Title: SYSTEM, CATHETER AND PLANNING METHOD FOR HYPERThERMIA-ADJUVANT BRACHYThERAPY

Abstract: The invention addresses the problem of optimally planning hyperthermia-adjunct brachytherapy in view of a prescribed temperature distribution and radiation dosage. It relates to a system (1) comprising an image acquisition device (3), and a catheter (5) being connected to a control device (15). By being adapted to determine in parallel a set of brachytherapy parameters as well as hyperthermia parameters, prior to introduction of said catheter into a patient, both as a function of predetermined temperature distribution and predetermined radiation dose, the system allows for efficient and reliable positioning of the catheter (5) and close approximation of temperature distribution and radiation dose to the prescribed limits. The invention further addresses the problem of radiation attenuation in hyperthermia-adjunct brachytherapy catheters by suggesting a catheter (5) comprising a main body (27) being adapted to accommodate a radiation source, wherein the main body (27) consists of a conductive polymer.
before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
System, catheter and planning method for hyperthermia-adjuvant brachytherapy

FIELD OF THE INVENTION

The invention relates to a system for image guided hyperthermia-adjuvant brachytherapy. Further, the invention relates to a catheter for use in image guided hyperthermia-adjuvant brachytherapy, in particular for use in such a system. Still further, this invention relates to a method for planning hyperthermia-adjuvant brachytherapy treatment of a patient, and a method of image guided hyperthermia-adjuvant brachytherapy treatment of a patient, comprising said planning method. Still further, this invention relates to a computer program for operating a system according to this invention.

BACKGROUND OF THE INVENTION

Brachytherapy and especially high dose rate (HDR) brachytherapy is a form of endo-radiotherapy commonly used as an effective treatment for cervical, prostate, breast, and skin cancer. It is also known to be used to treat tumors in other body parts. Brachytherapy is typically used alone or in combination with other therapies (adjuvant therapies) such as surgery, External Beam Radiotherapy (EBRT) and chemotherapy. In HDR brachytherapy, a small radioactive source on the tip of a wire, the so-called applicator, is temporarily inserted directly into the tumor tissue or in the close vicinity of the tumor tissue of the patient through one or more catheters, wherein often one single radioactive source is sequentially inserted into said catheters. Insertion of said source or sources of radiation into said catheters is typically achieved in automated fashion by robots called afterloaders. Said robots are employed to deliver the radioactive probe and programmed to allow for certain dwell times at certain insertion depths of the point source to realize a predefined radiation dose pattern. Radiation delivery is typically performed with the patient being inside a bunker, which is equipped with radioactive shielding. Loading of the catheters is accomplished after positioning of said catheters inside the patient environment. The catheters are typically positioned in the patient environment in an appropriate department (interventional radiology, surgery), prior to transfer of the patient to the bunker. Under patient environment, the body region comprising the tissue in need of treatment is understood.
Hyperthermia is known as a stand-alone cancer treatment modality, but even more importantly as adjuvant therapy with chemo or radiation therapy. A therapeutic effect is achieved by elevating the cell temperature in a specific region of the patient slightly, typically in the range from 42 °C through 46°C for a specified period of time, usually in the range from 30 through 60 minutes. Temperature values within this range are not immediately harmful to normal and tumor cells, but degenerated, malignant cells are sensitized to radio or chemo treatment due to the elevated temperatures. A number of clinical trials have been performed comparing the effect of radiotherapy alone and in combination with hyperthermia. Both tumor control and survival rate have been shown to significantly improve without considerable increase in side effects, as for example discussed by Wust, Hildebrandt, Sreenivasa, et al. in "Hyperthermia in combined treatment of cancer", The Lancet Oncology 2002 volume 3 number 8, pages 487-497. The combination of hyperthermia and radiotherapy may therefore be used to reduce overall dose and radiation-induced side effects.

The combination of HDR brachytherapy with interstitial RF hyperthermia has been demonstrated in prostate cancer, as discussed by Prionas et al. in "Thermometry of interstitial hyperthermia given as an adjuvant to brachytherapy for the treatment of carcinoma of the prostate", International Journal of Radiation Oncology Biology Physics 1994, volume 28, pages 151-162; and cervical cancer as discussed by Piotrkowicz et al. in "500 kHz hyperthermia assisted HDR brachytherapy in the treatment of recurrent cervical and endometrial cancer in previously irradiated fields", Reports of Practical Oncology and Radiotherapy 2005, volume 10 number 3, pages 131-134.

In order to achieve satisfactory treatment results, it is of importance that, especially in hyperthermia-adjuvant brachytherapy, the aforementioned mild temperature elevation of the tissue in need of treatment is correctly distributed over the entire volume of said tissue (tumor tissue). In current surgical practice, catheters are placed manually based on the practitioner's experience and intuitive choices, and parameters for temperature distribution such as RF current amplitudes and phases are afterwards adjusted for each electrode and catheter, leading to a perceived lack of precision by not using the optimal set of catheter locations.

A problem generally associated with catheters for dual use in both hyperthermia and brachytherapy treatment is the effect of radiation attenuation. When a catheter comprising conventional (metallic, often Pt or Au) electrodes for emitting RF currents in hyperthermia is loaded with a probe containing radioactive material for use in brachytherapy, the electrodes of known catheters attenuate, i.e. absorb significant amounts of
radiation emitted from the probe. Since for efficient hyperthermia, it may be desirable to apply more than one electrode, the attenuation phenomenon is amplified by the number of electrodes used. This leads to irregularities in radiation dosage which are difficult to monitor and compensate for.

