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— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

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(54) Title: SURGICALLY POSITIONED NEUTRON FLUX ACTIVATED HIGH ENERGY THERAPEUTIC CHARGED PARTICLE GENERATION SYSTEM

(57) Abstract:

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SURGICALLY POSITIONED NEUTRON FLUX ACTIVATED HIGH ENERGY THERAPEUTIC CHARGED PARTICLE GENERATION SYSTEM

CROSS REFERENCE TO RELATED APPLICATION

[0001] This application is a traditional application and claims priority to U.S. Provisional Patent Application No. 62/545,522, filed August 15, 2017.

BACKGROUND

1. Field

[0002] This invention pertains generally to the treatment of cancer and, more particularly to the treatment of highly localized carcinoma cells.

2. Related Art

[0003] The treatment of highly localized carcinoma cells, such as tumors, in the human body using ionizing radiation has proven to be quite effective. However, the application of ionizing radiation to the body typically involves having the radiation used pass through healthy tissue before it arrives at the intended target site. This results in damage to the healthy tissue. This limits the amount of damage that can be done to the tumor at one time, resulting in the need for multiple treatments and the accumulating adverse potential biological consequences and financial costs of the treatments. If the healthy cell damage repair does not keep up with the tumor growth rate and/or metastasis rate to allow for sufficient treatment, the victim is likely to perish from the consequences of the carcinoma.

SUMMARY

[0004] This invention overcomes the detrimental effects of the radiation treatment of cancer by providing a method of treating localized carcinoma cells in a body of an animal that includes the step of positioning a therapeutic source that is substantially nonradioactive when not exposed to a neutron source below a given activity, but becomes a source of highly ionizing but weakly penetrating radiation when exposed to a neutron field at or above the given activity, within the body in the vicinity of the carcinoma cells.

Preferably, the positioning step surgically implants the therapeutic source material on the carcinoma cells. The therapeutic source is irradiated from outside the body with a neutron field at or above the given activity for a prescribed period of time and the irradiation step is repeated at prescribed intervals. Preferably, the therapeutic source of highly ionizing but weakly penetrating radiation comprises B_4C, P-31 or other material that produces comparable high energy alpha or beta particles and either no or low energy gamma radiation. The therapeutic source should be insoluble in water, non-toxic to the body and have short half-lives. Desirably, if B_4C is used, the B_4C is enriched in B-10 content.

[0005] In one preferred embodiment the therapeutic source of highly ionizing but weakly penetrating radiation is configured so it substantially only irradiates the carcinoma cells. To achieve that end a radiation shield material is formed on a side of the therapeutic source not facing the carcinoma cells. Preferably, the step of irradiating the therapeutic source includes the step of using an electric neutron generator, such as a Neutristor, to irradiate the therapeutic source. One such embodiment employs a plurality of electric neutron generators positioned around the body to irradiate the therapeutic source from different angles.

[0006] In another embodiment the method includes the step of using a neutron moderating material between the electric neutron generator and the therapeutic source to adjust the neutron energy to optimize the highly ionizing, but weakly penetrating radiation produced by the therapeutic source. The neutron moderating material may be D_2O, C or other material having similar moderating properties. The neutron moderating material is placed outside the body between the electric neutron generator and the body.

[0007] In one such embodiment the therapeutic source is left within the body between treatments of treating the localized carcinoma cells, with the therapeutic source removed from the body once the treatments are complete. The therapeutic source may comprise one or more very thin disks or plates in the order of a micron's thickness with a sufficient combined surface area to ensure the entire volume of localized carcinoma cells will be affected by the highly ionizing but weakly penetrating radiation when one or more of the disks or plates are emplaced around the carcinoma cells and irradiated with the neutron field.

[0008] In still another embodiment the method includes the step of using a gamma spectrometer to monitor the intensity of gamma radiation emitted by a product of the neutron radiation of the therapeutic source material while a charged particle production rate can be monitored while the neutron irradiation is occurring. The monitored intensity of the gamma radiation and neutron activity of the neutron field can be used to determine a radiation dose that has been applied to the body. The method may also control the intensity of the neutron field based on the monitored gamma intensity and the radiation dose.

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] A further understanding of the invention can be gained from the following description of the preferred embodiments when read in conjunction with the accompanying drawings in which:

[0010] Figure 1 is a schematic of the apparatus that may be employed to practice the method of this invention.

