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[54] **METHOD AND APPARATUS FOR THE IN-VESSEL RADIATION TREATMENT OF BLOOD**

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[51] **Int. Cl.** **A61n 5/10**

[58] **Field of Search** ..... 128/1.1, 1.2, 2 A, 260, 128/335.5; 250/454, 456, 492, 493

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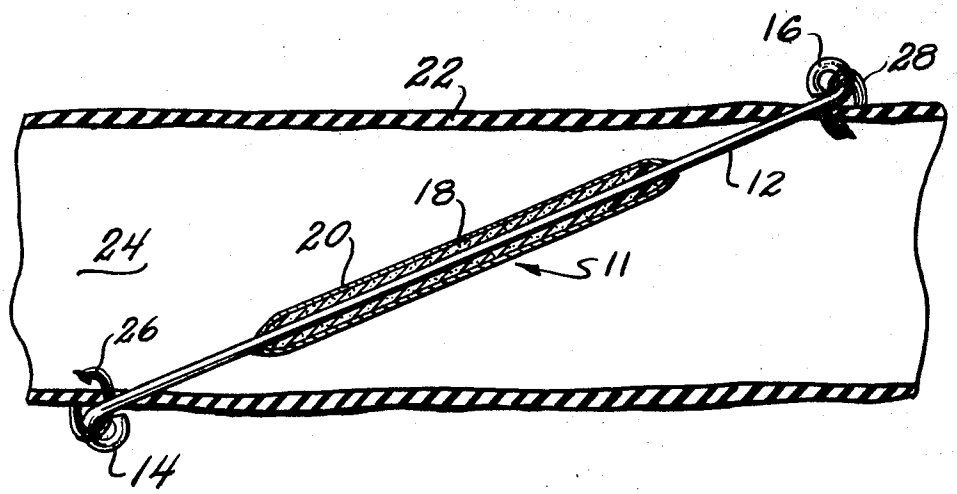
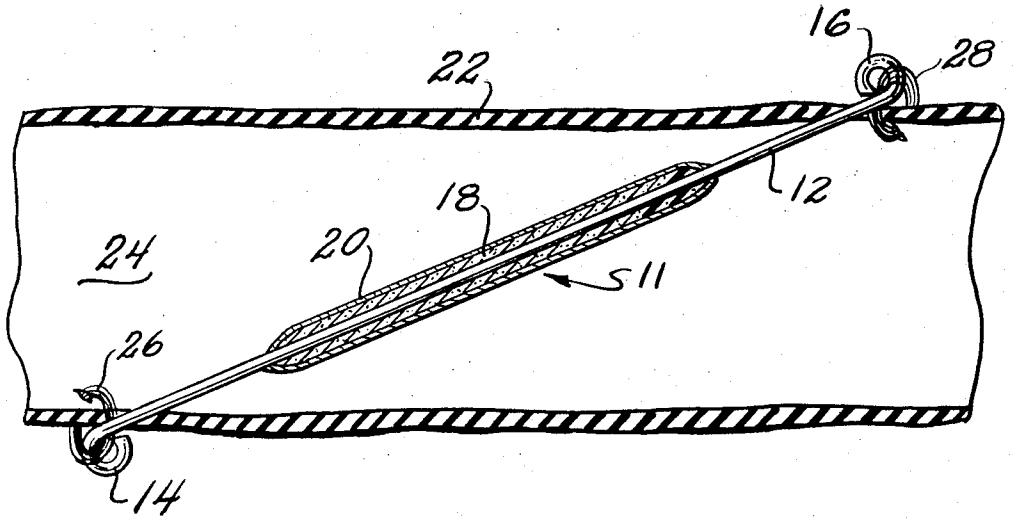
[57] **ABSTRACT**

An apparatus and a corresponding method for the in-vivo radio-therapy of blood by irradiation of the blood within the blood vessel. The device includes a wire which has a straight section and small oppositely facing loops at each of its two ends. An active radioisotope-layer is deposited over the center portion of the straight section of the wire and this radioisotope-layer is sealingly covered with a coating-layer to prevent any leaking of the radioisotope into the blood. The wire is adapted for surgical implantation diagonally transverse a blood vessel in a manner so that the active radioisotope-layer lies fully within the blood vessel, while the end of the wire projects such that the two loops lie fully exterior to the blood vessel. Following the depositing of the radioisotope-layer and the coating-layer on the wire and sterilization of the wire, the device is surgically implanted diagonally transverse the blood vessel and is anchored in place with respect to the blood vessel by suturing through the loops.