SUMMARY OF THE INVENTION

It is thus an object of the invention to provide for a system and method allowing for improved precision in catheter positioning such that optimal tissue treatment is achieved with possibly minimized admission of radiation to the patient.

It is a further object of the invention to provide for a catheter which, once positioned, allows for efficient radiation dosage inside the patient.

In a first aspect of the present invention, a system for image guided hyperthermia-adjuvant brachytherapy is presented, said system comprising an image acquisition device, preferably an MR device, adapted to provide image data to create a three-dimensional model of a patient environment, one or more catheters, said catheter or catheters being introducible into the patient environment and adapted to emit RF energy and to accommodate a brachytherapy radiation source, and a control device, said control device being adapted to determine in parallel a set of brachytherapy parameters as well as hyperthermia parameters, prior to introduction of said catheter, as a function of said model, a predetermined temperature distribution and a predetermined radiation dose. Under a model, in terms of the present invention a virtual computer model is understood. The patient-specific geometries of the model are obtained by (preferably MRI) image data processing. The control device and the image acquisition device cooperate in obtaining a model of the anatomy of tumor tissue and surrounding issue of so-called risk organs. Tissue types are classified and an electroanatomic model of electric conductivity and permittivity is created. A particular benefit of the invention according to this aspect is that the catheter positioning is made possible in the planning stage on the basis both of parameters for optimal heat distribution, important for hyperthermia, as well as parameters for optimal brachytherapy, leading to an optimized radiation dose distribution pattern.

In particular, it has been found that both applications, hyperthermia and radiotherapy, rely on several parameters when identifying an optimal setup of the respective application. Among these parameters, catheter positioning is a common parameter. The invention uses this common parameter as a link to perform an iterative optimization for both applications essentially simultaneously. Preferably, said brachytherapy parameters are
adapted to realize a prescribed radiation dose distribution, e.g. predetermined by a physician, said parameters being the position of the at least one catheter, and the dwell time of the radiation source used and/or the dwell position of the radiation source during the respective dwell times.

If in this document the wording "and/or" is used, it is understood that one of the elements or both elements are included.

Under dwell position, the location inside the catheter wherefrom the probe inside the patient environment emits radiation is understood. Dwell time accordingly is understood as the time span during which said probe is left at one dwell position before being removed or relocated to a further dwell position.

Said hyperthermia parameters are adapted to preferably realize a prescribed temperature distribution, e.g. predetermined by a physician, said parameters being the position of said at least one catheter, and the RF amplitude and/or RF phase of the RF current applied to the electrodes. Variation of RF phase is particularly interesting if more than one electrode is used for emitting RF current in hyperthermia treatment. If more than one catheter each comprising one or more electrodes, is used, it is particularly preferred to consider distinct RF amplitudes and RF phases, for each catheter/electrode and between distinct electrodes.

The control device is in a preferred embodiment adapted to perform an optimization process.

It is preferred if the control device is adapted to determine the location, volume and absorption characteristics of the tissue in need of treatment inside the three-dimensional model provided by the image acquisition device, and designate an initial catheter position for the at least one catheter, preferentially as a function of said location, volume and absorption characteristics. This initial positioning may be conducted based on practical experience of the physician and constitutes the physician's best guess.

The control device is preferably adapted to calculate, based upon said initial catheter positioning, an estimate radiation dose and an estimate temperature distribution using the further above-mentioned parameters. Temperature distribution is preferably calculated using Pennes bio-heat equation. The bio heat equation as discussed by Pennes in "Analysis of tissue and arterial blood temperatures in the resting human forearm", Journal of Applied Physiology 1948, volume 1, pages 93-122 is known as such and has been used widely to describe the heat flow by means of thermal conductance, convectional cooling by blood, absorbed power, and metabolic rate.
Radiation dose is calculated using a simplified model, in particular based upon
the assumption that from each dwell position, radiation is spread in all directions, wherein the
radiation intensity results from the equation
\[ I(r) = I_0 \cdot \frac{1}{r^2}. \]
In said equation, \( r \) is the distance from the radiation source, and \( I_0 \) is the
maximum intensity when \( r \) is zero.

The control device is preferably adapted to iteratively determine an optimized
catheter position, in particular by calculating, based upon said initial catheter position, a first
estimate radiation dose and a first estimate temperature distribution, calculating, based upon
at least one further catheter position different from the initial catheter position, at least one
further estimate radiation dose and at least one further estimate temperature distribution, and
by comparing each of the obtained further estimate radiation doses and estimate temperature
distributions with at least one of the previously determined estimates. After a number of
iteration loops, the further estimates no longer yield a significant improvement in temperature
distribution estimate and radiation dose distribution. Then, the catheter position relating to
the best temperature distribution and radiation dose distribution estimate are selected as the
optimized temperature distribution and radiation dose distribution.

Preferably, the control device is adapted to employ a fast algorithm for
calculating the radiation dose estimate, in particular by restricting the dose calculation to a
limited number of reference points on critical surfaces. These are surfaces of tumor and risk
organs, i.e. healthy organs that should not receive minimal and in any case not more than a
predescribed maximum dose (empirical values known in radiotherapy). This restriction
makes very fast optimization of seed dwell parameters and iteration of catheter positions
possible. As critical surfaces, in particular those surfaces may be considered where tumor
tissue borders on normal tissue. Reference points on these surfaces may be selected manually
by a physician.

The control device preferentially is adapted to vary said position or positions
of said catheter or catheters in said model with respect to anatomical boundary conditions, e.g.
constraints approved by the physician, such that feasible introduction pathways are obtained.