DESCRIPTION OF THE PREFERRED EMBODIMENT

[0011] In accordance with this invention for the treatment of highly localized carcinoma cells, one or more very thin (e.g., micron thickness) disks or plates of a therapeutic source with sufficient surface area to ensure that the entire volume of the localized carcinoma cells will be affected by the radiation emitted when one or more devices are implanted within the body of a patient proximate to, and preferably adjacent the tumor. As used herein, the term “patient” means an animal, such as, a human being. The therapeutic source material used should be one that produces high energy alpha or beta particles and either no or low energy gamma radiation. The material must be insoluble in water and non-toxic. The neutron reaction products of the material should also be non-toxic to the subject and have very short half-lives. The use of B_4C for the source material is an example of a material with these qualities and the reference to short half-lives, high energy alpha or beta particles and no or low energy gamma radiation refers to a material that has a half-life approximately as short as or shorter than B_4C, alpha or beta particle energy ranges as high or higher than B_4C and no or low gamma radiation energy approximately

equal to that of B_4C. The preferred embodiment of this material uses B_4C that is enriched in a B-10 content. The use of a compound containing a high concentration of P-31 is another acceptable selection. The therapeutic source material to be inserted for irradiation can be shaped using a number of commercially available fabrication techniques and, preferably, has a shielding over a side of the source material facing away from the carcinoma that is substantially transparent to neutrons, but shields at least some of the highly ionizing particles from the healthy tissue surrounding the carcinoma, such as a light metal-like aluminum.

[0012] An array of miniature electrically powered fast neutron generators similar in configuration to the "Neutristor" design developed by Sandia National Laboratory and described in a Snowmass 2013 White Paper entitled *Novel Compact Accelerator Based Neuron and Gamma Sources for Future Detector Calibration,* G. Jennings, C. Sanzeni, D.R. Winn, Fairfield University, Fairfield CT 06824, can be used to irradiate the therapeutic source material with a neutron field once the source material is implanted in the patient. Ideally, the array is configured as necessary to provide a neutron intensity at the source position sufficient to maximize the neutron reaction rate without providing too much neutron exposure to other parts of the subject's body. Ideally, the array is geometrically configured to provide neutrons incidents on the carcinoma at different angles to provide the maximum number of sufficiently thermalized neutrons from each generator in the array to reach the target location. This is accomplished through a combination of neutron source array geometry and variations in the thickness of the material used as a neutron moderator placed between the neutron array and the irradiation target. The calculations required to establish the optimum conditions can be performed by those skilled in the art using a number of different commercially available neutron transport calculation products, such as MCNP available from Los Alamos National Laboratory.

[0013] FIG. 1 is a schematic that illustrates an apparatus to practice certain methods of this invention. As shown in FIG. 1, a therapeutic source 10 is implanted within the body of a patient 12. An array of electric neutron generators 14 are configured to irradiate with a neutron field the therapeutic source 10 within the patient 12. A neutron moderator 16 is provided that is geometrically configured and placed between each electric neutron

generator 14 and the therapeutic source 10 target. The neutron moderator 16 includes a sufficient amount of a material, like D_2O or C, and is independently adjusted to achieve the goal of providing the maximum number of neutrons with the optimum energy for charged particle generation by neutron reactions with the target therapeutic source material.

[0014] A gamma spectrometer 18 is provided that measures the intensity of the gamma radiation emitted by the target isotope created in the neutron reaction so the charged particle production rate can be monitored while the neutron irradiation is occurring. This can be accomplished using a number of commercially available devices.

[0015] A computational control system 20 uses the measured gamma activity and the activity status of the neutron generators to determine radiation dose that has been applied to the patient relative to a dose target. The control system 20 has the ability to increase or decrease the intensity of the neutrons provided by any or all of the neutron generators in the array based on gamma intensity and measured dose measurements.

[0016] The approach and system for treating carcinoma described herein is different from other types of radiation treatments in that it relies on creating and implanting a non-radioactive target in or around a tumor versus the injection of a compound that provides a limited amount of therapeutic treatment deposition in the desired area. The ability this system provides to perform neutron activation of initially non-radioactive materials in a hospital environment maximizes the benefits of charged particle cancer treatment and minimizes the unwanted expense and radiation exposure to the patient and caregivers. This approach allows very precise and efficient cancer killing to occur. Additionally, the target source can be left in position without increasing the whole body radiation dose to the patient, until the tumor is completely dead. Multiple irradiations can occur with relative ease. The use of the electric neutron generator, e.g., Neutristor, provides the ability to perform the treatments in a hospital setting instead of a reactor or very large neutron source location. This greatly reduces treatment costs (or greatly increases treatment profitability) relative to existing radiation treatment methods.

[0017] While specific embodiments of the invention have been described in detail, it will be appreciated by those skilled in the art that various modifications and alternatives to those details could be developed in light of the overall teachings of the disclosure.

Accordingly, the particular embodiments disclosed are meant to be illustrative only and not limiting as to the scope of the invention which is to be given the full breadth of the appended claims and any and all equivalents thereof.

