(12) UK Patent Application (19) GB (11) 2 125 986 A

(21) Application No 8322218
(22) Date of filing 18 Aug 1983
(30) Priority data
(31) 57/151403
(32) 31 Aug 1982
(33) Japan (JP)
(43) Application published
14 Mar 1984
(51) INT CL³
A61B 17/32
(52) Domestic classification
G2J E
A5R EW
(56) Documents cited
GBA 2076993
GBA 2074343
GBA 2023004
GB 1573748
GB 1378986
GB 1320170
GB 1135956
GB 1073619
GB 1045868
(58) Field of search
G2J
A5R

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(54) Endoscope device for the treatment of cancers

(57) A device for the treatment of cancers comprising a pulsed laser beam source (24), an image detecting means (27, 28, 29, 32, 35, 36, 37) and an endoscope (21) which is arranged to transmit the pulsed laser beam from the pulsed laser beam source and to direct that beam onto a cancer focus (A) there to sterilize the cancerous cells. The endoscope (21) also serves to transmit light from the cancer focus (A) and the surface of the affected organism to the image detecting means (27, 28, 29, 32, 35, 36, 37) to enable diagnosis and observation of the cancer focus to be made.

FIG. 2

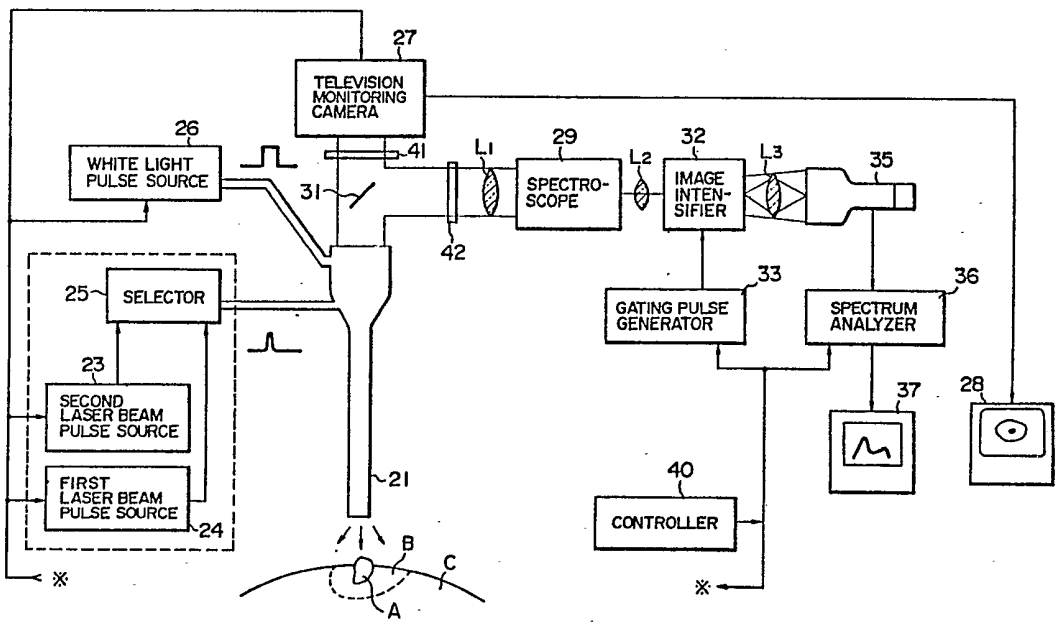

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FIG. 1

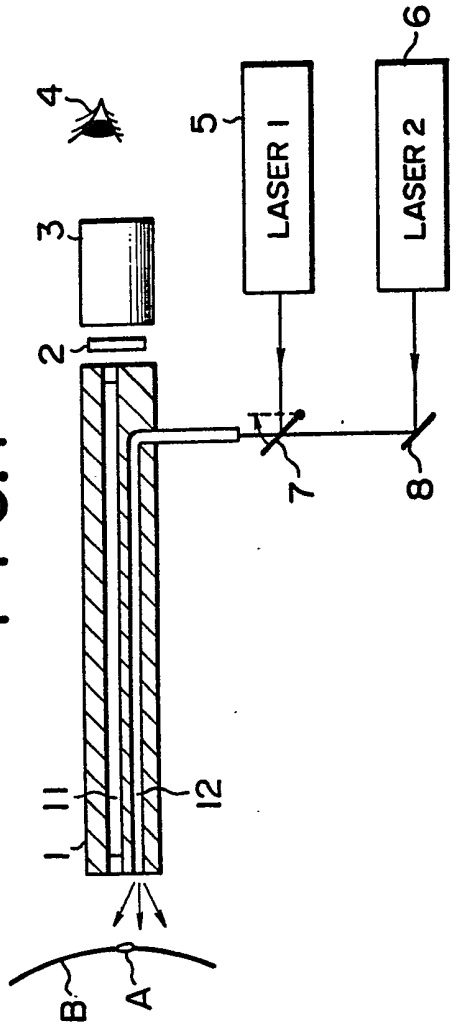


FIG. 3

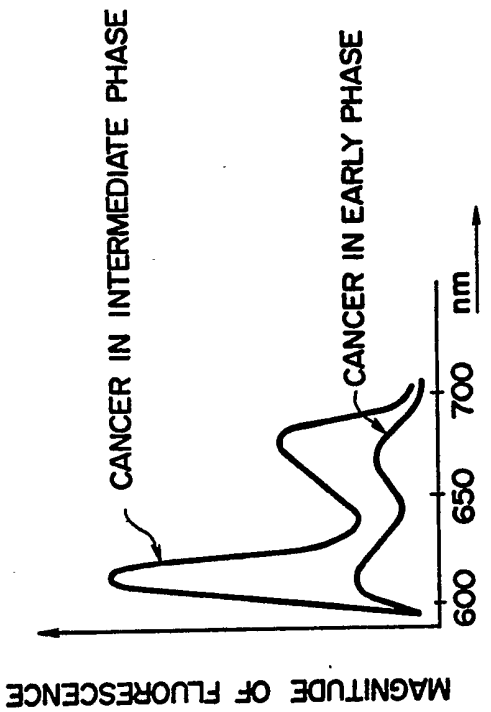


FIG. 4

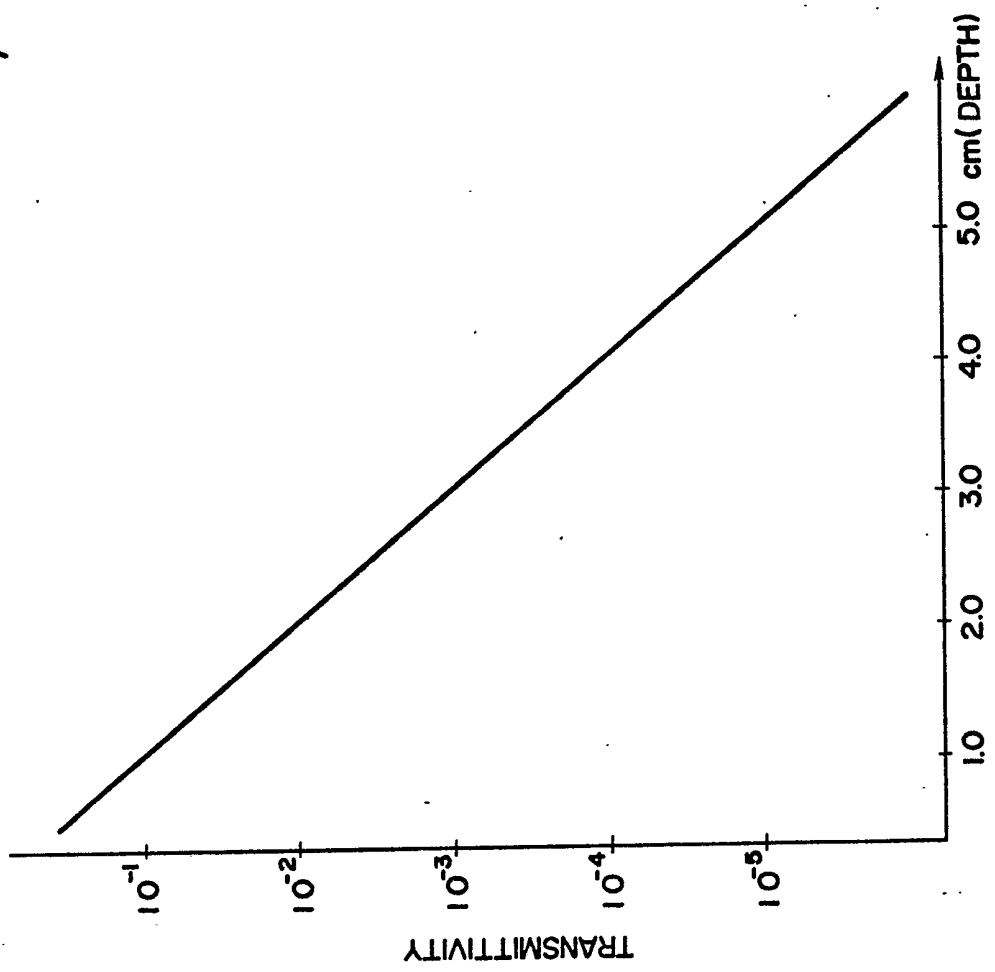


FIG. 2

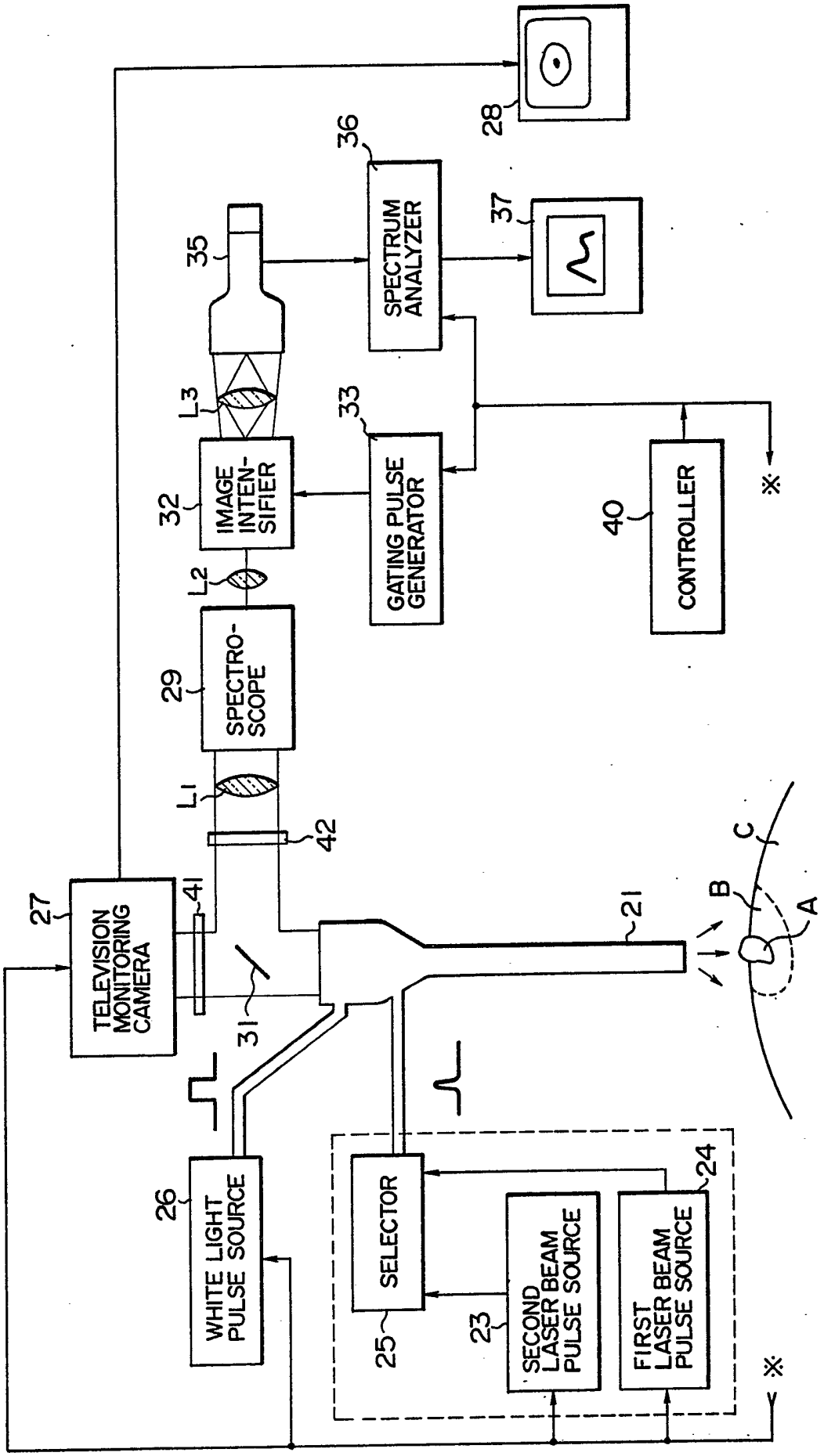

28
36
SPECTRUM ANALYZER
37
35
L3
33
GATING PULSE GENERATOR
32
IMAGE INTEN-SIFIER
40
CONTROLLER
※
L2
29
SPECTRO-SCOPE
L1
42
27
TELEVISION MONITORING CAMERA
41
31
21
C
B
A
26
WHITE LIGHT PULSE SOURCE
SELECTOR
25
23
SECOND LASER BEAM PULSE SOURCE
FIRST LASER BEAM PULSE SOURCE
24
※

