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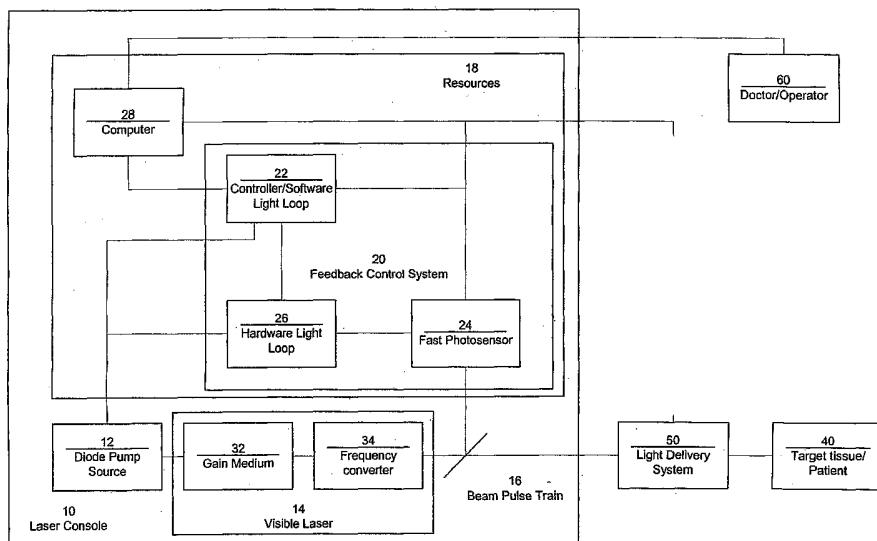
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(54) Title: LASER SYSTEM WITH SHORT PULSE CHARACTERISTICS AND ITS METHODS OF USE



(57) Abstract: A laser system that includes a diode pump source. A frequency doubled solid state visible laser is pumped by the diode pump source and produces a pulsed laser output with a train of pulses. Resources provide instructions for the creation of the pulsed output, with on and off times that provide for substantial confinement of thermal effects at a target site. This laser system results in tissue specific photoactivation (or TSP) without photocoagulation damage to any of the adjacent tissues and without causing full thickness retinal damage and the associated vision loss.

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LASER SYSTEM WITH SHORT PULSE CHARACTERISTICS AND ITS METHODS OF USE

BACKGROUND OF THE INVENTION

Field of the Invention:

5 This invention relates generally to laser systems, and their methods of use, that produce short and controlled pulse width trains, and more particularly to frequency doubled, cw laser systems, and their methods of use, that produce visible pulse trains of the appropriate pulselength, duty factor, and power to perform ophthalmology treatments currently being performed in the near-infrared.

10 Description of the Related Art:

Laser photocoagulation (PC) is the current standard of care for the treatment of certain retinal diseases such as diabetic macular edema (DME), proliferative diabetic retinopathy (PDR), extrafoveal, juxtafoveal and some types of subfoveal retinal neovascularization (SRNV). The laser PC protocols validated by the diabetic retinopathy study (DRS), the early treatment of diabetic retinopathy study (ETDRS) and the macula photocoagulation study (MPS) all provide evidence for the beneficial use of lasers. Most of these treatments have been conducted with visible lasers (green and red lasers). All of these laser treatments are based upon obtaining a visible endpoint as the optimal tissue reaction, which becomes visible during the laser treatment. These 20 laser pulsewidths are typically 50 to 300 milliseconds.

Current ophthalmic diode pumped solid state green lasers have pulsewidths of 10 to 60,000 milliseconds. This pulsewidth time domain is useful for the typical photothermal reactions normally requested in ocular Photocoagulation. In these applications the energy is absorbed by chromophores such as melanin or blood and 25 conducts away from the absorbing or pigmented layers into adjacent non-absorbing and non-exposed layers – thus causing thermal damage laterally and axially into the clear layers in addition to the pigmented layers.