7 Claims, 1 Drawing Figure

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METHOD AND APPARATUS FOR THE IN-VESSEL RADIATION TREATMENT OF BLOOD

CONTRACTUAL ORIGIN OF THE INVENTION

The invention described herein was made in the course of, or under, a contact with the UNITED STATES ATOMIC ENERGY COMMISSION.

BACKGROUND OF THE INVENTION

The present invention relates to radiotherapy and radiation treatment of blood and is particularly concerned with the in-vivo radiation treatment of blood. Specifically, the present invention is concerned with the radiation treatment of blood within the blood vessel. Still more particularly, the present invention relates to a method and a device for implantating a radiation source within the blood vessel which reduces the amount of shielding required and hence the complexity of the device and simplifies surgical procedure.

Radiotherapy including radiation treatment of blood as a potential cure or control of various diseases is well known in the art, radiotherapy being extensively used in the treatment of various forms of cancer. In particular, radiotherapy as a treatment for the control of leukemia has been studied and undertaken in the past.

Suppression of lymphocyte levels in circulating blood following irradiation of the total body with low doses of ionizing radiation is well known. It has been demonstrated that irradiation of blood in an exterior loop (extracorporeal irradiation of blood) suppresses lymphocyte levels without damage to other body tissues. It has consequently been shown that extracorporeal irradiation of blood is an effective adjunct or alternative to drug therapy for treating some forms of leukemia.

Immune reactions initiated by lymphocytes are usually the ultimate reason for failure of organ transplants. Current methods of suppressing these immune reactions include use of drug therapy, antilymphocyte antibodies, and irradiation. Typically, more than one of these approaches is used since there are problems associated with each.

Acceptance times of skin allografts have been extended by extracorporeal irradiation of blood and this technique has been evaluated for its applicability for immunosuppression relative to renal allografts. Significant reduction in early rejection eposodes and a significantly higher frequency of six-month renal graft survival has been reported for extracorporeal irradiation of blood-treated groups.

Most treatments of both experimental animals and humans have been accomplished by shunting blood through large fixed equipment such as cobalt-60, cesium-137 or X-ray sources, thereby necessitating specialized facilities. With the relatively long treatment regimes required, this severely limits the numbers of patients who can receive treatment and requires the inconvenience and expense of hospitalization. A small, inexpensive, portable irradiator is needed for the above reasons and also to permit chronic exposures of patients prior to and subsequent to kidney transplants.

A small implantable irradiator which would permit direct in-vivo irradiation of the blood is also desirable. One such portable irradiator consists of a small tube of shielding material coated on the inside with a radioactive isotope which is further coated to prevent leakage into the blood system. Small sections of an artery or vein are surgically removed and this tube inserted in substitution therefor, the insertion being accomplished by suturing the blood vessel to small fiber tubes located on each end of the device. These devices then serve as a small section of the blood vessel.

Alternatives to these devices are desirable as the surgical procedures involved in inserting them as a substitution for a section of a blood vessel are complex and these devices require shielding to prevent the undesirable radiation of surrounding tissues.

Therefore, it is an object of the present invention to provide a method and an apparatus for radiotherapy of blood.

It is a further object of the present invention to provide a method and apparatus for in-vivo irradiation of blood.

An additional object of the present invention is to provide a method and apparatus for the irradiation treatment of blood within the blood vessel itself.

Another object of the present invention is to provide a device which is less complex and requires less or no shielding and which can be implanted by simplified surgical procedures.

Other objects and advantages of the present invention will become apparent upon reading the following description and with particular reference to the specific embodiment described hereinbelow.