Preferably, the control device is adapted to determine a minimal number of
catheters necessary for treating the identified tissue. Minimization may be achieved by
considering that the tissue in need of treatment must on one hand side be subjected to a
minimum radiation dose, and at the same time, radiation dose, in particular in neighboring
tissue, must not exceed a maximum radiation dose. The control device is thus preferably adapted, based upon a first calculation of radiation dose with a first number of catheters, to calculate a second radiation dose for a second number of catheters the second number being lower than the first number of catheters.

If the desired radiation dose for the tissue in need of treatment is also achieved with the second number of catheters while not exceeding the maximum radiation dose and not falling below the minimum radiation dose for the tissue to be treated, said minimization step may be repeated by the control device until no further minimization is possible or desired.

Based upon the selected optimized catheter position, the control device is preferably adapted to calculate in parallel the exact dose distribution based upon the catheter positioning, once said positioning has been determined, and the exact temperature distribution inside the model of said tissue in need of treatment. Temperature distribution may be determined for example as laid out by van der Koijk et al. in "Dose uniformity in MECS interstitial hyperthermia", Physics in Medicine and Biology 1996, volume 41, pages 429-444.

Radiation dose calculation may be effected by a conventional planning algorithm calculating the exact dose distribution with the catheter arrangement obtained in the first optimization step. In contrast to the preliminary, fast calculation of the first step, the control device in the second step is adapted to calculate the radiation dose across the entire volume of the tissue to be treated, whereas in the first step, calculation was only effected for said limited number of reference points.

Fine-tuning of the catheter positions is now possible in that the control device is adapted to calculate optimum radiation dosage and temperature distribution, i.e. treatment plans, by again varying the catheter positions determined in the first step, though by lesser amounts than in the first (fast algorithm) step. By iterating such a calculation using the algorithms for exact temperature and radiation dose calculation, catheter positions can be found which yield the best possible treatment plan. A benefit of this procedure is that since a good "initial guess" for the catheter arrangement had already been determined in the first step, only a small number of iterations for this time-consuming calculation in the second step will be necessary.

In a further preferred embodiment, the system is adapted to monitor the temperature distribution inside the patient environment and to control RF emission currents and phases between electrodes of said catheter or catheters, preferably using thermometry
(preferably via the MR image acquisition device), and/or temperature sensing means provided on the at least one catheter. The combination of MR thermometry and local, catheter-based temperature monitoring allows for a more exact detection of temperature distribution inside the tissue in need of treatment and during treatment. An advantage hereof is that the system may be adapted to control more exactly the temperature distribution inside the tissue volume even after MR thermometry has been finished. This allows for exact control and continuation of hyperthermia treatment during transfer of the patient from the image acquisition (preferably MR) site to a bunker in which brachytherapy has to be performed. This allows for a more time-efficient and less strenuous procedure for the patient.

Preferably, the system, in particular the control device, is adapted to compare the calculated temperature distribution to the temperature measured by MR thermometry and/or said temperature sensing means provided by the catheter. This comparison data may be used to quantitatively and qualitatively assess deviations between the calculated and actual temperature distribution inside the tissue subjected to RF currents. The combination of MR thermometry and said catheter-based temperature sensing means is particularly useful since MR thermometry may be subject to artifacts. Additional temperature information provided by the catheter allows for validation and gauging of the MR thermometry.

As a preferred alternative to MR thermometry, ultrasound thermometry may be used.

It is further preferred if the system is adapted to adjust the temperature distribution by adapting RF currents and/or RF phases if the measured temperature distribution is different from the calculated temperature distribution.

In a further aspect of the present invention, a control device for use in a system for image guided hyperthermia-adjuvant brachytherapy according to as described hereinafore is presented, said control device being adapted to determine in parallel a set of brachytherapy parameters as well as hyperthermia parameters, prior to introduction of said catheter, as a function of a three-dimensional model of a patient environment, a predetermined temperature distribution and a predetermined radiation dose. The invention according to this embodiment preferentially has the same preferred embodiments as the system described hereinafore. Consequently, reference is made to the above description also for preferred embodiments of the control device alone.

In a further aspect of the present invention, a catheter for use in image guided hyperthermia-adjuvant brachytherapy, in particular in a system as described hereinafore, is presented. Said catheter comprises a main body, a lumen being formed inside the main body
and being adapted to accommodate a brachytherapy radiation source, preferably in the form of a HDR applicator, wherein the main body substantially consists of a conductive polymer.

A catheter comprising such a main body is superior to conventional catheters comprising ring-type metallic RF electrodes. Benefits of the catheter according to the invention are that conductive polymers are much more radio-translucent than those metals, which significantly decrease or even almost avoid attenuation of the radiation used for radiotherapy. Furthermore, the conductive polymer allows for the main body itself acting as electrode. As such, the polymeric electrode of the catheter according to the invention may be held flexible such that the electrode or electrodes of a catheter are allowed to extend along a much longer section of the catheter (in lengthwise direction) without limiting its bendability.

A further advantage of the catheter according to the invention is that metallic wires inside the catheter wall or shaft which would also attenuate the radiation are no longer required to connect to the catheter electrode. It has been found that, since in RF hyperthermia, the necessary RF currents per catheter are smaller than for example in cardiac RF ablation by about factor four, and because a large part of the cross-section of the hyperthermia catheter tube can be used for conduction, since their structure is much less complex than that of vascular catheters, transmission of electricity can be achieved along the main body without extra wiring. The obviation of extra wiring in turn helps to further decrease the effect of attenuation of radiation.

Preferentially, the conductive polymer is an intrinsically conductive polymer.

In a particularly preferred alternative thereto, the conductive polymer is selected from the group of polymers with conductive fillers. Polymers with conductive fillers consist of standard polymers (polyethylene, silicone, polyurethane, polypropylene), and flakes or grains of conductive materials (typically metals, but also carbon and carbon fibers).