FIG. 5

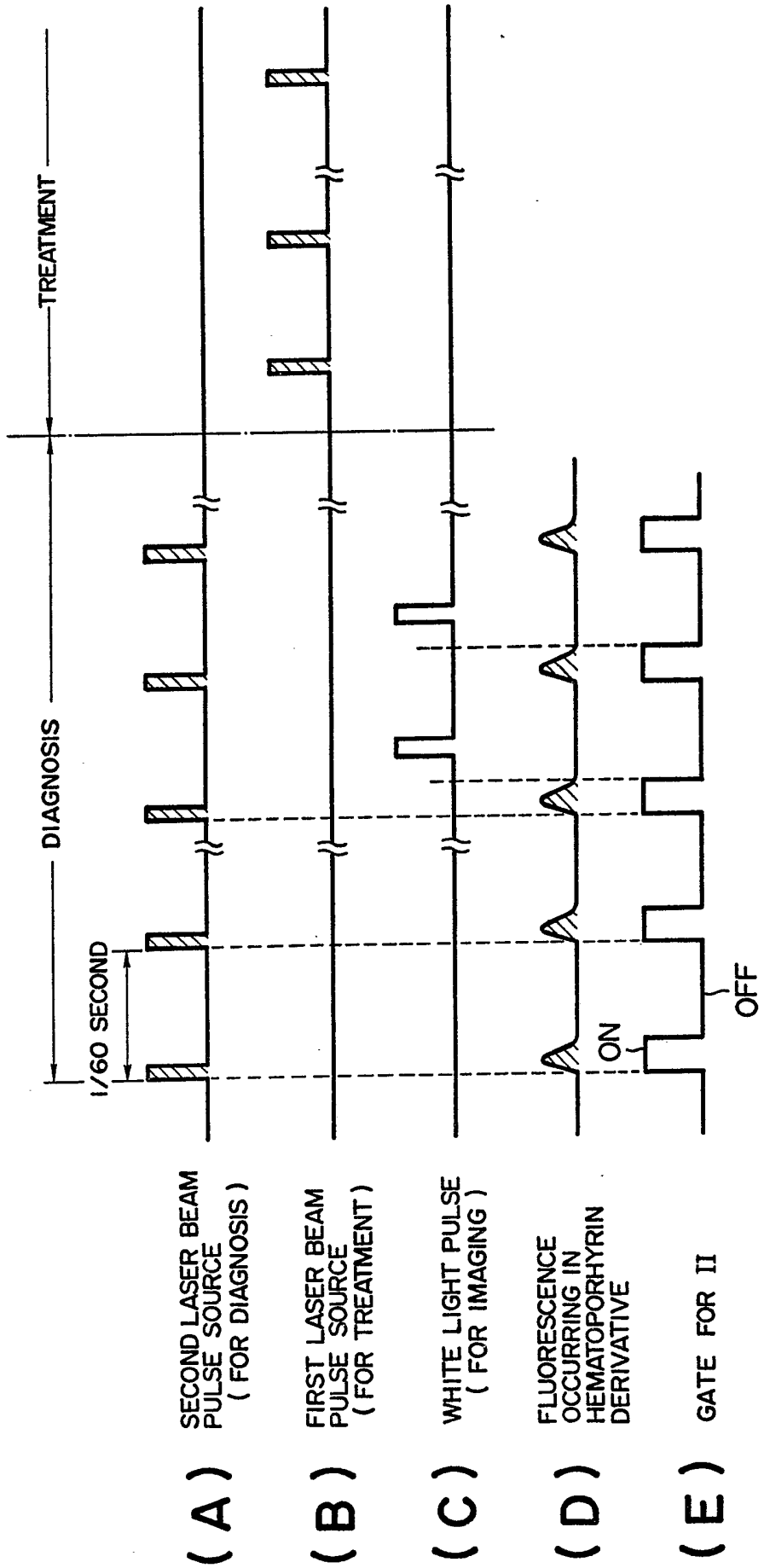
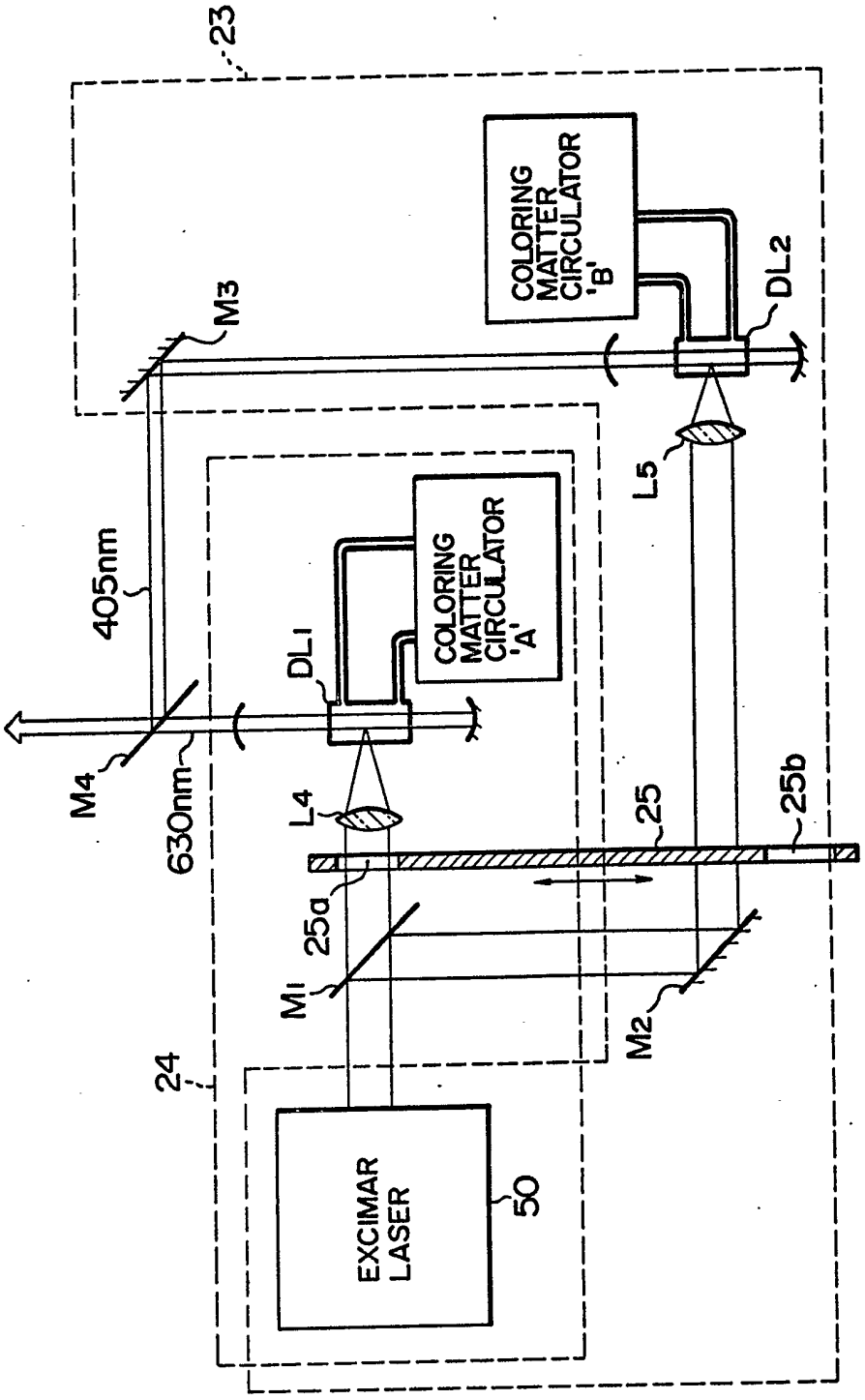

TREATMENT
DIAGNOSIS
1/60 SECOND
(A) SECOND LASER BEAM PULSE SOURCE (FOR DIAGNOSIS)
(B) FIRST LASER BEAM PULSE SOURCE (FOR TREATMENT)
(C) WHITE LIGHT PULSE (FOR IMAGING)
(D) FLUORESCENCE OCCURRING IN HEMATOPORHYRIN DERIVATIVE
(E) GATE FOR II
ON
OFF

FIG. 6


23
COLORING MATTER CIRCULATOR 'B'
DL2
M3
L5
405nm
COLORING MATTER CIRCULATOR 'A'
DL1
M4
630nm
L4
25
25b
25a
M1
M2
24
EXCIMAR LASER
50