What is claimed is:

1. A method of treating localized carcinoma cells in a body of an animal (12) comprising the steps of:

positioning a therapeutic source (10) that is substantially nonradioactive when not exposed to a neutron source below a given activity, but becomes a source of highly ionizing but weakly penetrating radiation when exposed to a neutron field at or above the given activity, within the body in the vicinity of the carcinoma cells;

irradiating the therapeutic source (10) from outside the body with a neutron field at or above the given activity for a prescribed period of time; and

repeating the irradiating step at prescribed intervals.

2. The method of treating localized carcinoma cells of Claim 1 wherein the therapeutic source (10) of highly ionizing but weakly penetrating radiation comprises B_4C, or P-31.

3. The method of treating localized carcinoma cells of Claim 2 wherein the B_4C is enriched in B-10 content.

4. The method of treating localized carcinoma cells of Claim 1 wherein the therapeutic source (10) of highly ionizing but weakly penetrating radiation is configured so it substantially only irradiates the carcinoma cells.

5. The method of treating localized carcinoma cells of Claim 4 wherein a radiation shield material that shields at least some of the highly ionizing radiation, but is substantially transparent to neutrons, is formed on a side of the therapeutic source (10) not facing the carcinoma cells.

6. The method of treating localized carcinoma cells of Claim 1 wherein the positioning step includes the step of surgically implanting the therapeutic source (10) approximately on the carcinoma cells.

7. The method of treating localized carcinoma cells of Claim 1 wherein the step of irradiating the therapeutic source (10) includes the step of using an electric neutron generator (14) to irradiate the therapeutic source (10).

8. The method of treating localized carcinoma cells of Claim 7 wherein the electric neutron generator (14) is a Neutristor.

9. The method of treating localized carcinoma cells of Claim 7 wherein the electric neutron generator (14) includes a plurality of electric neutron generators positioned around the body to irradiate the therapeutic source (10) from different angles.

10. The method of treating localized carcinoma cells of Claim 7 including the step of using a neutron moderating material (16) between the electric neutron generator (14) and the therapeutic source (10) to adjust the neutron energy to optimize the highly ionizing, but weakly penetrating radiation produced by the therapeutic source (10).

11. The method of treating localized carcinoma cells of Claim 10 wherein the neutron moderating material (16) comprises D_2O or C.

12. The method of treating localized carcinoma cells of Claim 10 wherein the step of using the neutron moderating material (16) includes the step of placing the neutron moderating material (16) outside the body.

13. The method of treating localized carcinoma cells of Claim 1 including the step of leaving the therapeutic source (10) within the body between treatments of treating the localized carcinoma cells.

14. The method of treating localized carcinoma cells of Claim 13 including the step of removing the therapeutic source (10) from the body once treatment of the localized carcinoma cells is completed.

15. The method of treating localized carcinoma cells of Claim 1 wherein the therapeutic source (10) comprises one or more very thin disks or plates in the order of a micron's thickness with a sufficient combined surface area to ensure the entire volume of localized carcinoma cells will be affected by the highly ionizing but weakly penetrating radiation when one or more of the disks or plates are emplaced around the carcinoma cells and irradiated with the neutron field.

16. The method of treating localized carcinoma cells of Claim 1 wherein the therapeutic source (10) is configured from a material that produces high energy alpha or beta particles and either no or low energy gamma radiation.

17. The method of treating localized carcinoma cells of Claim 16 wherein the therapeutic source material is insoluble in water, non-toxic to the body and has short half-lives.

18. The method of treating localized carcinoma cells of Claim 1 including the step of using a gamma spectrometer (18) to monitor the intensity of gamma radiation emitted by a product of the neutron radiation of the therapeutic source material while a charged particle production rate can be monitored while the neutron irradiation is occurring.

19. The method of treating localized carcinoma cells of Claim 18 using the monitored intensity of the gamma radiation and neutron activity of the neutron field to determine a radiation dose that has been applied to the body.

20. The method of treating localized carcinoma cells of Claim 19 controlling the intensity of the neutron field based on the monitored gamma intensity and the radiation dose.

