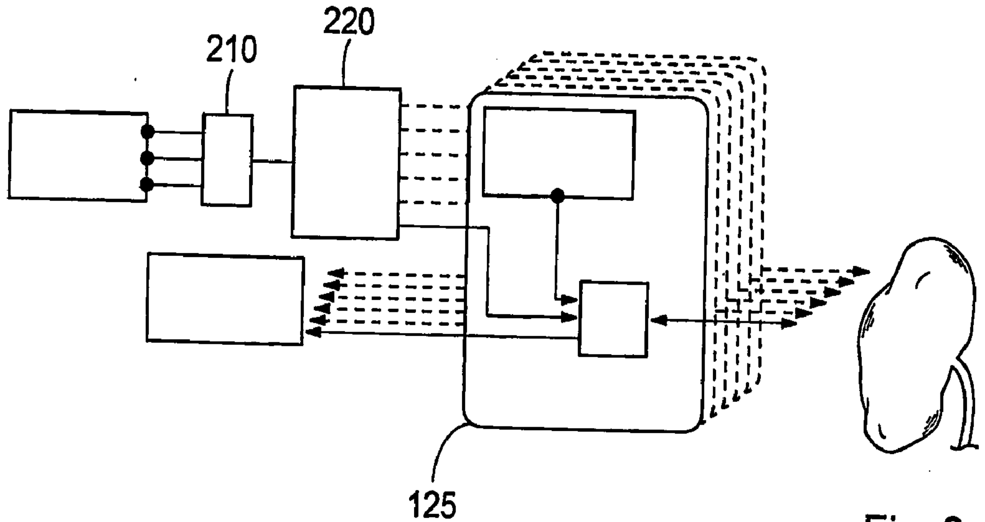
210
220
125

Fig. 2

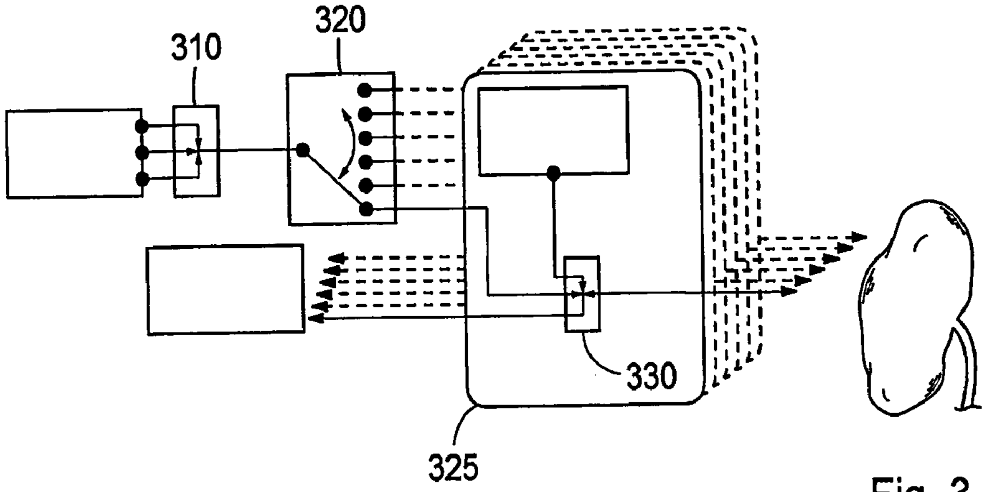

Fig. 3

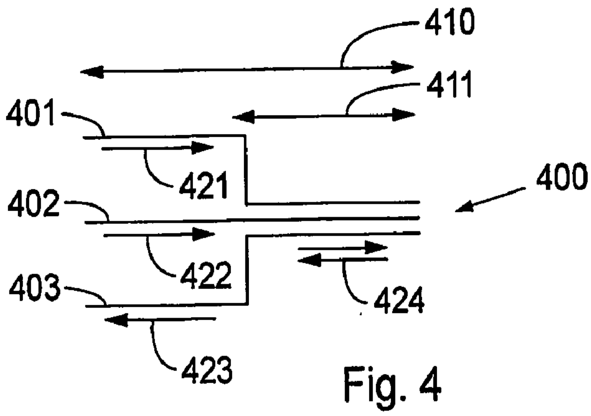

Fig. 4

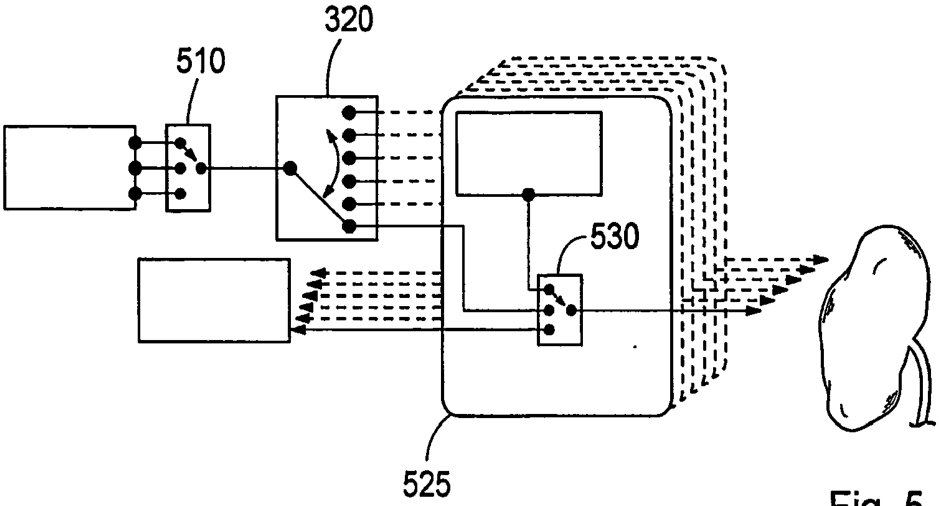

Fig. 5

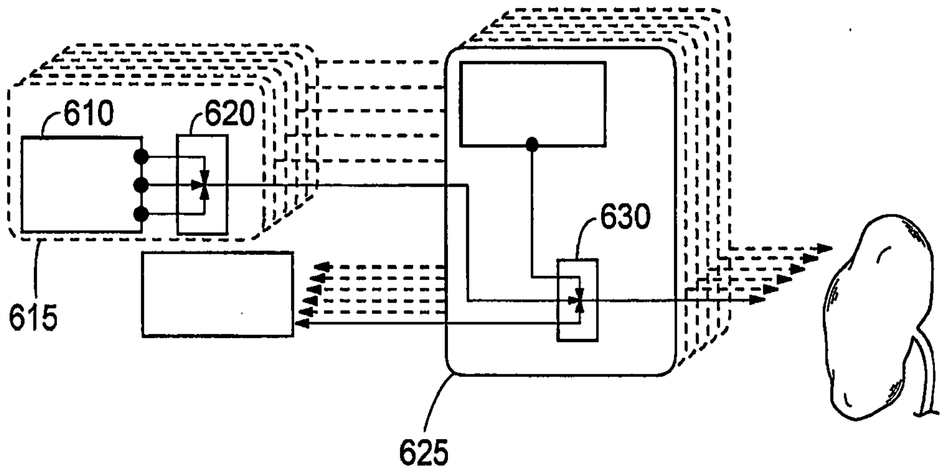

Fig. 6

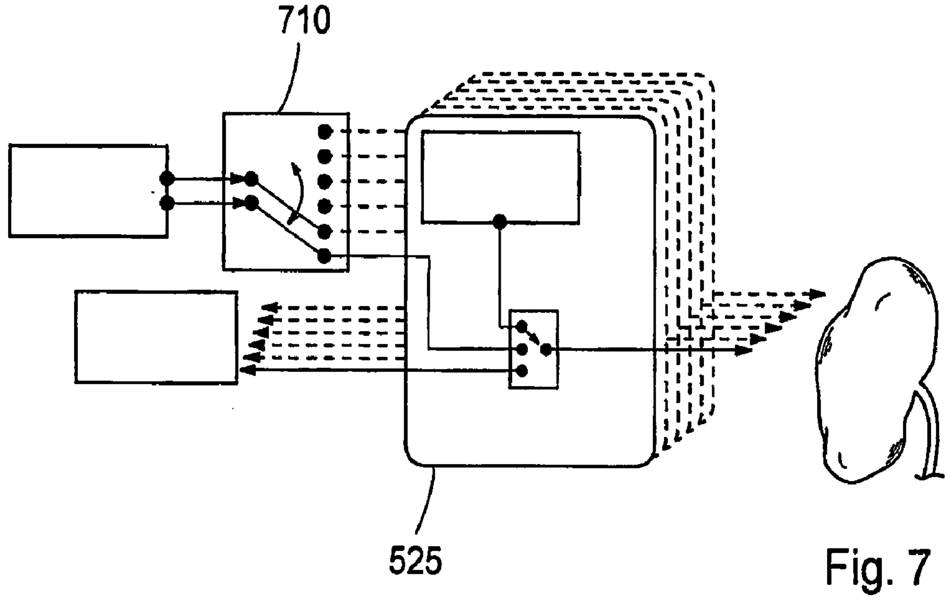

Fig. 7

SYSTEM AND METHOD FOR THERAPY AND DIAGNOSIS COMPRISING OPTICAL COMPONENTS FOR DISTRIBUTION OF RADIATION

FIELD OF THE INVENTION

[0001] The invention relates generally to a system and a method for therapy and diagnosis in a subject. More particularly, the system and method relate to a system and method for tumour therapy and diagnosis in a human or animal subject. Even more particularly, the invention relates to a system and method for photodynamic therapy (PDT) and/or photothermal therapy (PTT) and/or photodynamic diagnosis (PDD) of a site on and/or in a human or animal body, wherein electromagnetic non-ionising radiation is conducted to the site for reaction with the radiation, wherein the system comprises an operation mode selector for distribution of radiation from at least one source of radiation to a reaction site, and/or from the reaction site to at least one radiation sensor, respectively, and wherein the reaction site generally is a tumour site with a tumour, such as a malignant tumour.

BACKGROUND OF THE INVENTION