5/7

FIG. 7

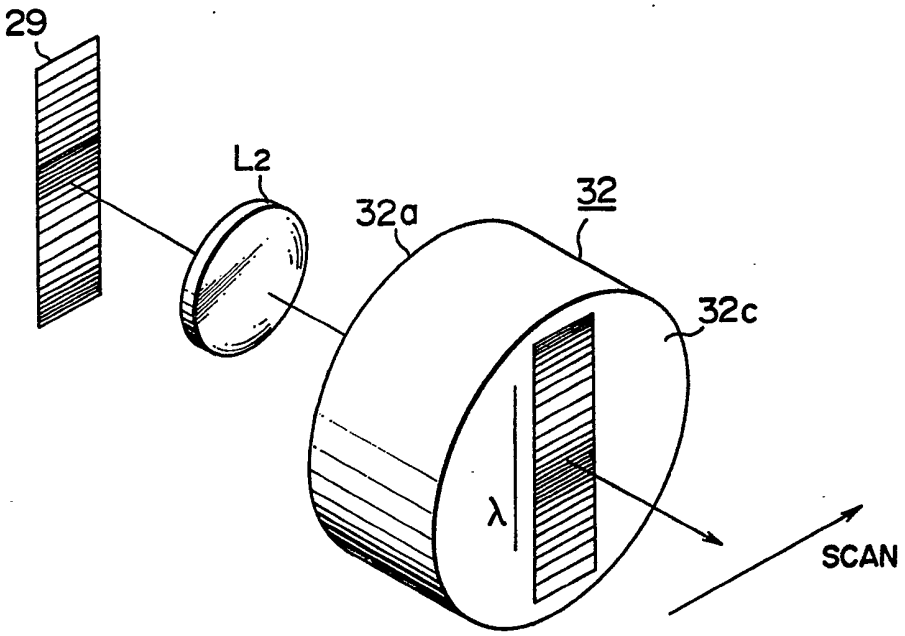
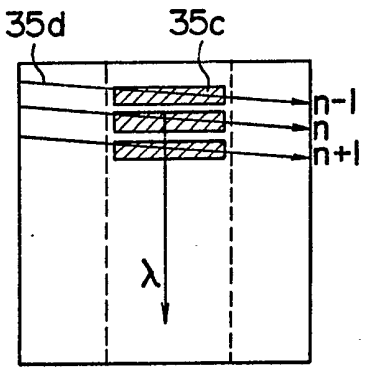


FIG. 9



6/7

FIG. 8

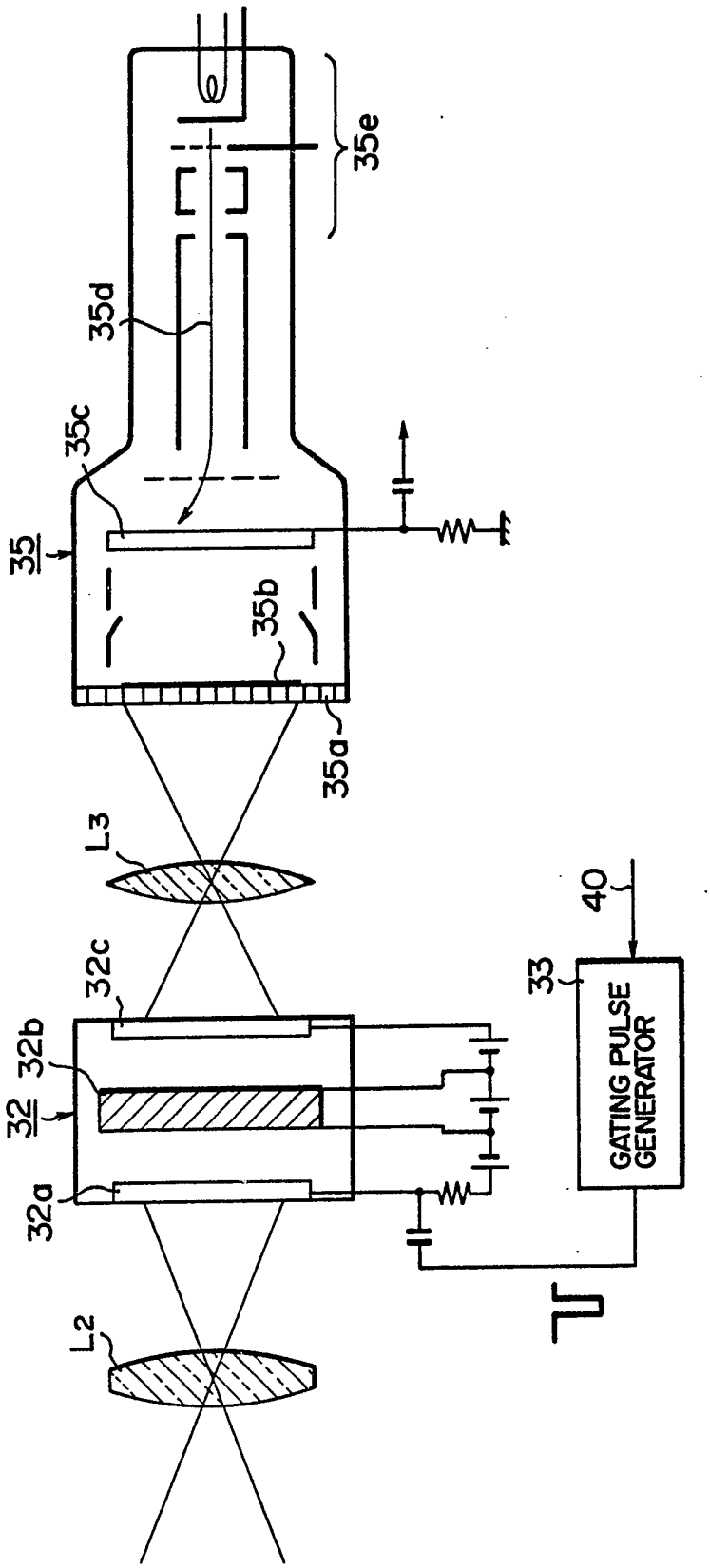

35e
35d
35c
35
35b
35a
L3
32c
32b
32
32a
L2
40
33
GATING PULSE GENERATOR

FIG.10(A)

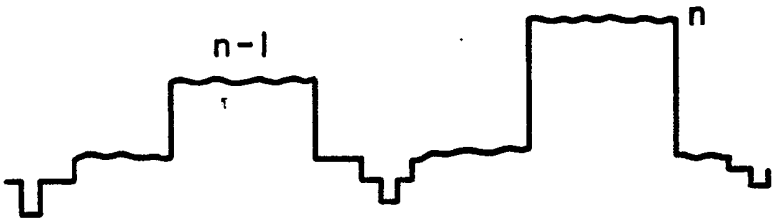


FIG.10(B)