Microsecond short pulsed visible lasers have been demonstrated by Pankratov, "Pulsed delivery of laser energy in experimental thermal retinal photocoagulation", Proc. 30 SPIE, V1202, pp. 205-213, 1990, Roider et. al., "Microphotocoagulation: Selective

effects of repetitive short laser pulses", Proc. Natl. Acad. Sci, V90, pp 8643-8647, 1993, Roider et. al., "Retinal Sparing by Selective Retinal Pigment Epithelial Photocoagulation", Arch Ophthalmol, V117, pp1028-1034, 1999, and US patent 5,302,259 by Birngruber issued in 1994. These short pulse laser treatments have 5 demonstrated beneficial effects while minimizing choroidal damage by using a pulse train with a low duty factor to confine the thermal effects to the absorbing layer or structure. Pankratov used an acousto-optical modulator to chop a continuous wave laser with pulse trains of 0.1 to 1.0 seconds and pulsedwidths from 10 to 900 microseconds. However, the longer pulsedwidths with high duty cycles behaved like 10 CW. Only the shorter pulsedwidths of 10 to 50 microseconds had beneficial effects of minimal to no visible lesions. The others used Q-switched green lasers with pulsedwidths of 1.7 to 5 microseconds.

The Q-switched lasers have been used for certain thermal confinement applications such as selective laser trabeculoplasty (SLT) treatment for Glaucoma and 15 selective retinal treatment (SRT) for clinically significant diabetic macular oedema (CSMO). In this case the energy is absorbed by the chromophores in such a short time that it cannot conduct away into adjacent tissue during the laser exposure time. The chromophore is heated to damaging levels and in certain cases will boil or explode – causing local mechanical damage in addition to the thermal damage to adjacent 20 tissues. For these treatments, thermal confinement (or lack of thermal conduction) can only be achieved for pulses shorter than the time constant of the absorbing layer, which is on the order of 1 to 30 microseconds for the retinal pigment epithelium (RPE).

Pioneering studies using Near-Infrared (NIR) diode lasers to treat retinal diseases without using the full energy of the traditional PC laser applications have been 25 shown by Reichel et. al., "Transpupillary Thermotherapy of occult subfoveal choroidal neovascularization in patients with age-related macular degeneration", Ophthalmol, V106, pp1908-1914, 1999 and by Mainster, et. al., "Transpupillary Thermotherapy: long-pulse photocoagulation, apoptosis and heat shock proteins", Ophthalmic Surg lasers, V31, pp359-373, 2000. These laser treatments use energies below the 30 threshold of visible tissue reaction. Procedures using these treatments are called Minimum Intensity Photocoagulation or MIP procedures. The loss of vision associated

with the traditional PC treatments is mitigated due to the lower energies being used and thus not coagulating the retina photoreceptors in the neighboring clear layers.

There are two variations of these MIP treatments – one is called Transpupillary ThermoTherapy or TTT. This performs a long, CW, sub-threshold treatment – typically

5 for 60 seconds – as described in the above references.

The other is a CW NIR laser with short and controlled pulse widths. It generates a pulse train of short pulses (typically 100 to 10,000 microseconds) with higher power during the pulse, but significant off time between pulses (typically 5 to 25% duty factor) – allowing the energy to be confined in a small volume using the Arrhenius principle.

10 The thermal confinement results in tissue specific photoactivation because the specific absorbing tissue, which is being heated by the pulses to temperatures above the standard photocoagulation threshold, are activated but not coagulated, since the heat can dissipate fast enough that no coagulation takes place. This tissue specific photoactivation (or TSP) allows significant treatment without causing full thickness

15 retinal damage and the associated vision loss.

The use of photoactivation in TSP instead of photocoagulation is meant to distinguish between these new subthreshold MIP treatments and the standard photocoagulation treatment. The standard treatment thermally heats the tissue until it starts to denature the protein structures and, hence, is called photocoagulation. This

20 denaturization initiates a healing response, which ameliorates the disease.

The new MIP treatments heat the tissue and initiate some signal carrier cells, which initiate a healing response and this healing response ameliorates the disease being treated without coagulating any of the retinal layers and without the associated vision loss. Hence, activating the healing response without coagulating tissue and thus

25 losing vision is a better treatment method.

Both of these treatments have been developed and are currently being used in many countries with Infrared lasers.