[0002] Within the field of medical therapy of tumour diseases, a plurality of treatment modalities has been developed for the treatment of malignant tumour diseases: operation, cytostatic treatment, treatment with ionising radiation (gamma or particle radiation), isotope therapy and brachytherapy employing radioactive needles are examples of common treatment modalities. In spite of great progress within therapy, the tumour diseases continue to account for much human suffering, and are responsible for a high percentage of deaths in western countries. A relatively new treatment modality, photodynamic therapy, commonly abbreviated PDT, provides an interesting complement or alternative in the treatment field. A tumour-seeking agent, normally referred to as a precursor or sensitizer, is administered to the body e.g. intravenously, orally or topically. It generally accumulates in malignant tumours to a higher extent than in the surrounding healthy tissue. The tumour area is then irradiated with non-thermal red light, normally from a laser, leading to excitation of the sensitizer to a more energetic state. Through energy transfer from the activated sensitizer to the oxygen molecules of the tissue, the oxygen is transferred from its normal triplet state to the excited singlet state. Singlet oxygen is known to be particularly toxic to tissue; cells are eradicated and the tissue goes in necrosis. Because of the localisation of the sensitizer to tumour cells a unique selectivity is obtained, where surrounding healthy tissue is spared. The clinical experiences, using in particular haematoporphyrin derivative (HPD) and delta aminolevulinic acid (ALA) have shown good results.