Especially suitable materials are polyethylene filled with carbon and carbon fibers (conductivity of 25-40 (Ohm cm)^{-1}) as discussed by Thongruang et al. in "Bridged double percolation in conductive polymer composites: an electrical conductivity, morphology and mechanical property study", Polymer 2002, volume 43 number 13, pages 3717-3725. An advantage of using polymers with conductive fillers is their increased chemical stability and ease of processing as compared to intrinsically conductive polymers.

Preferably, the catheter according to the invention comprises at least one insulation element consisting of a non-conductive polymer, said insulation element or elements being provided at the surface of said main body and adapted to separate the main
body into multiple electrodes. The same variants of conductive polymers as described for the main body can be used for the making the electrodes.

In a preferred embodiment, at least one carbon fiber insert, preferably in the form of a carbon fiber bundle i.e. carbon fiber tow, is located inside the main body such that it at least partly covers the cross section of the catheter and is connected to the at least one electrode.

A catheter comprising multiple electrodes requires a corresponding number of separate pathways for RF current in order to supply each electrode with a designated RF current, amplitude and phase. Preferably, the catheter in such embodiment comprises a multitude of carbon fiber inserts located inside the main body, one connected to each electrode.

Preferably, each carbon fiber insert partly covers the cross section of the catheter. It is particularly preferred if each insert covers an angle of about $60^\circ$. In this case, preferably up to four electrodes may be located on the catheter while still leaving enough spacing in between the RF current pathways. Generally, the smaller the angle covered by one electrode is, the higher the number of RF current pathways may be.

The RF current pathways are preferentially embedded in the main body and spaced from the lumen inside the main body as well as spaced from the outside surface of the catheter. This way, the inserts are protected from mechanical damage which might else be caused e.g. by the applicator or external influences.

The catheter according to the invention preferably comprises temperature sensing means for locally monitoring temperature in the patient environment, wherein preferably said temperature sensing means comprises at least one fiber-optic temperature sensor. The use of fiber optic temperature sensors instead of electric temperature sensors leads to a further improvement of radio-translucency, thus decreasing the unwanted effect of radiation attenuation.

The main body of said catheter is preferentially elongate and has a circular cross section. Under elongate it is understood that the main body extends, in unbent condition, in a lengthwise direction along a central axis. When bent, the central axis is a curved line forming the neutral fiber of the catheter. The cross section of the catheter mentioned hereinabove is perpendicular to said axis or neutral fiber.

Said main body preferably may have an inner diameter in the range of 1-1.5 mm, particularly preferred of 1.2 mm, a wall thickness in the range of 200-400 $\mu$m, particularly of 300 $\mu$m, and length in the range of 10-25 cm, particularly of 20 cm. Using
polyethylene filled with carbon and carbon fibers as main body material, a resistance in the range of 56 to 35 Ohms, may respectively be achieved. This is sufficiently low to apply current levels for hyperthermia while preventing excessive heating of the catheter itself.

As carbon fiber insert, carbon fiber tows may be embedded in the tube to further lower the resistance. This is beneficial especially for catheters comprising several electrodes arranged along the main body of the catheter to allow for more degrees of freedom when adapting the RF current distribution. Such carbon fiber tows, available for example as carbon fiber bundles, may be used for pultrusion of the catheter main body. Alternatively, the carbon fibers may be routed in a corresponding lumen of the main body to allow for more flexibility of the catheter. Since the conductivity of pure carbon fibers is about 670 (Ohm cm)$^{-1}$, the catheter cross section may be reduced correspondingly, and connection of several electrodes can be realized. With e.g. a tow comprising about 760 fibers of 10 μm diameter each, a resistance of 50 Ohm may be achieved.

According to a further aspect of the invention, a method for planning hyperthermia-adjuvant brachytherapy treatment of a patient is presented, said method comprising the steps of:

- providing a three-dimensional model of a patient environment,
- determining in parallel a set of brachytherapy parameters as well as hyperthermia parameters, prior to introduction of said catheter, as a function of said model, a predetermined temperature distribution and a predetermined radiation dose.

The method according to this aspect profits from the same advantages as the system according to the invention described further hereinafter, to which thus reference is made. This also holds true for the preferred embodiments of the method as described hereinafter.

Preferably, said brachytherapy parameters are adapted to realize a prescribed radiation dose distribution, e.g. predetermined by a physician, said parameters being the position of the at least one catheter, and the dwell time of the radiation source used and/or the dwell position of the radiation source during the respective dwell times.

Said hyperthermia parameters preferably are adapted to realize a prescribed temperature distribution, e.g. predetermined by a physician, said parameters being the position of said at least one catheter, and least one of RF amplitude and RF phase. Variation of RF phase is particularly interesting if more than one electrode is used for emitting RF current in hyperthermia treatment.

The optimization preferentially is performed in an optimization process.
Preferentially before this optimization procedure, the step of determining the location, volume and absorption characteristics of the tissue in need of treatment inside the three-dimensional model, is performed; and as first step of the optimization procedure, the step of designating an initial catheter position for said at least one catheter, preferably as a function of said location, volume and absorption characteristics of the tissue in need of treatment is performed. In an iterative routine, preferably the steps of calculating, based upon said initial catheter position, a first estimate radiation dose and a first estimate temperature distribution, calculating, based upon at least one further catheter position different from the initial catheter position, at least one further estimate radiation dose and at least one further estimate temperature distribution, and comparing each of the obtained further estimate radiation doses and estimate temperature distributions with at least one of the previously determined estimates are performed.