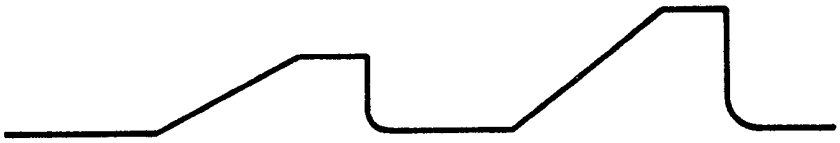
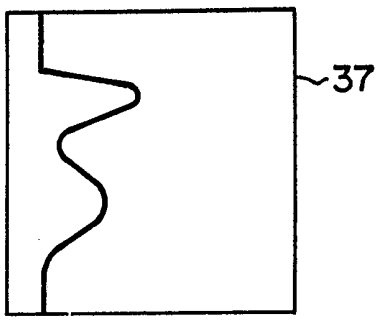


FIG.11



SPECIFICATION

Device for the treatment of cancers

This invention relates to a device for use in the treatment of cancer foci, and particularly to such devices which may be used to direct a laser beam upon a cancer focus at which a photo-sensitive material such as a hematoporphyrin derivative having an affinity to cancer foci and other tumors has beforehand been absorbed.

Continuous krypton laser beams have been used for cancer diagnosis, and continuous argon laser beams have been used for treatment of cancer foci. Devices for these purposes have been proposed in for example Japanese Utility Model Application Publication No 64307/1983 (filed by Yoshihiro Hayata, Katsuo Aizawa and Harubumi Kato).

Figure 1 of the accompanying drawings shows a schematic diagram of the device described in the above mentioned Japanese Utility Model application. Before the use of the device to diagnose cancer a hematoporphyrin derivative is absorbed at the focus A and the peripheries B of the cancer. In operation the endoscope 1 is directed towards the focus A and its peripheries B and a visible krypton laser beam from beam source 5 is selectively transmitted through mirror 7 to light pipe 12, and emerging therefrom is incident upon focus A and its peripheries B. An image of focus A and its peripheries B is observed by the transmission of light from the focus and its peripheries along image guide 11 to image intensifier 3 through a bandpass (color) filter 2.

From the treatment of the diagnosed cancer, a visible laser beam from an argon dye laser source 6 is transmitted through light pipe 12 and onto the affected site.

This device permits cancer diagnosis and treatment to be carried out in a new mode. However, the argon laser beam used for the treatment may not be able to penetrate the affected site by a distance sufficient to treat the focus of the cancer as such foci may be well within the body rather than close to the body surface.

Treatment with an argon dye laser beam can be achieved at approximately 5 mm below the body surface as described in "Laser Induced Photochemical Effects for Cancer Treatment" by Daisuke Kato, Laser Research, Vol. 10, No. 2, pp. 165—172 (May 1982). Thus it has not been easy to eradicate a cancer completely from the body.

We have now found that the laser beam from a conventional continuous source is of insufficient energy to penetrate within a body sufficiently to treat a non-superficial cancer focus as the transmission of the beam to the focus decreases exponentially with increasing depth of the focus within the body. However we have now surprisingly found that not only can sufficient penetration to treat a non-superficial focus be achieved with a pulsed laser source which emits a beam of higher energy (during the pulses) than the energy of a conventional continuous beam but the use of such pulsed beams also serves to increase the concentration of a reactant for the photochemical sterilization reaction and the rate of the reaction.

We obtained the transmittivity data of an organism exposed to a laser beam and correlated this data with the depth within the organism to which the beam could penetrate sufficiently to treat a cancer. This data correlation is illustrated in Figure 4 of the accompanying drawings.

The mechanism of the photochemical reaction and its sterilization of cells affected by cancer appears not to have been analyzed thoroughly for the case of cells in which hematoporphyrin derivatives have been absorbed.

Our investigations showed that the reaction velocity of the photochemical reaction occurring within a time interval between laser beam pulses generally increases with the instantaneous magnitude (i.e. the energy during pulse) of the laser beam. The photochemical reaction generally appeared to have a non-linear effect on cancer affected cells with the amount of a reactant increasing with the instantaneous magnitude of the laser beam.

The objective of the present invention is therefore to provide a cancer treatment device providing an increased attainable depth by use of a laser pulse beam source as an emitter thereby allowing substantially complete eradication of superficial and non superficial cancers.

According to the invention there is provided a device for the treatment of cancers comprising a light source, an image detecting means and an endoscope, said endoscope being arranged to transmit a light beam generated by said light source to a light transmitting exit of said endoscope and to transmit light incident on said endoscope at or near said exit to said image detecting means, wherein said source comprises a pulsed laser beam source.

The cancer treatment device in accordance with the present invention suitably contains an endoscope comprising a light pipe used to transmit the light beams from the light source and an image guide used to observe the flesh of the organism during both diagnosis and treatment. The tip of the endoscope is faced to the foci where a photosensitive material having an affinity to cancer foci has been absorbed so that a treatment for cancer can be performed by exposing the organism affected by cancer to the pulsed laser beam.

In a preferred embodiment the device of the invention further comprises a pulse laser, suitably an excimer laser, arranged to stimulate a dye laser capable of emitting at approximately 630 nm when so stimulated. 630 nm is a particularly effective wavelength for cancer treatment.