[0003] Sensitizers may also exhibit a further useful property; when the substance is excited with visible or ultraviolet radiation it will yield a characteristic fluorescence signal, shifted towards longer wavelengths. This signal clearly appears in contrast to the endogenous fluorescence of the tissue, which is also called autofluorescence, and is used to localise tumours and for quantifying the size of the uptake of the sensitizer in the tissue.

[0004] The limited penetration in the tissue of the activating red radiation is a big drawback of PDT. The result is that only tumours less than about 5 mm thickness can be treated by surface irradiation. In order to treat thicker and/or deep-lying tumours, interstitial PDT (IPDT) can be utilised. Here, light-conducting optical fibres are brought into the tumour using, e.g. a syringe needle, in the lumen of which a fibre has been placed.

[0005] In order to achieve an efficient treatment, several fibres have been used to ascertain that all tumour cells are subjected to a sufficient dose of light so that the toxic singlet state is obtained. It has been shown to be achievable to perform dose calculations of the absorptive and scattering properties of the tissue. E.g., in the Swedish patent SE 503 408 an IPDT system is described, where six fibres are used for treatment as well as for measurement of the light flux which reaches a given fibre in the penetration through the tissue from the other fibres. In this way an improved calculation of the correct light dose can be achieved for all parts of the tumour.

[0006] According to the disclosure of SE 503 408, the light from a single laser is divided into six different parts using a beamsplitter system comprising a large number of bulky mechanical and optical components. The light is then focused into each of the six individual treatment fibres. One fibre is used as a transmitter while the other fibres are used as receivers of radiation penetrating the tissue. For light measurement light detectors are mechanically swung into the beam path which thus is blocked, and the weak light, which originates from the fibres that collected the light which is administered to the tissue, is measured.

[0007] However, such open beam paths result in a strongly lossy beamsplitting and the resulting losses of light drastically impair the light distribution as well as the light measurement. Furthermore, such a system must often be adjusted optically, which is also an important drawback in connection with clinical treatments. The system is also large and heavy and difficult to integrate into a user-friendly apparatus.

[0008] EP-A2-0280397 discloses a sterilizable endoscope of small diameter having a central coherent fibre bundle for carrying an image to a viewing means. The fibre bundle is surrounded by light fibres. The proximate end of the endoscope is provided with a coupling means for aligning the optical fibre bundle with the optical system of the viewing means and for providing an interface with light transmitting means to transmit light from a light source along the light fibres to a body cavity to be inspected. The device can be used for detection of cancer cells and treatment thereof by phototherapy. A dye is attached to the tissue being examined and subsequently exposed to an exciting laser light frequency. Cancer cells will emit fluorescent light at a characteristic fluorescence frequency. The fluorescence light is detected and displayed on the video monitor and light with the same frequency as this fluorescent light is then transmitted through the light fibres to the cell for phototherapy treatment. However, only the use of a single wavelength light source is disclosed, it is thus not possible to have multiple diagnostics performed without manually exchanging the light source. Moreover, it is not possible to switch between different constellations of the light fibres, i.e. all fibres always have the same function (light in or light out). The coupling means mentioned in EP-A2-0280397 is only used to adjust the path of light through a two-part endoscope when it is assembled prior to use. In addition, different fibres are used for directing therapeutic light to a cancer location and to direct diagnostic light back through the endoscope. No distribution is performed between different operating modes. This solution offers for instance neither interactive treatment nor tomographic mapping of tumours. WO-A1-02074339 discloses a device and method for photodynamic diagnosis of tumour tissue by using fluorescent cobalamins. These fluorescent cobalamins are used as diagnostic and prognostic markers (a) to distinguish cancer cells and tissues from healthy cells and tissues, and (b) to determine if an individual responds positively to chemotherapy using cobalamin-therapeutic bioconjugates. An apparatus is disclosed that includes a camera coupled to the proximal end of a surgical telescopic device. The surgical telescopic device is used for illuminating tissue with non-white light and detecting the emitted fluorescence for diagnostic purposes. The use of a dual light sources including a red (non-white) and a white light source is disclosed. The white light source is used for conventional illumination of the tissue. A switch is mentioned for switching between the alternative light sources. The switch might be voice-actuated, mechanically-operated (foot pedal), optically-operated, or electronically-operated. The switch is not described in more detail, except that a mirror or prism under mechanical or electromechanical control can be used to switch between the two light sources. Alternatively, a light source with two physically separated outputs is disclosed. In this case the light input to the surgical telescopic device has to be moved between the two outputs in order to switch illumination source for the tissue. The device is not suitable for therapy. Therapy has to be performed conventionally by a surgeon removing the cancerous tissue detected by means of fluorescence. Therefore, this device is not suited for interactive diagnosis and therapy. Furthermore, there is no indication for a switch suitable for switching between different modes of diagnosis or therapy. Furthermore, the disclosed device offers only substantially superficial diagnosis or treatment, interstitial tissue cannot be diagnosed or treated. The device is also limited to existing body cavities and has the drawback that endoscopic probes are bulky and large compared to single optical fibres.

[0009] EP-A2-0195375 discloses a catheter for laser angiosurgery. The device is used for detecting atherosclerotic plaque deposits by means of detecting fluorescent light as a reaction on excitation light sent through the catheter comprising optical fibres for this purpose. The same fibre may be used for sending excitation light to the plaque and for receiving fluorescent light from the plaque. When plaque is detected, it may be removed by sending high energy light through selected fibres in the catheter. However, this system is not suited for diagnosis or treatment of tumours. Fibres to be illuminated are selected by purely mechanical arrangements either moving the light source or the fibres in order to align the two towards each other. This device is also bulky compared to single fibres, similar to the above mentioned endoscope, bound to existing body cavities and works substantially superficial. Furthermore it is not selective, i.e. all tissue aimed at is destroyed, independently if it is noxious or healthy.