Preferably, an estimate radiation dose and an estimate temperature distribution using the further above-mentioned parameters are calculated based upon said initial catheter positioning.

Temperature distribution is preferably calculated using the bio-heat equation. Radiation dose preferentially is calculated using a simplified model, in particular based upon the assumption that from each dwell position, radiation is spread in all directions, wherein the radiation intensity results from the equation

\[ I(r) = I_0 \cdot \frac{1}{r^2}. \]

In said equation, \( r \) is the distance from the radiation source, and \( I_0 \) is the maximum intensity when \( r \) is zero.

Preferably, a fast algorithm is employed for calculating the radiation dose, in particular by restricting the dose calculation to a limited number of reference points on critical surfaces. These are surfaces of tumor and risk organs, i.e. healthy organs that should not receive minimal and in any case not more than a predescribed maximum dose (empirical values known in radiotherapy). This restriction makes very fast optimization of seed dwell parameters and iteration of catheter positions possible.

The method preferably further comprises the step of
varying the position or positions of said catheter or catheters in said model with respect to anatomical boundary conditions, e.g. constraints approved by the physician, such that feasible introduction pathways are obtained.

The method comprises in a preferred embodiment the step of determining a minimal number of catheters necessary for treating the identified tissue in need of treatment.

In a preferred embodiment, upon a first calculation of radiation dose with a first number of catheters, a second radiation dose for a second number of catheters is calculated, the second number being lower than the first number of catheters.

If the desired radiation dose for the tissue in need of treatment is also achieved with the second number of catheters while not exceeding the maximum radiation dose and not falling below the minimum radiation dose for the tissue to be treated, said minimization step may be repeated until no further minimization is possible or desired.

The method preferentially further comprises the steps of

- selecting an optimized catheter position from the obtained estimates, and
- calculating in parallel the exact dose distribution based upon the optimized catheter position, and the exact temperature distribution inside the model of said tissue in need of treatment.

Radiation dose calculation may be effected by a conventional planning algorithm calculating the exact dose distribution with the catheter arrangement obtained in the first optimization step. In contrast to the preliminary, fast calculation of the first step, the radiation dose is in the second step calculated across the entire volume of the tissue to be treated, whereas in the first step, calculation was only effected for said limited number of reference points.

Fine-tuning of the catheter positions is now possible in that optimum radiation dosage and temperature distribution, i.e. treatment plans, are calculated by again varying the catheter positions determined in the first step, though by lesser amounts than in the first (fast algorithm) step. By iterating such a calculation using the algorithms for exact temperature and radiation dose calculation, catheter positions can be found which yield the best possible treatment plan.

In a further aspect of this invention, a method of image guided hyperthermia-adjuvant brachytherapy treatment of a patient is presented. Said method comprises the planning method as described hereinabove, in particular the steps of

- providing a three-dimensional model of a patient environment,
- determining in parallel a set of brachytherapy parameters as well as hyperthermia parameters, prior to introduction of said catheter, as a function of said model, a predetermined temperature distribution and a predetermined radiation dose.; and the steps of:

- introducing at least one catheter into the patient environment, preferably at least one catheter as described hereinabove,
- accommodating at least one brachytherapy radiation source in said catheter or catheters, preferably at least one HDR applicator, and
- emitting RF energy with said catheter or catheters.

Preferably, the step of introducing said at least one catheter is performed using image guidance. With image guidance (preferably through MR), the practitioner monitors online on a display device the advancement of said catheter or catheters inside the patient environment.

Optionally, said display device displays, supplied by the control device of the system according to the invention, the established and optimized positions for each catheter, allowing a quick and precise catheter placement.

The method according to this aspect preferably further comprises the steps of:

- monitoring the temperature distribution inside the patient environment, and
- controlling RF emission currents and/or phases between electrodes of said catheter or catheters, preferably using thermometry via the image acquisition device and/or temperature sensing means provided on the at least one catheter.

Preferably, both image-based thermometry and internally located temperature sensing means provided on the catheters are used for monitoring temperature distribution inside the patient environment in order to achieve optimum control of the temperature distribution. A particular advantage of said method is seen in deactivating image-based thermometry after a predetermined time interval, but continuing to operate the temperature sensing means applied on the at least one catheter during continued hyperthermia application, while the patient is being transferred from a first location where the image acquisition device is located to a second location, e.g. a bunker, where the brachytherapy is to be applied.

In a further aspect, a computer program for operating a system for image guided hyperthermia-adjuvant brachytherapy as described hereinabove is presented, the computer program comprising program code means for performing the method steps of the method for planning hyperthermia-adjuvant brachytherapy treatment of a patient according to the invention as described hereinabove, and/or comprising program code means for performing the method steps of the method for image guided hyperthermia-adjuvant
brachytherapy treatment of a patient as described hereinabove when the computer program is run on a computer controlling said system for image guided hyperthermia-adjuvant brachytherapy.

It shall be understood that the system for image guided hyperthermia-adjuvant brachytherapy according to the invention, in particular of claim 1, the control device, in particular according to claim 9, for use in said system, the catheter for use in image guided hyperthermia-adjuvant brachytherapy, in particular in a system according to this invention, in particular the catheter of claim 10, the method for planning hyperthermia-adjuvant brachytherapy treatment of a patient according to the invention, in particular of claim 11, the method of image guided hyperthermia-adjuvant brachytherapy treatment of a patient according to the invention and the computer product according to the invention, in particular according to claim 15, have similar and/or identical preferred embodiments, in particular, as defined in the dependent claims.

It shall further be understood that a preferred embodiment of the invention can also be any combination of the dependent claims with the respective independent claim.

These and other aspects of the invention will be apparent from and elucidated with reference to the embodiments described hereinafter.