SUMMARY OF THE INVENTION

In accordance with the present invention, a method and apparatus is provided for in-vivo radiotherapy of blood by irradiation of the blood within a blood vessel. A layer from an active radioisotope is deposited on the center portion of a wire which includes a straight section and small oppositely facing loops at each of its two ends. A coating-layer is deposited over the active radioisotope-layer to sealingly cover the radioisotope and prevent leaking of the radioisotope into the blood. Following sterilization of the device, the device is implanted in a blood vessel by surgically inserting the wire diagonally transverse a blood vessel in a manner such that the active layer lies fully within the blood vessel while the ends project such that the two loops lie fully exterior to the blood vessel. The device is anchored in place with respect to the blood vessel by suturing to the blood vessel through the loops at the end of the wire.

BRIEF DESCRIPTION OF THE DRAWINGS

An understanding of the features and operation of the present invention can be obtained from a reading of the following description and with reference to the drawing which is a sectional view through a blood vessel showing the device partially in section implanted in accordance with the present invention.

DETAILED DESCRIPTION OF THE INVENTION

Referring now to the drawing, there is shown a device in accordance with the present invention implanted through a blood vessel. A wire indicated generally at **11** includes a straight section **12** and two loops **14** and **16**, one located on each end of the straight section **12** of the wire **11**. Loops **14** and **16** are oppositely facing loops, meaning these loops lie on or project from opposite sides of straight section **12**.

The central portion of the straight section **12** of the wire **11** has deposited thereon an active radioisotope-

layer **18.** A coating-layer **20** coats the central portion of the straight section **12** and sealingly covers the radioisotope-layer **18** so as to prevent any leaking of the radioisotope from the device into the bloodstream.

The device is shown as implanted in a blood vessel **22.** The device is adapted for implantation diagonally transverse blood vessel **22** and is implanted in a manner such that active layer **18** lies fully within blood vessel **22,** i.e., active layer **18** lies within the interior **24** of the blood vessel **22** between the walls thereof. The device is further implanted such that the loops **14** and **16** at the two ends of the straight section **12** lie fully outside and exterior to the blood vessel **22.** The device is anchored in place with respect to the blood vessel such as by sutures **26** and **28** through loops **14** and **16,** respectively. The device is anchored in order to prevent the undesirable loss of the device in the body and to prevent undesirable movement relative to the blood vessel **22.**

The active radioisotope-layer **18** can be deposited on the center portion of the wire in any manner known and practiced in the art including, among others, electroplating from a solution containing the radioisotope. Similarly, the coating-layer can be deposited over the active radioisotope-layer in various manners well known in the art including, among others, vacuum sputtering of a metal. Following depositing of the coating-layer and prior to implantation, the device must be sterilized, sterilization by gamma irradiation being one of the many possible methods which can be employed. The device is then implanted in a blood vessel by surgically inserting the device so as to lie diagonally transverse the blood vessel, as described hereinabove. While various means of surgical implantation can be used, two examples of surgical methods which have been found particularly adaptable to the present device are insertion through the blood vessel in a hypodermic needle followed by withdrawal of the hypodermic needle, leaving the device in place, and insertion of the device across the blood vessel through two surgical incisions in the wall of the blood vessel, the incisions being made on opposite sides of the blood vessel and diagonally spaced so as to accommodate the device diagonally thereacross. If the device is implanted by the latter method wherein incisions are made in the blood vessel wall, the sutures used to close the surgical incisions in the blood vessel can also be employed to anchor the device in place with respect to the blood vessel by making the sutures through the loops on the respective two ends of the straight section.

This device offers versatility in that the choice of the radioisotope to be used can be made based upon the desired intensity of radiation and the desired energy of radiation. Since the coating-layer can be made very thin as by vacuum sputtering a metal, it is possible to use either alpha emitters or beta emitters for the radioisotope. Since the device is inserted directly into the bloodstream and is surrounded by blood, extensive radiation shielding is not required, as the radiation emitted will be absorbed by the blood itself with no damage to surrounding tissues. This device permits surgical implantation by means of much simpler surgical procedures and is therefore far less traumatic than other known implantation procedures.

DESCRIPTION OF PARTICULAR EMBODIMENT

While the invention is hereinafter described in connection with a particular specific embodiment, it will be understood that it is not intended to limit the invention to only that specific embodiment, but it is intended to cover all alternatives, modifications and equivalents as may be included within the spirit and scope of the invention as defined by the appended claims.