A preferred embodiment of the device of the invention will now be described by way of example with reference to the accompanying drawings, in which:—

Figure 1 shows a schematic diagram of a conventional cancer diagnosis and treatment device;

Figure 2 is a block diagram of a preferred embodiment of the cancer treatment device in accordance with the present invention;

Figure 3 is a graph showing fluorescence spectra for cancer foci in which a hematoporphyrin derivative is absorbed;

Figure 4 is a graph showing the attainable depth of a laser beam within an organism;

Figure 5 depicts a timing chart showing the operation of a cancer treatment device in accordance with the present invention;

Figure 6 is a block diagram showing the structure of the laser beam pulse sources of a device in accordance with the present invention;

Figure 7 is a perspective view of an image on the photoelectric layer of an image intensifier of a device in accordance with the present invention;

Figure 8 is a schematic diagram showing the image intensifier and imaging tube of a device in accordance with the present invention;

Figure 9 depicts a schematic diagram showing the relation of the spectral response to the scanning lines in the television monitoring system of a device in accordance with the present invention;

Figure 10 shows waveforms of a signal and its integrated signal in the (n-1)th and nth scanning lines of Figure 9; and

Figure 11 shows an example of a spectral response obtained by use of a device in accordance with the present invention.

Figure 2 shows a block diagram of a preferred embodiment of the cancer treatment device in accordance with the present invention. Marks A, B and C represent a cancer focus, its peripheries, and the unaffected flesh of an organism respectively.

A hematoporphyrin derivative with a pH of 7.4 formed by dissolving hematoporphyrin hydrochloride, which has an affinity to cancer foci, in a mixture of sulfuric acid and acetic acid is used as a solution for intravenous injection. Prior to diagnosis and treatment, this hematoporphyrin derivative is injected into the vein of the patient.

The hematoporphyrin derivative is a substantially harmless material which is selectively absorbed in the parts of an organism affected by cancer but not in those parts of the organism which are not affected by cancer.

When a laser beam pulse with a wavelength of approximately 405 nm is incident upon the hematoporphyrin derivative absorbed in the cancer foci, fluorescence occurs at wavelengths of both 630 nm and 690 nm. The cancer foci can be diagnosed by the use of these characteristic fluorescence emissions in the manner described below.

Endoscope 21 contains a light pipe to transmit the light pulse to be incident upon the cancer foci and its peripheries and an image guide by which light from the cancer foci incident on the endoscope is transmitted to an image detecting means.

The preferred embodiment of the cancer treatment device is provided with a first laser beam pulse source 24 used for a treatment, a second laser beam pulse source 23 for a precise diagnosis, and a white light pulse source 26 for overall diagnosis.

In operation visible light from the first or second laser beam pulse source 24 or 23 is selectively applied to a light pipe and white light from the white light pulse source 26 is applied to another light pipe. This visible light is then directed through endoscope 21 onto the cancer focus.

Figure 6 shows an example of first and second laser beam pulse sources 24 and 23. In Figure 6, the first laser beam pulse source which is capable of emitting visible light at 630 nm is shown enclosed within broken line 24 and the second laser beam pulse source which is capable of emitting visible light at 405 nm is shown enclosed within broken line 23.

In the arrangement shown an excimer laser 50 is used to stimulate both first and second laser beam pulse sources 24 and 23. The first laser beam pulse source 24 contains a first dye laser DL1 which comprises a solution of rhodamine 610 in ethanol and can emit visible light at 630 nm when stimulated by excimer laser 50. The second laser beam pulse source 23 contains a second dye laser DL2 which comprises a solution of PBBO (2-(4-biphenylyl)-5-phenylbenzoxazole) in a mixture of toluene and ethanol and can emit visible light at 405 nm when stimulated by excimer laser 50. L4 and L5 are condenser lenses, M1 and M4 are semi-transparent mirrors, M2 and M3 are total reflection mirrors, and selector 25 is a shutter with two openings 25a and 25b which can manually be operated. During the use of the device of the invention to treat a cancer focus, dye laser DL1 is stimulated by the laser beam which passes from excimer laser 50 along a light path formed by opening 25a and lens L4. Dye laser DL2 is stimulated by the laser beam which passes from excimer laser 50 along a light path formed by opening 25b and lens L5.

Excimer laser 50 can emit light pulses with energy ranging from several milli-joules to 100 milli-joules with a pulse width of 30 ns at a wavelength of 308 nm at a repetition rate of 60 Hz or a fraction of 60 Hz.

The light beam at a wavelength of 630 nm selected as the first laser beam pulse is not readily absorbed by living tissue; however light of 630 nm wavelength is efficiently absorbed by the hematoporphyrin derivative which is absorbed into the cancer affected tissue.

When light of wavelength 405 nm from the second laser beam pulse source 23 is directed onto a cancer focus at which the hematoporphyrin derivative is absorbed, fluorescence occurs. Figure 2 shows fluorescence spectra for cancer foci in the early and intermediate stages of development.

For general observation and diagnosis visible

light from the white light pulse source 26 may be directed through the second light pipe of the endoscope and onto the body surface. Images of portions A and B can be observed under the light from the white light pulse source 26, and these may be displayed on a television picture monitor as described hereinafter.

The entire cancer treatment device shown in Figure 2 is controlled by controller 40 which can generate a basic timing signal clocked at 60 Hz so that excitation of laser beam pulse sources, reproduction of images, and spectrum analysis can synchronously be performed. The basic timing signal will be described later with the explanation of the operation of the device.

A semi-transparent mirror 31 is place facing the outlet of the image guide in endoscope 21. Light from the image guide passes through or is reflected by the semi-transparent mirror 31. Light passing through the semi-transparent mirror 31 passes into television camera 27 through shutter 41 which is opened only during diagnosis. An image of portion A or B obtained by the laser beam from the second laser beam pulse source 23, the light pulse from white light pulse source 26, or from both of these pulses can be picked up by the television monitoring camera 27 during diagnosis and can be displayed on television picture monitor 28. Light reflected from the semi-transparent mirror 31 passes into spectroscope 29 through shutter 42 and condenser lens L1. Spectroscope 29 is used to analyze the image of portion A or B. An image from spectroscope 29 is incident upon photo-electric layer 32a of image intensifier 32 through condenser lens L2. Figure 7 depicts a schematic diagram showing how the image from spectroscope 29 is incident upon the photoelectric layer of image intensifier 32.