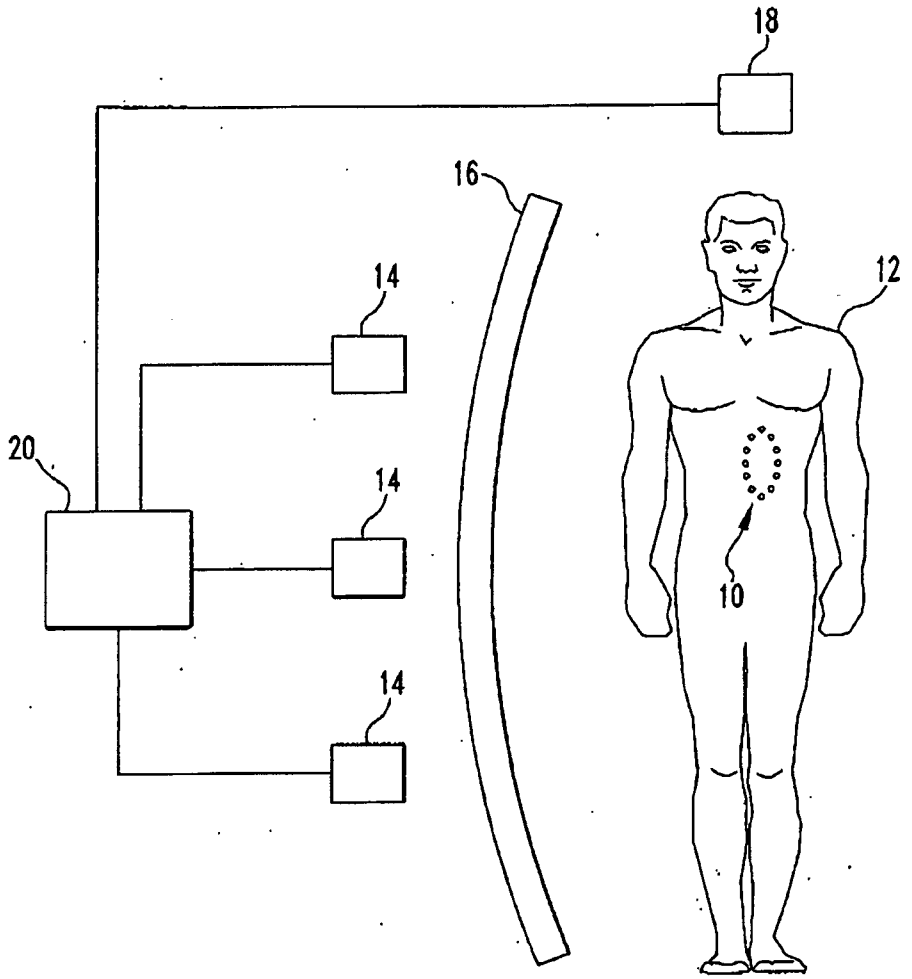

FIG.1

PATENT COOPERATION TREATY

PCT

DECLARATION OF NON-ESTABLISHMENT OF INTERNATIONAL SEARCH REPORT

(PCT Article 17(2)(a), Rules 13*ter*.1(c) and (d) and 39)

Applicant's or agent's file reference	**IMPORTANT DECLARATION**	Date of mailing (*day/month/year*)
WECFY2017001		30 October 2018 (30.10.2018)
International application No.	International filing date (*day/month/year*)	(Earliest) Priority date (*day/month/year*)
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International Patent Classification (IPC) or both national classification and IPC

A61N 5/10(2006.01)i, A61K 41/00(2006.01)i

Applicant

WESTINGHOUSE ELECTRIC COMPANY LLC

This International Searching Authority hereby declares, according to Article 17(2)(a), that **no international search report will be established** on the international application for the reasons indicated below.

1. ☒ The subject matter of the international application relates to:
   - a. ☐ scientific theories
   - b. ☐ mathematical theories
   - c. ☐ plant varieties
   - d. ☐ animal varieties
   - e. ☐ essentially biological processes for the production of plants and animals, other than microbiological processes and the products of such processes
   - f. ☐ schemes, rules or methods of doing business
   - g. ☐ schemes, rules or methods of performing purely mental acts
   - h. ☐ schemes, rules or methods of playing games
   - i. ☒ methods for treatment of the human body by surgery or therapy
   - j. ☐ methods for treatment of the animal body by surgery or therapy
   - k. ☐ diagnostic methods practised on the human or animal body
   - l. ☐ mere presentation of information
   - m. ☐ computer programs for which this International Searching Authority is not equipped to search prior art
2. ☐ The failure of the following parts of the international application to comply with prescribed requirements prevents a meaningful search from being carried out:
   ☐ the description ☐ the claims ☐ the drawings
3. ☐ A meaningful search could not be carried out without the sequence listing; the applicant did not, within the prescribed time limit:
   - ☐ furnish a sequence listing in the form of an Annex C/ST.25 text file, and such listing was not available to the International Searching Authority in a form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
   - ☐ furnish a sequence listing on paper or in the form of an image file complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it; or the sequence listing furnished did not comply with the standard provided for in Annex C of the Administrative Instructions.
   - ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rule 13ter.1(a) or (b).
4. Further coments:

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