Physicians have not used green lasers for long sub-threshold treatments (like TTT) because of concerns regarding retinal phototoxicity. They have not used green

30 lasers for pulse trains of short pulses, because current green lasers are unable to deliver similar pulse-width trains as those provided by the above referenced NIR laser with short and controlled pulse widths. By way of illustration, current green lasers

employ a fast photodetector or photosensor to sense the output power level of the laser cavity. A software control light loop measures laser output on the millisecond time scale, and increases or decreases the requested energy by increasing or decreasing the requested drive current to the pump diode. This allows a relatively stable laser

5 output, within a few percent, over long time periods such as pulses of tens to hundreds or even thousands of milliseconds.

In addition to the software light loop, a hardware light spike safety protection design has been used. This is an analog circuit that can respond to light energy changes in the microsecond regime. This is used to provide safety against a high

10 power light spike, if some failure or current spike occurs. This protects the patient from spikes being delivered through the delivery system.

However, the hardware light loop threshold is generally set at 10 to 20% above the desired energy level, since it is a safety factor. There are numerous types of laser power fluctuations or changes that occur on this short time scale that can be smaller

15 than this threshold or that bounce back and forth between transverse modes of the laser. These mode hops can cause power fluctuations of up to 10 to 20% before the hardware light loop kicks in. The software light loop is not able to respond to these quick changes and only make the fluctuations worse by trying to respond and varying the requested power.

20 There is a need to provide a system, and its methods of use, that can respond to these quick changes without making the fluctuations worse.

SUMMARY OF THE INVENTION

Accordingly, an object of the present invention is to provide an improved system, and its methods of use, that produces short and controlled pulse width trains.

25 Another object of the present invention is to provide a frequency doubled, cw laser system that produces short and controlled pulse width trains, and its methods of use, with reduced mode hops.

30 A further object of the present invention is to provide a frequency doubled, cw laser system that produces short and controlled pulse width trains, and its methods of use, with reduced power fluctuations.

Yet another object of the present invention is to provide a frequency doubled, cw laser system that produces short and controlled pulse width trains, and its methods of use, with power fluctuations less than 10%.

Still a further object of the present invention is to provide a frequency doubled, 5 cw laser system, and its methods of use, that produces visible pulse trains of the appropriate pulselength, duty factor, and power to perform ophthalmology treatments currently being performed in the near-infrared.

Another object of the present invention is to provide a frequency doubled, cw laser system, and its methods of use, that deliver pulse rise times as short as 25 10 microseconds, pulselengths in the 25 microseconds to 10 milliseconds range, and pulse trains of these pulses for hundreds of pulses.

Yet another object of the present invention is to provide a frequency doubled, cw laser system, and its methods of use, suitable for treatment of the retina with a pulse train of visible pulses to cause change without coagulating the neurosensory elements 15 of the retina.

These and other objects of the present invention are achieved in a laser system that includes a diode pump source. A frequency doubled solid state visible laser is pumped by the diode pump source and produces a pulsed laser output with a train of pulses. Resources provide instructions for the creation of the pulsed output, with on 20 and off times that provide for substantial confinement of thermal effects at a target site.

In another embodiment of the present invention a method of treatment provides a diode pumped, frequency doubled solid state laser system. The solid state laser system produces a pulsed output that has a train of pulses with on times optimized for confinement of thermal effects. A plurality of pulses is directed to a target site. A 25 temperature rise at the target site is non-additive from pulse to pulse.

In another embodiment of the present invention, a method is provided for treating biological tissue by laser surgery. A frequency doubled solid state visible laser system is provided that has a frequency doubler. Instructions are provided to the laser system to create a pulsed output that has a train of pulses with on and off times that 30 substantially confine thermal effects. A pulsed output is produced and directed to a target site.

In another embodiment of the present invention, a laser treatment system includes a diode pump source that pumps a frequency doubled solid state visible laser. The frequency double solid state visible laser produces a pulsed output. A controller system is provided that is responsive to a photodetector. The controller system provides instructions to the visible laser to create the pulsed output. The pulsed output has a train of pulses with on and off times that substantially confine thermal effects.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic diagram of one embodiment of a frequency doubled, cw laser system of the present invention.