[0010] Thus, there is a need for a new compact device allowing distributing of radiation in a system for PDD, PDT and PTT for implementing a smart way of performing interactive interstitial treatment. One solution would be to use smart mechanical constructions for switching between different modes avoiding e.g. the lossy beamsplitters and allowing e.g. automatic calibration.

[0011] Such a mechanical solution to the above mentioned problems has been proposed in PCT/SE02/02050, wherein a distributor for radiation having two discs rotating relative to each other is described. The radiation distributor couples optical fibres between different modes by rotational movement of fibres in these discs relative each other. For switching between several light sources to one fibre going to the patient, an assembly with a total of four discs is described.

[0012] However, although these mechanical constructions are improvements to the above described known IPDT system and although the above described problems are solved, these mechanical solutions have other limitations, related to e.g. mechanical inertia limiting the switching time between the different modes of a therapy and diagnosis system such as an interactive interstitial treatment system.

[0013] Thus, there is a need for a new compact device allowing distributing of radiation in a system for therapy and diagnosis in a human or animal, wherein the therapy and diagnosis comprises PDT, PTT, and PDD.

[0014] Further problems to be solved by the invention are to provide an alternative solution eliminating the service of components e.g. due to wear of components, thus improving reliability of a device for therapy and diagnosis comprising PDT, PTT, and PDD. Also, the rotation of the fibres should be avoided, which further reduces the necessary size of the device and increases reliability. Furthermore, another problem solved by the invention is that sounds or noises that are generated in operation of known devices when switching between different operation modes are substantially reduced or eliminated.

SUMMARY OF THE INVENTION

[0015] The present invention overcomes the above identified deficiencies in the art and solves at least the above identified problems by providing a system and a method according to the appended patent claims, wherein a very practical and efficient implementation of interactive IPDT is achieved in that different optical measurements for diagnostics and dosimetry can be performed in an integrated and simple way by means of a system requiring minimal space. An important application of the invention is interactive, interstitial photodynamic therapy, and/or interactive photothermal tumour therapy.

[0016] The term "radiation" used hereinafter in this specification refers to radiation suitable for the field of the invention, i.e. for photodynamic therapy (PDT) and/or photothermal therapy (PTT) and/or photodynamic diagnosis (PDD). More specifically this radiation is "optical" radiation, i.e. non-ionising electromagnetical radiation within the wavelength-range of infrared (IR), visible or ultraviolet light. This also concerns radiation sources, radiation conductors, radiation sensors, radiation switches etc. within the scope of the embodiments and claims defining the invention, i.e. these sources, conductors or sensors for "radiation" are adapted to generate, conduct, measure, etc. the above-mentioned non-ionising radiation.

[0017] According to one aspect of the invention, a system for therapy and/or diagnosis of a human or animal comprises at least one first radiation source for emission of a diagnostic radiation and at least one second radiation source for emission of a therapeutic radiation, and at least one first radiation conductor adapted to conduct radiation to a site of the human or animal. The system comprises an operation mode selector means for optically directing either said therapeutic radiation or said diagnostic radiation to said site through said at least one first radiation conductor.

[0018] According to an embodiment of the invention, the system for therapy and/or diagnosis of a human or animal is a system and method for interactive interstitial photodynamic tumour therapy and/or photothermal tumour therapy and/or tumour diagnosis.

[0019] The use of non-mechanical switching elements based on optical principles offers several advantages over mechanical arrangements. Among others, these advantages comprise: high switching speed between different system operation modes (diagnosis, photodynamic therapy, thermal therapy); compactness and stability of the system; excellent optical parameters; long life of the system due to no mechanical wear of the components and due to many more switching cycles during a life-cycle of the elements of the system; and no switching noise, thus offering increased patient comfort.

BRIEF DESCRIPTION OF THE DRAWINGS

[0020] In order to explain the invention more detailed, a number of embodiments of the invention will be described below with reference to the appended drawings, wherein

[0021] FIG. **1** is a schematic view illustrating an embodiment of the invention for interactive IPDT;

[0022] FIG. **2** is a schematic view illustrating another embodiment of the invention;

[0023] FIG. **3** is a schematic view over a further embodiment of the invention comprising optical combiners and a non-mechanical optical switch;

[0024] FIG. **4** is a schematic view illustrating the principle of an optical combiner used in an embodiment of the invention;

[0025] FIG. **5** is a schematic view illustrating another embodiment of the invention comprising non-mechanical optical switches;

[0026] FIG. **6** is a schematic view showing yet a further embodiment of the invention comprising modules with multiple diagnostic radiation sources; and

[0027] FIG. **7** is a schematic view showing yet a further embodiment of the invention comprising a 2×N non-mechanical optical switch.

DESCRIPTION OF EMBODIMENTS

[0028] Different embodiments of the system according to the invention are now described with reference to the drawings. In order to simplify the description of the embodiments, reference numerals for similar elements shown in the drawings are not repeated throughout all the figures.

[0029] A general description of a system **100** according to a first embodiment of the invention is given with reference to FIG. **1**. Accordingly, a system **100** for interactive IPDT comprises at least one diagnostic radiation source **110**. The diagnostic radiation source **110** generates a diagnostic radiation. The optical radiation from at least one diagnostic optical radiation source **110** enters a diagnostic optical radiation coupling module **120**. The optical radiation is preferably transmitted by means of optical radiation conductors **111**. In general, the radiation conductors, described in this description of embodiments, are light guides such as optical fibres. The diagnostic radiation coupling module **120** distributes the radiation further through one or more radiation conductors **122** to at least one corresponding operation mode selection module **140**. The coupling of the diagnostic radiation to the radiation conductors **122** is accomplished by means of the diagnostic radiation coupling module **120**, which e.g. comprises a non-mechanical optical switch or alternatively an optical combiner in series with a non-mechanical optical switch or alternatively with an optical combiner. This will be explained in more detail below.