A device was constructed and implanted in accordance with the present invention. The device was formed of a Type 302 stainless steel spring wire 0.010 inch in diameter and just over 2 inches long. The wire was formed with opposing 0.040-inch-diameter loops at each end, the centers of the loops being 2 inches apart.

The wire was ultrasonically cleaned in approximately 10 percent solution of Delex -- a commercial detergent -- and ultrasonically rinsed in distilled water twice, followed by a tripple rinse in reagent-grade acetone, and thoroughly air-dried.

A layer of $^{238}PuO_2$ was electroplated on the center 1 inch of the straight section of the wire. Electroplating was based on procedures recommended by Handley and Cooper, *Analytical Chemistry*, Vol. 41, No. 2, February 1969, page 381. Similar procedures have been used in the past for production of standard samples of other radioactive actinides.

The electroplating cell was filled with approximately 10 cc of dimethyl sulfoxide. A D-C power supply was connected to a platinum anode and the irradiator wire serving as a cathode with small alligator clips. A magnetic stirrer was adjusted to rotate the stirring bar such as to give good mixing without causing a noticeable vortex in the liquid. 80 micrograms of dried $^{238}PuO_2$ was dissolved in 25 microliters of 6 N nitric acid and transferred to the cell. The power supply was adjusted so as to apply 3.5 volts across the cell and adjusted so that the current flow through the cell was 0.1 milliamp. The current was applied and continued for 20 minutes. In order to prevent redissolution of some of the $^{238}PuO_2$, the liquid was decanted with a syringe to below the level of the wire before reducing the voltage.

While the current, voltage and electrode spacing are probably not critical and are interdependent as in any cell, in order to obtain very smooth deposits, it is important to adjust the current flow and stirring speed to prevent the formation of bubbles on the wire. On previous attempts using higher voltage and current, a few bubbles were produced on the wire, resulting in deposits which appeared thicker to the naked eye and were black. On microscopic examination, these deposits were found to be rough with high peaks and with the appearance of a sponge. On such a deposit, a containment layer thick enough to assure a nonsmearable device would cause a large reduction in available alpha energy.

In the present example, after removal of the wire from the cell, the wire active area deposit had the appearance of a satinfinished stainless steel with a slight brownish tint, very similar to a mildly baked stainless-steel vacuum system. An examination through a high-powered reading glass showed a smooth velvety deposit apparently well adhering and of high density. At this time, the alpha radiation level from the wire was measured using a "yellow face Juno" and a reading of approximately 60 rads per hour uncorrected as read on the Juno was obtained.

Sputter deposition of each coating or containment layer was done in two steps in a MRC Model 8620 RF sputtering system located in a glove box. The active wire was mounted on a simple holding fixture consisting of two support wires silver-brazed to a 5-inch stainless steel disk and bent to support the wires 1/4 inch above the disk. It was necessary to open the chamber and to turn the wire over to sputter the containment on the reverse side. The chamber was evacuated to 3×10^{-7} Torr before back-filling to 4.5 millitorr of argon. The first platinum containment layer of approximately 7,500 A was sputter-deposited at a power of 250 watts on a 5-inch-diameter target, zero bias, 800 volts RF peak to peak. The 7,500 A estimate is based on deposition rates for platinum previously established at 3.22 microns per hour at 500 watts by metallographic techniques. The chamber was vented to argon, opened, the wire turned over, and pumped down and platinum sputtered on the other side.

After the first complete containment layer had been sputtered on, the wire was removed to an open-faced hood and smearability and activity checked. After a light rub on the wire, a Q-tip counted 200–300 disintegrations per minute. Alpha activity on the yellow face Juno had dropped to 25 rads per hour uncorrected. The wire was then carefully rubbed with tweezer tips which had been wrapped with optical lens paper in order to knock off any high peaks of plutonium oxide.

The wire was then placed back in a sputtering chamber and approximately 3,500 A of platinum was deposited using the same sputtering conditions as for the first containment layer. After sputtering, the wire was smeared with Q-tips and facial tissue and only background count was noted, which is less than **25** disintegrations per minute. The alpha activity as read on the yellow face Juno was 12.5 rads per hour on one side and **15** rads per hour on the other side.