Image intens...
of the images of the cancer foci from photoelectric layer 32a to phosphor layer 32c through a microchannel plate 32b which is shown clearly in Figure 8.

Figure 8 shows the locational relation between image intensifier 32 and SIT (silicon intensified target) imaging tube 35. SIT imaging tube 35 consists of a faceplate 35a, a photo-electric layer 35b formed on the inner face of faceplate 35a, an image target 35c, and an electron gun 35e and is used to generate a graphical signal of the spectral response. The image formed on image target 35c, which corresponds to that impinging on photoelectric layer 35b of imaging tube 35, is scanned by electron beam 35d. Figure 9 shows the relation between the electron beam and spectra. The output of imaging tube 35 which is issued every scanning line is integrated by spectrum analyzer 36 and displayed on display unit 37.

Figure 10(A) shows the video signal in the (n-1)-th and n-th scanning lines of Figure 9 and Figure 10(B) shows the integrated signal in each scanning line for spectrum analyzer 36. In these figures, the magnitude of the spectral response at the wavelength corresponding to the n-th scanning line is greater than that corresponding to the (n-1)-th scanning line, that is, the magnitude of the spectral response in the corresponding line is determined by integrating the corresponding spectral response sampled in accordance with the spatial relation. The total integrated signal is shown in Figure 11, and it can be output as digital data after being converted by an A/D converter.

Operation of the cancer treatment device in accordance with the above-mentioned configuration will be described by referring to the operation of the controller 40.

The cancer treatment device can operate in three modes: a first diagnosis mode in which cancer can be detected; a treatment mode in which, following absorption of a hematoporphyrin derivative into the cancer focus, the cancer can be eradicated from an affected organism by irradiation with laser beam pulses from the first laser beam pulse source 24; and a second diagnosis mode in which healing from cancer after treatment is completed can be confirmed.

Mode selection can be performed in a cyclic way.

Figure 5 shows a timing diagram for light pulse emission from the first and second laser beam pulse sources and white light pulse source, and for image pick up for the diagnosis and treatment operation modes. The pulse sources 23, 24, 26 are synchronously operated by controller 40 so as to emit light pulses synchronizing with the vertical drive at 60 Hz in the television monitoring system.

In the first and second diagnosis modes, visible light from second laser beam pulse source 23 is emitted at a wavelength of approximately 405 nm with a pulse width of approximately 30 ns during vertical blanking in the television monitoring system, synchronizing with said vertical drive.

Fluorescence occurs in cancer foci into which a hematoporphyrin derivative has been selectively absorbed when the foci are irradiated by the laser beam from the second laser beam pulse source 23. Fluorescent light emitted from the cancer foci and incident on the endoscope is analysed by the spectroscope assembly (29, 32, 33, 35, 36, 37) enabling a diagnosis to be performed with minimal background radiation resulting from diffused light and fluorescence from unaffected sites in the organism.

In Figure 5, (D) and (A) show the timing relation of fluorescence occurring in the cancer focus as a result of stimulation by the laser beam pulses from the second laser beam pulse source 23.

(E) and (D) in Figure 5 show the time periods when the gate of image intensifier (II) 32 is open and the timing relation between these open periods and the fluorescence emission from the cancer focus. As the gate is open only during fluorescing periods, noise from background radiation is minimized.

An image of the cancer obtained when the focus is lit by white light, may be used to make a qualitative diagnosis based upon visual perception.

The white light pulses are emitted between the

light pulses from the second laser beam source 23, the relative timing relation being as shown in (A) and (C) of Figure 5.

A precise diagnosis can be made using a graph of the spectral response, and a qualitative decision can be made by using television picture monitor 28.

Treatment of the cancer foci is carried out by irradiation with laser beam pulses from the first laser beam pulse source 24.

The advantages of the cancer treatment device in accordance with the present invention over the conventional devices are expected to comprise the following:

The increased energy of the laser beam obtained by use of pulsed laser beam sources results in increased penetration into an organism, and thus enables cancer foci in a location deep in an organism to be treated.

We have confirmed by experiment that cancer foci in a mouse were sterilized by irradiating, through a piece of pork with a thickness of 50 mm, with a 630 nm wavelength pulsed laser beam obtained by stimulating a rhodamine 610 dye laser with pulses of energy 100 mJ/pulse from a XeCl gas excimer laser. The reason for the use of pork was that the flesh of the human body is similar to pork in terms of laser beam transmission.

Thus cancer foci in a location deep in an organism, e.g. in the lungs, can be sterilized by the cancer treatment of the present invention.

CLAIMS

1. A device for the treatment of cancers comprising a light source, an image detecting means and an endoscope, said endoscope being arranged to transmit a light beam generated by said light source to a light transmitting exit of said endoscope and to transmit light incident on said endoscope at or near said exit to said image detecting means, wherein said source comprises a pulsed laser beam source.

2. A device as claimed in claim 1 wherein the said light source is a source capable of generating a light beam of a wavelength that stimulates a sterilizing photochemical reaction in body tissue in which a hematoporphyrin derivative is absorbed.

3. A device as claimed in either of claims 1 and 2 wherein said light source comprises a dye laser capable of emitting at approximately 630 nm when stimulated by a pulse laser, and said device further comprises a pulse laser arranged to stimulate said dye laser.

4. A device as claimed in claim 3, wherein said pulse laser is an excimer laser.

5. A device for the treatment of cancers comprising a pulsed laser beam source substantially as herein described.

6. A device for the treatment of cancers comprising a pulsed laser beam source substantially as herein described with particular reference to Figures 2 and 5 to 11.

Printed for Her Majesty's Stationery Office by the Courier Press, Leamington Spa, 1984. Published by the Patent Office, 25 Southampton Buildings, London, WC2A 1AY, from which copies may be obtained.