[0030] The diagnostic radiation is further conducted to one of the operation mode selection modules **140**, as shown in FIG. **1**. The purpose of each operation mode selection module **140** is to guide diagnostic radiation from one of the diagnostic radiation sources **110** or therapeutic radiation from therapeutic radiation sources **130** through one of radiation conductors **142** to a treatment site **101** in a patient. All these radiation conductors **142** can transmit radiation to the reaction site **101** and receive radiation from said site. Thus, several measurements can be recorded and read out simultaneously. Each of the fibres **142** is proximally coupled to a separate operation mode selection module **140**, e.g. fibre **141** is coupled to the operation mode selection module **140** illustrated as the first operation mode selection module of a plurality **125** of operation mode selection modules **140**/ therapeutic radiation sources **130** in FIG. **1**. The distal end of fibres **142** are appropriately positioned in different locations at the treatment site in order to enable an effective diagnosis or treatment of the patient. Moreover, the operation mode selection modules **140** couple radiation, which is transmitted from the distal end of fibres **142** back towards the operation mode selection module **140**, further towards at least one radiation detector **150**. Alternatively a plurality of radiation detectors is used, either with different sensitivities or e.g. one detector for each operation mode selection module. The radiation coming from the treatment site **101** is transmitted to the radiation detectors **150** by means of radiation conductors **152**, wherein a radiation conductor **151** is illustrated going from the topmost illustrated operation mode selection module **140** to radiation detector **150**. The operation mode selection module **140** may comprise e.g. a non-mechanical optical switch or an optical combiner. An embodiment of an operation mode selection module **140** based on an optical combiner is described in more detail below with reference to FIG. **4**.

[0031] FIG. **2** illustrates another embodiment of an interactive interstitial treatment system, wherein the diagnostic radiation coupling module **120** is subdivided into two radiation distributor components **210** and **220**. Radiation distributor **210** is as illustrated, a (N×1) radiation distributor, i.e. a radiation distributor having N radiation inputs and one radiation output. In the illustrated example, the radiation distributor **210** is a 3×1 radiation distributor, which single output is coupled to a (1×n) radiation distributor **220**, wherein n is the number of operation mode selection modules **125** as well as the number of radiation conductors **142** going to/from the treatment site **101**. Radiation distributors **210**, **220** may comprise, similar to operation mode selection module **140**, e.g. a non-mechanical optical switch or an optical combiner. Exemplary radiation distributors **210**, **220** are described in more detail below with reference to FIGS. **3** and **5** illustrating different combinations of non-mechanical optical switches and/or combiners for radiation distributors **210**, **220** and selection module **140** have different advantages concerning e.g. performance of the system.

[0032] In FIG. **3**, a system is shown comprising an optical 3×1 combiner **310** and an non-mechanical optical 1×6 switch **320** as well as an optical combiner **330** as a operation mode selector in six modules **325**. For interstitial treatment six therapeutic radiation sources **130**, preferably laser light modules, are coupled to the six optical combiners **330**. Each optical combiner **330** works in such a manner that the therapeutic radiation in therapy operation mode is coupled through the corresponding radiation conductor **142** to the treatment site **101**. For switching to the diagnostic operation mode, the therapeutic radiation source is switched off and subsequently one of the three diagnostic radiation sources **110** is activated. Thus, diagnostic radiation is conducted to combiner **310**, where the radiation from the active diagnostic radiation source is coupled to the output of the combiner leading to the non-mechanical optical switch **320**. The non-mechanical optical switch **320** couples the input radiation to an output radiation conductor **122** leading to the corresponding optical combiner **330** comprised in one of modules **325**. From combiner **330**, the diagnostic radiation is sent to the treatment site via a radiation conductor **142** connected to combiner **330**, as shown in FIG. **3**. Thus the diagnostic radiation is spread in the treatment site and partly to the remaining five radiation conductors **142** and partly reflected back. The diagnostic radiation from the patient is via combiner **330** sent to radiation detector **150**. Thus five (=(n−1)) measurement values are obtained. Subsequently the non-mechanical optical switch **320** switches the incoming diagnostic radiation from the radiation source **110** to the next combiner **330** comprised in the next module **325**. Thus five further measurement values are obtained. This measurement procedure is repeated until all six modules **325** have been activated, resulting in six times five (=30) measurement values. These thirty measurement values obtained may be used as input data for a tomographic modelling of the optical dose build up in the different parts of the tumour during the course of the treatment. This measurement procedure may be repeated with the remaining diagnostic radiation sources, yielding three times thirty (N*(n−1)) or ninety tomographic measurement values. Also the diagnostic radiation reflected at site **101** from the illuminating radiation connector may be used for diagnostic purposes.

[0033] The combiner **310** may be a fibre combiner commercially available from, e.g., Polymicro Technologies or Sedi Fibres Optiques.