An alpha-energy analysis was run on the completed device, using a 400-channel alpha-energy analyzer. The results showed the absence of any alphas having the 5.5 MeV energy characteristic of Pu^{238}, which was convincing evidence that the activity is contained until such time that the platinum containment is either damaged through handling or eroded away by the blood flow. A peak was located at about 4.82 MeV and calculation of the thickness of the containment layer based on the energy analysis indicated a thickness in reasonable agreement with that projected from the deposition rate data.

Following sterilization with 400,000 rads of gamma radiation, the device was implanted in a beagle dog. In the present case, insertion was accomplished, while the dog was anesthetized as for any surgery, by passing a long steel needle obliquely through the artery and drawing the irradiator device through the needle by means of a suture thread and suturing, through the loops of the device at both ends, to the wall of the blood vessel following removal of the steel needle. With this technique, there is little disturbance of the blood vessel. Radiographs taken subsequent to implantation showed the wire continuing in place. The other surgical procedure contemplated for use with the present device will be to dissect the descending aorta, make two small slits on opposite sides of the blood vessel and 2 inches diagonally apart, insert the wire and anchor it with sutures also used to close the slits. This procedure is much simplified over the previously used method of removing a part of the aorta and suturing in its place a multilayered tube with woven fiber ends.

Two of the devices were implanted in dogs. The first device was nonradioactive and was implanted to develop techniques and to check thrombic effects of the wire itself. The device with the radioactive layer was subsequently implanted. After 65 days, there was no gross evidence of thrombic effect in either animal but total absence of clotting can be confirmed only after the animal is sacrificed. While Pu^{238} was used as the source in the present instance, it is possible that because of the very short range of alpha particles and the difficulty of detecting any leakage, should a leakage subsequently develop, it is possible that beta emitters will prove to be preferable as the active radioisotope. A beta emitter would provide a radiation which is sufficiently penetrating to give a sufficiently high dose rate to the blood and yet is not so penetrating that it would be damaging to surrounding tissue. Use of more penetrating beta radiation would also have the advantage that a thicker containment layer could be used, insuring its integrity and containment of the radioisotope without reducing the radiation level to unacceptably low values.

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. An in-vivo radioisotope blood irradiator for in-vessel radiation treatment of blood comprising: a wire including a straight section and a small oppositely facing loop at each of the two ends thereof; an active radioisotope-layer deposited over the center portion of said straight section of the wire; and a coating-layer sealingly covering said active radioisotope-layer; said wire adapted for implantation diagonally transverse a blood vessel in a manner so that said active layer lies fully within said vessel and said ends project such that said two loops lie fully exterior to said vessel.

2. The blood irradiator of claim **1** further comprising suture means associated with each of said loops for anchoring said wire with respect to said blood vessel.

3. The blood irradiator of claim **1** wherein said wire is stainless steel spring wire about 0.01 inch in diameter and slightly in excess of 2 inches in length, said loops are about 0.04 inch in diameter, the centers of said two loops are about 2 inches apart, and the active radioisotope-layer is deposited over the center **1** inch of said wire.

4. The blood irradiator of claim **3** wherein said active radioisotope-layer comprises $^{238}PuO_2$ and said coating-layer comprises platinum.

5. A method for in-vivo radiotherapy of blood by irradiation of the blood within a blood vessel comprising:

a. depositing a layer of an active radioisotope on the center portion of a wire which includes a straight section and a small oppositely facing loop at each of the two ends thereof;

b. depositing a coating-layer over said active radioisotope-layer so as to sealingly cover said radioisotope;

c. sterilizing said wire; and

d. implanting said wire in said blood vessel by surgically inserting the wire diagonally transverse said blood vessel in a manner so that said active layer lies fully within said vessel and said ends project

such that said two loops lie fully exterior to said vessel.

6. The method of claim 5 further comprising: suturing through said loops to anchor said wire with respect to said blood vessel.

7. The method of claim 5 wherein a layer of $^{238}PuO_2$ is deposited on the center portion of a stainless steel wire by electroplating from a solution containing $^{238}PuO_2$ and a thin coating-layer of platinum is deposited over said $^{238}PuO_2$ by vacuum sputtering.

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