BRIEF DESCRIPTION OF THE DRAWINGS

In the following drawings:

Fig. 1 shows schematically and exemplarily a system for image guided hyperthermia-adjuvant brachytherapy,

Fig. 2 shows schematically and exemplarily a three-dimensional model of a patient in environment acquired with the system of Fig. 1.

Fig. 3 shows schematically and exemplarily a part of a catheter for use in a system according to Fig. 1,

Fig. 4 shows schematically and exemplarily an alternative view of the catheter according to Fig. 3,

Figs. 4a-b schematically and exemplarily show cross sectional detail views of the catheter according to Figs. 3 and 4,

Fig. 5 shows schematically and exemplarily a flow chart of a method of image guided hyperthermia-adjuvant brachytherapy treatment of a patient, and

Fig. 6 shows schematically and exemplarily a flow chart concerning a part of the method according to Fig. 5.
DETAILED DESCRIPTION OF EMBODIMENTS

In Fig. 1, a system according to a first aspect of the invention for image guided hyperthermia-adjuvant brachytherapy is shown. Said system 1 comprises an MR image acquisition device 3 being adapted to provide a three-dimensional model of a patient environment 21. Further, said system 1 comprises at least one catheter, one catheter 5 being shown in Fig. 1, wherein in Fig. 1 that catheter 5 has been introduced into the patient environment. Said catheter 5 is connected to a catheter control unit 7. Said catheter control unit 7 comprises an energy application unit 9 and a measurement unit 11. Said energy application unit 9 and the catheter 5 are adapted and cooperate to apply radio frequency (RF) energy within a person 17 towards the patient environment in a hyperthermia procedure. The measurement unit 11 and the catheter 5 are adapted to and cooperate to measure the temperature inside the patient environment 21. For more details concerning the catheter 5, it is referred to Figs. 3, 4, 4a to b hereinafter.

The system 1 further comprises a control device 15 connected to the MR image acquisition device 3 and preferably also to the catheter control unit 7. Said control device 15 and said catheter control unit 7 may optionally be formed as one integrated control system. The control device 15 is adapted to determine a position of said catheter or more catheters inside the model generated by the image acquisition device 3 of said patient environment 21 prior to introduction of said catheter 5 or catheters. In particular, the position of said catheter is being optimized by the control device 15 as a function of brachytherapy parameters as well as hyperthermia parameters.

Fig. 2 shows an exemplarily virtual model as acquired by the image acquisition device 3 shown in Fig. 1. The model comprises the patient environment 21. The image data acquired by the control device 15 has been analyzed. A tumor 23 has been identified adjacent a region of normal tissue 25.

A multitude of catheters, in particular four catheters 5a, 5b, 5c, 5d have been introduced into the patient environment 21 and are located adjacent said tumor 23, essentially surrounding it. The catheters 5a-d have been placed under consideration of physical boundaries predetermined by a practitioner. Positioning of said catheters 5a-d has been optimized by the control device 15 in order to as closely as possible approximate the tumor tissue 23 and at the same time provide the opportunity to homogenously subject the tumor tissue with both RF energy and brachytherapy radiation. The optimization process is described hereinafter with respect to Figs. 5 and 6.
Fig. 3 shows the tip region of a catheter 5. Said catheter 5 comprises a main body 27. The main body 27 of said catheter 5 substantially consists of a conductive polymer which is a radio-translucent. On the surface of said main body 27, Fig. 3 shows an elongated hollow cylindrical surface element 29 consisting of a non-conductive material. The surface element 29 functions as an insulating element and limits the tip region of said catheter 5 such that there is a spatially defined electrode 31.

Inside the catheter 5, there is a lumen 39 adapted for accommodating a source of radioactive material suitable for brachytherapy. Preferentially, said lumen 39 is adapted for receiving a probe or applicator comprising said material by way of afterloading from robot connecting to the end of the catheter which is opposite to the catheter tip.

Furthermore, Fig. 3 shows temperature sensing means 33 which are attached to said main body 27. Signal transmission means 37 are located inside a corresponding cavity of the main body 27. It is preferred if the temperature sensing means comprise a fiber optic temperature sensor.

Fig. 4 shows a larger part of a catheter 5. Fig. 4 in particular demonstrates that almost the entire catheter surface consists of electrodes 31a, b, c which are specially separated from each other only by comparatively thin hollow cylindrical non-conductive surface elements 29a, b, c. Figs. 3 and 4 show the catheter 5 in straight orientation. Due to the flexibility of the conductive polymer material of main body 27, the catheter is, however, bendable to accommodate for anatomical boundary conditions.

Fig. 4a and 4b show a cross section along the lines A-A of Fig. 4. It is schematically shown that a carbon fiber insert 41 is provided in a correspondingly shaped side lumen spatially separated from the main lumen 39 of the main body 27. The carbon fiber insert 41 covers an angle a. In alternative embodiments, said carbon fiber insert may be inserted into a corresponding recess of the main lumen 39 formed in the main body 27 of the catheter 5. Fig. 4b is an enlarged view of the carbon fiber insert 41 already shown in Fig. 4a.

With reference to Fig. 5 and 6, the methods according to the invention are described in the following. Starting with Fig. 5, there is a method or MR guided hyperthermia-adjuvant brachytherapy treatment of a patient shown. The method comprises a planning method for planning the hyperthermia-adjuvant brachytherapy treatment. At first, in step 101, a three-dimensional model of a patient environment is provided, preferably by an image acquisition device such as the image acquisition device 3 of system 1 (Fig. 1).