[0034] As a basis for the non-mechanical optical switch **320** one may use a commercially available optical fibre switch from Piezosystem Jena Inc or Agiltron Inc. The working principle of the combiner **330** is illustrated in FIG. **4**. The combiner **330** may also be based upon a commercially available fibre combiner from Polymicro Technologies. The combiner has three input fibres **401-403**, wherein radiation is transmitted along these fibres in the directions as indicated by arrows **421-423**. The fibres **401-403** are drawn together to a single fibre along a length as indicated by arrow **411** or fused at the junction of **401**, **402**, **403**, and **424**. The whole combiner has a length as indicated by arrow **410**. Thus optical radiation is transmitted via the fibres **401** and **402** to the single fibre at **400** and radiation from the single fibre at **400** is transmitted in the opposite direction mainly to fibre **403**. In the embodiment according to FIG. **3**, fibre **401** is connected to the therapeutic radiation source, fibre **402** is connected to the diagnostic radiation source and fibre **403** is connected to the radiation detector. The combiner **330** can be made to transmit the main part of the diagnostic radiation emerging from the tissue site **101** via fibre **400** to fibre **403**, assuring an efficient use of the occasionally faint diagnostic radiation. The combiner does not transmit radiation directly from fibres **401**,**402** to fibre **403**.

[0035] FIG. **5** is a schematic diagram illustrating a further embodiment of the present invention, wherein a non-mechanical optical switch **510** switches between different diagnostic radiation sources **110**. A further non-mechanical optical switch **530** works as an operation mode selector, wherein either the therapeutic radiation source is coupled to the treatment site, the diagnostic radiation source is coupled to the treatment site, or the treatment site is coupled to the radiation detector. The non-mechanical optical switch **320** works similar as described above. This embodiment has the advantage that the time for switching from one diagnostic radiation source to another is not determined by the diagnostic radiation sources. Compared to an optical combiner, the non-mechanical optical switch **510** determines the time needed for switching between different radiation sources. This is in general more reproducible than turning off a light source at one input of a combiner and turning on another light source at another input of a combiner, wherein both light sources are coupled to the same output of the combiner. Furthermore a non-mechanical optical switch generally exhibits lower radiation losses than an optical combiner, which means that less powerful diagnostic radiation sources may be used than with optical combiner **310**. However, a non-mechanical optical switch has to be actively controlled, whereas an optical combiner is a passive component. Moreover, the non-mechanical optical switch **530** prevents reflected diagnostic radiation from entering the radiation detector **150** via a combiner, e.g. combiner **330**. This unintended diagnostic radiation going to the detector may lead to "blooming" (saturation) of the detector **150**. Instead of using a plurality of detectors **150** in order to avoid this phenomena, a single detector may be sufficient, which limits costs of the system according to the present embodiment.

[0036] FIG. **6** is a schematic diagram illustrating yet a further embodiment of the present invention. An optical combiner **630** is used similarly to the optical combiner **330**. A plurality of diagnostic radiation sources **610**, each having a corresponding combiner **620** in a plurality of diagnostic radiation source modules **615**, is comprised in this embodiment instead of an optical switch distributing the diagnostic radiation to a plurality of operation mode selection modules **140**. Thus the cost for an optical switch, e.g. switch **320**, is avoided. Furthermore the diagnostic radiation sources **610** may be modulated, so that the diagnostic radiation may be detected simultaneously by means of e.g. a lock-in technique or by multiplexing the signals.

[0037] FIG. **7** is a schematic diagram illustrating yet another embodiment of the present invention. The embodiment comprises an optical 2×n switch **710** coupling two diagnostic input radiation sources to n outputs of the switch **710**. The switch **710** has two inputs, which may arbitrarily be directed to the different outputs. Such components are commercially available from e.g. Pyramid Optics. The operation mode selector/therapeutic radiation source module is an operation mode selector module **525** as described with reference to FIG. **5**, but might also be replaced by a combiner module **625**. In this way a more compact solution is achieved, as there is one component less in the system, e.g. combiner **310** or switch **510**. An optical switch has also lower losses than a combiner, as already mentioned above.

[0038] The radiation conductors may be coupled to or connected to the different elements of the system according to the invention by any suitable method or means, including fibre optic connectors of different types, such as SMA, ST or FC connectors. Alternatively, the radiation conductors may be fixed in holes by appropriate methods, e.g. glueing or mechanically fastening by, e.g., spring loaded elements.

[0039] For calibration purposes of the system according to the invention, the overall performance of the system is recorded prior to the treatment by direct measurements on a calibrated tissue phantom made of, e.g., a sterile intralipid-water solution or a sterile solid phantom made of, e.g., Delrin®. The performance of the therapeutic radiation sources may either be monitored by internal and/or external power meters.

[0040] The non-mechanical optical switches described may work according to different principles. The switching and beam deflection is based on optical principles without mechanical movement of components such as prisms or mirrors. Examples of switching principles are for instance beam deflection by an acousto-optical means, or acousto magnetic means, or by an electrically controlled variation of the refractive index of a material through which the beam travels, thereby deflecting an optical beam to different output/input fibres. Examples for materials having a variable refractive index suitable for electro-optical switches are e.g. $LiNbO_3$, $LiTaO_3$, GaAs, HgS, CdS, KDP, ADP or SiO_2. The Agiltron™ company provides commercially available optical switches of this type, namely the CrystaLatch™ Solid-State Fiber Optic Switch family or the NanoSpeed™ Optical Switch Series. These optical switches feature fast response and ultra-high reliability exceeding 100 billion switching cycles. The Agiltron™ are an example for truly non-mechanical (zero moving parts) optical switches, which are activated by an electrical pulse inside an inorganic optical crystal to facilitate state-of-the-art switching. Switching is furthermore performed intrinsically stable against temperature fluctuation and fatigue, providing another advantage of non-mechanical switches. In addition, the Agiltron switches provide fail-safe latching capability, thereby maintaining their position indefinitely when power is removed The switches are conveniently controllable by a direct low voltage signal or digitally.

[0041] In the following section, basic principles related to the system according to the invention will be described, wherein the description is based on an exemplary system with three diagnostic radiation sources **110** and six patient radiation conductors **142**, preferably optical fibres.