10 DETAILED DESCRIPTION OF THE EMBODIMENTS

In one embodiment of the present invention, illustrated in Figure 1, a laser system 10 includes a diode pump source 12. A frequency doubled solid state visible laser 14 is pumped by the diode pump source 12 and produces a pulsed output 16 with a train of pulses. Resources 18 provide instructions for the creation of the pulsed output, with on and off times that provide for substantial confinement of thermal effects at a target site. An off time of the train of pulses is of sufficient duration to provide that the target site has sufficient time to cool down from the delivery of a previous pulse before a next pulse is delivered to the target site 40 by the delivery system 50.

In one embodiment, the resources 18, including a computer 28 to store input from a doctor/operator 60 and to calculate laser parameters, provide the correct parameters, and a trigger to the diode pump source 12, to provide for the pulsed output having the train of pulses with on times that are optimized for confinement of thermal effects. The instructions can include the following steps, set a starting current for the diode pump source 12, set a target power from the laser system 10, and trigger the diode pump source 12 to start. The resources 18 are configured to provide repetitive pulses at one target site. In one embodiment of the present invention, the resources 18 includes hardware and software components that work together to reduce uncertainty and fluctuation of energy down to the few percent range.

The resources 18 includes a feedback control system 20 which can include a controller 22 that is responsive to a device including but not limited to a photodetector

24. This feedback control system 20 has a software light loop as part of the controller 22 and a hardware light loop 26. The controller 22 produces a control signal used to adjust the pulsed output 16. The feedback control system 20 monitors the laser light delivered to the target site 40, and the pulsed output 16 is modified in response to the 5 monitoring. In one embodiment, the train of pulses is optimized to confine the thermal effects of a target tissue 40 in a medical treatment.

In one embodiment, the controller 22 includes a processor that compares a signal, such as from the photodetector 24, to a target power and uses this comparison to determine the on and off times. The controller 22 can include a high speed circuit 10 and/or a processor, that compares the signal, such as the signal from the photodetector 24, to a target power, and uses this comparison to determine the on and off time of each pulse.

The visible laser 14 has a gain medium 32. In various embodiments, the gain medium 32 can be made of a variety of materials, including but not limited to, Nd:YAG, 15 Nd:YVO₄, Nd:YLF, Ho:YAG, Er:YAG, Yb:YAG, Yb:YVO₄, and the like.

The visible laser 14 also contains a frequency converter 34. In various embodiments, this frequency converter 34 can be made of a variety of materials, including but not limited to, KTP, LBO, BBO, and the like.

In one embodiment, the train of pulses has a thermal relaxation time less than a 20 thermal relaxation time of the target site. In one embodiment of the present invention, the train of pulses have a pulse width that is less than 10 milliseconds. In another embodiment of the present invention, the train of pulses has pulses greater than 25 microseconds. In one specific embodiment, the train of pulses is optimized to confine the thermal effect to the RPE without affecting the neurosensory retina of the eye.

25 In one embodiment, the pulsed output 16 has a wavelength in the visible range suitable for a diode pumped solid state laser. The pulsed output 16 can have a pulse on time of 25 microseconds to 10,000 microseconds, a pulse off time of 75 to 100,000 microseconds, and the like.

In one embodiment of the present invention, each pulse length is controlled in 30 the microsecond regime. In one embodiment of the present invention, the turn-on time of laser system 10 is less than 1 to 10 milliseconds. In one embodiment, the resources 18 with this new hardware/software combination light loop, the turn-on time can be

decreased to 25 microseconds. The turn-off time is even shorter than the turn-on time. The control of total on-time can be implemented with a timer chip included with the resources, with sub-microsecond accuracy to time the pulse length and shut off the pulse at the appropriate time. In one embodiment of the present invention, micropulses 5 of 25 up to 10,000 microseconds are provided by laser system 10 with power levels of up to 3W. By way of illustration, and without limitation, pulse trains of up to 500 of these pulses with a variable duty factor from 5% to 25% are provided.

In one embodiment of the present invention, laser system 10 is utilized for a variety of different methods of treatment, particularly medical treatments. Suitable 10 target, treatment sites 40 include but are not limited to, RPE, capullochoris and choroids of the eye, and the like. In this embodiment, laser system produces the pulsed output 16 with a train of pulses that have on times optimized for confinement of thermal effects to sites adjacent to the target site 40. A plurality of pulses is directed to the target site 40. A temperature rise at the target site 40 is non-additive from pulse to pulse. By way 15 of illustration, and without limitation, the target site 40 can have an area of about 50 microns to 3 mm. In this method of treatment, the pulsed output has a wavelength range in the visible, and the pulsed output 16 can have a wavelength range of 520 to 615 nm.