Alternatively, said model may be provided through data storage means.
Once obtained, in step 103 the position of at least one catheter inside the model of said patient environment is/are determined prior to introduction of said catheter or catheters. The position for said catheters is being optimized as a function of brachytherapy parameters as well as hyperthermia parameters as laid out herein above. Fig. 6 illustrates in more detail the optimization step 103.

After determining the positioning for the at least one catheter, the planning method is completed, and terminates a first phase, so-called phase 0. In this phase, MRI has been used to create an image anatomy of tumor and surrounding tissue. Tissue types have been classified and an electro anatomic model of electric connectivity and permittivity has been adapted. Catheter positions, dwell positions, dwell times, and RF current parameters have been calculated such that both the radiation dose distribution and the RF hyperthermia field distribution have been optimized. In a next phase, so-called phase 1, said at least one catheter 5 (Figs. 3, 4, 4a-b) is introduced into the patient environment 21 (Fig. 1) which may be accomplished under MR guidance. Next, in step 107, the emission of RF radiation with said catheter or catheters is commenced.

Simultaneously, the system 1 commences temperature monitoring through MR thermometry in step 109a and through temperature sensing means provided on the catheters in step 109b.

Both temperature sensing means monitor the temperature distribution inside the patient environment 21, in particular inside the tumor tissue 23. After a predetermined time interval, in particular at a time when all catheters have been applied to the patient, step 107 is terminated, and the patient is being transferred in step 111 from the MR station where the system 1 is located to a second location, preferably a bunker, where the brachytherapy will be applied in step 115. MR thermometry which had begun in step 109a is terminated in step 113 after beginning transfer of the patient. The temperature sensors provided on the catheter or catheters 5, however, may remain in operation and continue temperature monitoring.

This is particularly useful if the hyperthermia treatment is continued interstitially by the catheters during transfer and radiation treatment of the patient.

Optionally, temperature monitoring may be followed through until brachytherapy begins in step 115 or even until the end of the entire procedure.

The optimization step 103 of the method according to Fig. 5 is shown in more detail in Fig. 6. Preferably, the optimization process may be described as separated into two steps. The first step consists of several sub-steps. At step 201, the location, volume and
absorption characteristics of the tissue in need of treatment (tumors and healthy tissue) inside the three-dimensional model are determined, preferably by control device 15. Next, based upon a prescription of radiation dose and temperature distribution provided by e.g. a physician, an initial catheter position for said at least one catheter, preferably for a predetermined set and number of catheters is selected as a function of said location, volume and absorption characteristics of the tissue in need of treatment. At step 205, a preliminary calculation based on simplified starting parameters is performed for evaluating roughly the temperature distribution and radiation dose distribution inside the tissue in need of treatment. Preferably, preliminary calculation of temperature distribution and radiation dose distribution is performed in parallel. At the beginning of the iterative optimization process that is step 103, step 207 is bridged to lead directly to step 208, in which the position of said catheters is varied. Step 205 is then repeated for the new orientation of said catheter or catheters. In step 207, the previously existing results determined in step 205 are compared. If the newer catheter positioning has led to an improvement of the preliminary evaluated distribution results, a further iteration loop is run, again varying the position of the catheters in step 208 before calculating estimations for the radiation distributions anew. This process is continued until the variations of position do not lead to further increases in the preliminary calculation results, i.e. a better approximation of the radiation and temperature distribution according to the above-mentioned prescription, e.g. predetermined by a physician.

Then, based on the established catheter positioning, the exact temperature distribution profile and radiation dosage distribution profile are being determined, in particular as described hereinabove. This is conducted in steps 211a and 211b in parallel for both the hyperthermia pattern and the brachytherapy pattern. The exact determination of said profiles is considered the second step of said two-step procedure.

Optionally, in between steps 207 and 211a-b, an additional step 209 is provided wherein it is evaluated if the number of catheters being employed can be minimized. Procedures like the provision of a three-dimensional model of a patient environment, determination and optimization of a position of at least one catheter, determination of the location, volume and absorption characteristics of the tissue in need of treatment, calculation of radiation doses and temperature distributions et cetera performed by one or several units or devices may be performed by any other number of units or devices.

In the above description of the invention, an MR guided image acquisition device has been exemplarily been described. According to further preferred embodiments, an
ultrasound image acquisition device may be used in addition to or instead of the MR image acquisition device.

The procedures and/or the control of the system for image guided hyperthermia-adjunct brachytherapy in accordance with the method for planning hyperthermia-adjunct brachytherapy treatment of a patient can be implemented as program code means of a computer program and/or as dedicated hardware.

Other variations to the disclosed embodiments can be understood and effected by those skilled in the art in practicing the claimed invention, from a study of the drawings, the disclosure, and the appended claims.

A computer program may be stored/distributed on a suitable medium, such as an optical storage medium or a solid-state medium, supplied together with or as part of other hardware, but may also be distributed in other forms, such as via the Internet or other wired or wireless telecommunication systems.

In the claims, the word "comprising" does not exclude other elements or steps, and the indefinite article "a" or "an" does not exclude a plurality.

A single unit or device may fulfill the functions of several items recited in the claims. The mere fact that certain measures are recited in mutually different dependent claims does not indicate that a combination of these measures cannot be used to advantage.

Any reference signs in the claims should not be construed as limiting the scope.
CLAIMS:

1. A system (1) for image guided hyperthermia-adjuvant brachytherapy, said system (1) comprising:
   an image acquisition device (3) adapted to provide image data to create a three-dimensional model of a patient environment (21),
   at least one catheter (5, 5a-d), said catheter being introducible into the patient environment (21) and adapted to emit RF energy and to accommodate a brachytherapy radiation source, and
   a control device (15),
   said control device (15) being adapted to determine in parallel a set of brachytherapy parameters as well as hyperthermia parameters, prior to introduction of said catheter, as a function of said model, a predetermined temperature distribution and a predetermined radiation dose.