[0042] By a reaction or treatment site we mean in the present context a site, where photodynamically active compounds will react in a tumour when subject to therapy radiation e.g. conducted by radiation conductors being forwarded through e.g. the lumen of injection needles which are placed in the tumour. These radiation conductors **142** are then fixed in the reaction site **101**. Then the radiation conductors are moved forward to arrive outside the distal end of the needle. The same radiation conductor **142** is used continuously during the treatment for integrated diagnostics and dosimetry as well as to avoid that the patient be subjected to multiple pricks.

[0043] Preferably the diagnostic radiation sources **110** are lasers and/or light emitting diodes, out of which one is of the same wavelength as the lasers **130** utilised for the laser irradiation for photodynamic tumour therapy, but could be of lower output power. Suitable filters can be arranged to be inserted into the light path of the radiation sensor **150** in order to secure that the correct dynamic range is utilised for all measurement tasks and in order to prevent the above mentioned "blooming" of the radiation detector.

[0044] Certain of the diagnostic radiation sources **110** are utilised in order to study how radiation (light, as defined above) of the corresponding wavelength is penetrating through the tissue of the tumour at the treatment site **101**. When radiation from a radiation source is transmitted through the particular radiation conductor via the above described arrangements into the tissue, one of the radiation conductors **142**, functions as a transmitter into the tumour, and the other five radiation conductors **142** in the tumour will act as receivers and collect the diffuse flux of radiation reaching them. The radiation collected is again conducted to the radiation sensor **150**, as described above, and five different radiation intensities can be recorded on the detector array.

[0045] As an alternative to a specific wavelength, radiation from an optically broad light source such, as a white light source, and/or broadband light emitting diodes and/or line light sources can be coupled into the particular active radiation conductor **142**. On passage through the tissue to the receiving radiation conductor **142** in the patient, the well-defined spectral distribution of the radiation source will be modified by the tissue absorption. Then, oxygenated blood yields a different signature than non-oxygenated blood, allowing a tomographic determination of the oxygen distribution utilising the thirty different spectral distributions which are read out, five spectra at a time in the six possible different constellations. Such a determination of the oxygenation in the tumour is important, since the PDT process requires access to oxygen in the tissue.

[0046] Finally, in the case of **140** being a combiner a radiation source either for visible or ultraviolet light, e.g. a laser, can be coupled to the particular active radiation conductor **142**. Then fluorescence is induced in the tissue, and a sensitizer administered to the tissue displays a characteristic fluorescence distribution shifted towards longer wavelengths. The strength of the corresponding signal allows an approximate quantification of the level of the sensitizer in the tissue.

[0047] Since the short wavelength radiation has a very low penetration into the tissue, the induced fluorescence from such a source will be a local measurement at the distal tip of the radiation conductor. For this task a filter may be inserted in front of detector **150** to reduce the reflected radiation at site **101** since the reflected radiation will be many magnitudes larger than the fluorescent radiation. A suitable self-contained equipment for doing this is described in Rev. Sci. Instr. 71, 510004 (2000).

[0048] By switching the diagnostic radiation source **110** sequentially through the different modules **125**, the fluorescence that is a specific function of the concentration of the sensitizer, is measured sequentially at the tips of the six radiation conductors. Since the sensitizer is bleached by the strong red treatment light, being particularly strong just around the tip of the radiation conductor **142** conducting radiation to the patient, it is essential to make this measurement before the start of the treatment.

[0049] If the tips of the radiation conductors **142** in addition are treated with a material, the fluorescence properties of which are temperature dependent, sharp fluorescence lines are obtained upon excitation, and the intensity of these lines and their relative strength depend on the temperature at the tip of the radiation conductor **142** being employed for treatment. Examples of such materials are salts of the transition metals or the rare earth metals. Thus also the temperature can be measured at the six positions of the six radiation conductors, one at a time or simultaneously. The measured temperatures can be utilised to find out if blood coagulation with an associated light attenuation has occurred at the tip of the radiation conductor **142** and for studies regarding the utilisation of possible synergy effects between PDT and thermal interaction. Since the lines obtained are sharp, they can easily be extracted from the more broad-banded endogenous fluorescence distribution from the tissue.

[0050] The sensitizer level can for certain substances be measured in an alternative way. Then the red light used for the light propagation studies is used to induce red or near-infrared fluorescence. This fluorescence penetrates through the tissue to the tips of the receiving radiation conductors **142**, and is displayed simultaneously as spectra obtained in the radiation sensor **150**. A tomographic calculation of the sensitizer distribution can be performed based on in total thirty measurement values at each measurement occasion.

[0051] After diagnostic measurements and calculations have been performed, the fibres **142** optically coupled to the patient can be utilised for therapy by switching off the diagnostic radiation sources and switching on the therapeutic radiation sources **130**, as well as switching optical switches, if present in the system, accordingly so that therapeutic radiation sources are coupled to the patient fibres **142**. The therapeutic radiation sources are preferably laser sources with a wavelength, chosen to match the absorption band of the sensitizer. At the photodynamic tumour treatment a dye laser or a diode laser is preferably used, with a wavelength which is selected with regard to the sensitizer employed. For e.g. Photofrin® the wavelength is 630 nm, for 8-aminolevulinic acid (ALA) it is 635 nm and for phthalocyanines it is around 670 nm, several other Sensitizers exist having such characteristic wavelengths. The individual lasers are regulated during the treatment to a desirable individual output power. If desired, they may have built-in or external monitoring detectors.

[0052] The therapeutic treatment may be interrupted and new diagnostic data may be processed in an interactive method until an optimal treatment has been reached. This method may include synergy between PDT and hyperthermia, where an increased temperature is reached at increased fluxes of laser radiation. The whole process is controlled using a computer, which does not only perform all the calculations but also is utilised for regulation and control of the system.

[0053] The present invention has been described above with reference to specific embodiments. However, other embodiments than the preferred above are equally possible within the scope of the appended claims, e.g. different optical coupler elements than those described above, performing the above method by hardware or software, etc.

[0054] Furthermore, the term "comprises/comprising" when used in this specification does not exclude other elements or steps, the terms "a" and "an" do not exclude a plurality and a single processor or other units may fulfil the functions of several of the units or circuits recited in the claims.

1-24. (canceled)

25. A system for interactive interstitial photodynamic or photothermal tumor therapy or tumor diagnosis of a human, comprising at least a first and a second light source for emission of light within the wavelength-range of infrared (IR), visible or ultraviolet light; at least one light detector, for detection of light; and a plurality of first optical fibers adapted to conduct light to or from tumor site of the human, whereby the distal ends of the optical fibers are positioned at different locations of the tumor site in order to enable an effective diagnosis and treatment, wherein at least one non-mechanical operation mode selector means for optically directing:

said therapeutic light to said tumor site, whereas one therapeutic light source is coupled to each of said optical fibers for transmission of said therapeutic light to said site through each of said optical fibers, during which the diagnostic light sources are inactivated, and said diagnostic light to said tumor site through at least one first optical fiber, whereas light is guided through at least one optical fiber from the tumor site to light detectors, during which the therapeutic light sources are inactivated.

26. The system according to claim 25, wherein said operation mode selector means is a non-mechanical optical switch.

27. The system according to claim 26, wherein said non-mechanical optical switch is an electro-optical switch based on electrically controlled refractive index variations.

28. The system according to claim 26, wherein said non-mechanical optical switch is an acousto-optical switch based on sound generated Bragg deflection.

29. The system according to claim 26, characterized in that said non-mechanical optical switch is magneto-optical switch.

30. The system according to claim 25, characterized in that said operation mode selector means is an optical combiner.

31. The system according to claim 25, wherein a plurality of said diagnostic light sources are coupled to a first operation mode selector means for transmission from said diagnostic light sources to said site, and a second operation mode selector means being coupled to transmit diagnostic light from said tumor site to said at least one light detector, wherein light from said therapeutic light source is blocked from transmission to said site by said operation mode selector means.

32. The system according to claim 31, wherein one active diagnostic light source is coupled to said first mode selector means by means of a device selected from the group comprising: an optical combiner, a non-mechanical optical switch, two non-mechanical optical switches, and a 2×N non-mechanical optical switch.

33. The system according to claim 25, wherein each operation mode selector means having a similar plurality of diagnostic light sources is coupled to each of said operation mode selector means for transmission to said site, wherein in use only one diagnostic light source is active simultaneously or said operation mode selector means is configured to couple only one diagnostic light source at a time for transmission of said diagnostic light to said site.

34. The system according to claim 33, wherein a similar plurality of diagnostic light sources are coupled to each of said operation mode selector by means of an optical combiner.

35. The system according to claim 34, wherein the light conductors second ends are treated by a material with temperature sensitive fluorescence emission.

36. The system according to claim 35, wherein said light sources are sources for coherent light of a single fixed wave-length and/or light emitting diodes.

37. The system according to claim 35, wherein fluorescence is recorded through the same light conductor as the one transmitting diagnostic light to the site.

38. The system according to claim 37, wherein for interactive photodynamic therapy one or several of the light fibers which are treated with the material with a temperature sensitive fluorescence emission are configured to measure the temperature at the site, the light which in use is sent to the site heats the treatment site, the intensity of the light sent in use is controlled by the measured temperature in order to regulate the temperature of the site at the individual light fibers.

39. The system according to claim 25, wherein said interactive therapy and diagnosis comprises the following operation modes selectable by said operation mode selector means:

interactive interstitial photodynamic tumor therapy, photothermal tumor therapy using hyperthermia, and tumor diagnostics, whereby these operation modes in use are alternatively used during the same occasion of treatment of said tumor site.

40. A method for interactive interstitial photodynamic tumor therapy or photothermal tumor therapy or tumor diagnosis, wherein at least one light detector and light fiber are connected to a tumor site and the light fiber is used as a transmitter or a receiver for conduction of light to or from a tumor site for diagnosis and therapy of a tumor at the tumor site, wherein the switching between tumor therapy and tumor diagnostics is achieved in an automated way by switching between diagnostic light and therapeutic light by means of at least one non-mechanical operation mode selector means in a system according to claim 25, and the results from the diagnostics control the therapy process by regulating a therapeutical light intensity depending on the results of the diagnostics until an optimal treatment of the tumor site has been achieved.

41. The method according to claim 40, wherein utilizing interactive interstitial photodynamic tumor therapy, photothermal tumor therapy using hyperthermia, and tumor diagnostics during the same occasion of treatment of said tumor site.

42. Use of non-mechanical optical switches and/or optical combiners in a system for interactive therapy and diagnosis of a human according to claim 25.

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专利名称(译)	用于治疗和诊断的系统和方法包括用于辐射分布的光学组件		
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摘要(译)

一种用于人或动物的交互式治疗和诊断的系统和方法，包括用于发射诊断辐射的至少一个第一辐射源，用于发射治疗辐射的至少一个第二辐射源，以及适于进行传导的至少一个辐射导体辐射到所述人或动物处或其中的肿瘤部位。非机械操作模式选择器通过辐射导体将治疗辐射和/或诊断辐射引导到肿瘤部位。操作模式选择器装置最好是非机械光学开关和/或光学组合器。该系统可用于交互式间质光动力肿瘤治疗。