2. The system (1) according to claim 1, wherein said brachytherapy parameters are:
   - position of the at least one catheter (5), and
   - dwell time of the radiation source and/or dwell position of the radiation source;
   and
   wherein said hyperthermia parameters are
   - position of the at least one catheter (5), and
   - RF amplitude and/or RF phase.

3. The system (1) according to claim 1, wherein the control device (15) is adapted to perform an optimization process, the control device (15) being adapted to
   - determine the location, volume and absorption characteristics of the tissue (23, 25) in need of treatment inside the three-dimensional model provided by the image acquisition device (3), and
   - designate an initial catheter position for the at least one catheter (5, 5a-d),
   - calculate, based upon said initial catheter position, a first estimate radiation
dose and a first estimate temperature distribution, calculate, based upon at least one further catheter position different from the initial catheter position, at least one further estimate radiation dose and at least one further estimate temperature distribution, and to compare each of the obtained further estimate radiation doses and estimate temperature distributions with at least one of the previously determined estimates.

4. The system (1) according to claim 1, wherein the control device (15) is adapted to select an optimized catheter position from the obtained estimates and calculate in parallel the exact dose distribution based upon the optimized catheter position, and the exact temperature distribution inside the model of said tissue (23, 25) in need of treatment.

5. The system (1) according to claim 1, wherein the system (1) is adapted to monitor the temperature distribution inside the patient environment (21) and to control RF emission currents and/or phases between electrodes (31, 31a-c) of said at least one catheter (5).

6. The system (1) according to claim 1, wherein said catheter (5) comprises a main body (27), a lumen being formed inside the main body (27) and being adapted to accommodate a brachytherapy radiation source, wherein the main body (27) consists of a conductive polymer.

7. The system according to claim 6, wherein the catheter (5) comprises at least one insulation element (29, 29a-c) consisting of a non-conductive polymer, said insulation element or elements being provided at the surface of said main body (27) and adapted to separate the main body (27) into multiple electrodes (31a-c).

8. The system according to claim 6, wherein at least one carbon fiber insert (41) is located inside the main body (27) such that it at least partly covers the cross section of the catheter (5) and is connected to the at least one electrode (31, 31a-c).
9. A control device (15) for use in a system (1) for image guided hyperthermia-
adjuvant brachytherapy according to claim 1,
said control device (15) being adapted to determine in parallel a set of
brachytherapy parameters as well as hyperthermia parameters, prior to introduction of said
catheter, as a function of a three-dimensional model of a patient environment, a
predetermined temperature distribution and a predetermined radiation dose.

10. A catheter (5, 5a-d) for use in image guided hyperthermia-adjuvant
brachytherapy, in a system (1) according to claim 1, comprising a main body (27), a lumen
being formed inside the main body (27) and being adapted to accommodate a brachytherapy
radiation source, wherein the main body (27) consists of a conductive polymer.

11. A method for planning hyperthermia-adjuvant brachytherapy treatment of a
patient, comprising the steps of:
- providing a three-dimensional model of a patient environment (21),
- determining in parallel a set of brachytherapy parameters as well as
hyperthermia parameters, prior to introduction of at least one catheter (5, 5a-d), as a function
of said model, a predetermined temperature distribution and a predetermined radiation dose.

12. The method according to claim 11, wherein the optimization is performed in
an optimization process, said process comprising the steps of
- determining the location, volume and absorption characteristics of the tissue
(23, 25) in need of treatment inside the three-dimensional model,
- designating an initial catheter position for said at least one catheter (5, 5a-d)
- calculating, based upon said initial catheter position, a first estimate radiation
dose and a first estimate temperature distribution,
- calculating, based upon at least one further catheter position different from the
initial catheter position, at least one further estimate radiation dose and at least one further
estimate temperature distribution, and
- comparing each of the obtained further estimate radiation doses and estimate
temperature distributions with at least one of the previously determined estimates.
13. The method according to claim 12, comprising the step of varying the position or positions of at least one catheter (5, 5a-d) in said model with respect to anatomical boundary conditions such that feasible introduction pathways are obtained.

14. The method according to claim 12, comprising the steps of
- selecting an optimized catheter position from the obtained estimates, and
- calculating in parallel the exact dose distribution based upon the optimized catheter position, and the exact temperature distribution inside the model of said tissue in need of treatment.

15. A computer program for operating a system (1) for image guided hyperthermia-adjuvant brachytherapy according to claim 1, the computer program comprising program code means for performing the method steps of the method for planning hyperthermia-adjuvant brachytherapy treatment of a patient according to claim 11 when the computer program is run on a computer controlling said system (1) for image guided hyperthermia-adjuvant brachytherapy.
FIG. 5
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

INVENTION:

A61N 1/06

APPLICATION:

PCT/IB2013/058586

A. CLASSIFICATION OF SUBJECT MATTER

INVENTION:

A61N 1/06

DOCUMENTATION SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

A61N  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 practicable, search terms used)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category Citation of document, with indication, where appropriate, of the relevant passages


abstract; claims 1,44 1-8,

paragraph [0038] 12-14

paragraph [0632] - paragraph [0639]

paragraph [0673] - paragraph [0675]


abstract
col umn 34, line 11 - col umn 37, line 22

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A the whole document 3,4

Further documents are listed in the continuation of Box C.

See patent family annex.

Date of the actual completion of the international search

7 February 2014

Date of mailing of the international search report

17/02/2014

Name and mailing address of the ISA/Authorized officer

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Beck, Ewa

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