EXAMPLE 1

20 In this example, the resources 18 have a hardware light loop threshold set at 3 to 5% above the desired power level. At the start of each pulse, the requested light level is set to maximum and held there until the laser power reaches the desired level. This generates the fastest possible rise time. When the laser power reaches the desired level, the resources 18 hold the power just above the desired level. The resources 18 25 then ramps the requested power level down until the laser power is equal to or below the desired level. If it is equal to or below the desired level, it steps back up slowly. If it is above, it steps down slowly. The resources 18 make a new measurement before each decision to raise or lower the requested level.

At this point the resources 18 requested level is close to the proper level and the 30 combination of hardware and software keep the light within 3 to 5% as long as the pulse is on. The end result is a very fast turn on and stable light level throughout the entire

pulse for each pulse of the pulsed output 16. The resources 18 makes a measurement before each decision to raise or lower the requested level, it can only be off of the correct level by one DAC number. The pulse energy stability for short pulses is improved.

5

EXAMPLE 2

In this example, laser system 10 is utilized to treat RPE, capullochoris and choroids of the eye. Pulsed output 16 is directed to target site 40 of the eye and a temperature rise at the target site is non-additive from pulse to pulse. The target site 40 is an area of 50 microns to 3 mm. The pulsed output 16 has a wavelength range of 520 10 to 615 nm. The pulsed output 16 has a pulse on time of 25 microseconds to 10,000 microseconds, and a pulse off time of 750 to 10,000 microseconds.

EXAMPLE 3

In this example, laser system 10 is utilized to treat RPE, capullochoris and choroids of the eye. The pulsed output 16 is directed to a target site of the eye and a 15 temperature rise at the target site is non-additive from pulse to pulse. The target site 40 is an area of 50 microns to 3 mm. The controller 22 has a high speed circuit that compares a signal from the photodetector 24, to a target power, and uses this comparison to determine the on and off time of each pulse. The signal from photodetector 24 is compared to a target power to determine the on and off times.

20

The pulsed output 16 has a wavelength range of 520 to 615 nm. The pulsed output 16 has a pulse on time of 25 microseconds to 10,000 microseconds, and a pulse off time of 750 to 10,000 microseconds.

EXAMPLE 4

In this example, laser system 10 is utilized to treat RPE, capullochoris and 25 choroids of the eye. The pulsed output 16 is directed to a target site of the eye and a temperature rise at the target site is non-additive from pulse to pulse. The target site 40 is an area of 50 microns to 3 mm. The train of pulses 16 is optimized to confine the thermal effect to the RPE target site without affecting the neurosensory retina of the

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eye. An off time of the train of pulses is of sufficient duration to provide that the RPE target site has sufficient time to cool down from a delivery of a previous pulse before a next pulse is delivered to the RPE target site.

The pulsed output 16 has a wavelength range of 520 to 615 nm. The pulsed
5 output 16 has a pulse on time of 25 microseconds to 10,000 microseconds, and a pulse off time of 750 to 10,000 microseconds.

The foregoing description of embodiments of the invention has been presented for purposes of illustration and description. It is not intended to be exhaustive or to limit the invention to the precise forms disclosed. Obviously, many modifications and
10 variations will be apparent to practitioners skilled in this art. It is intended that the scope of the invention be defined by the following claims and their equivalents.

What is claimed is:

CLAIMS

1. A laser system, comprising:

a diode pump source; and

5 a frequency doubled solid state visible laser pumped by the diode pump source, the frequency double solid state visible laser producing an pulsed laser output; and resources that provide instructions for the creation of the pulsed output that has a train of pulses with on and off times that provide for substantial confinement of thermal effects at a target site.

10 2. The system of claim 1, wherein the train of pulses have a thermal relaxation time less than a thermal relaxation time of the target site.

3. The system of claim 1, wherein the train of pulses have a pulse width that is less than 10 milliseconds.

15 4. The system of claim 1, wherein the train of pulses has pulses greater than 25 microseconds.

5. The system of claim 1, wherein the resources include a feedback control system.

6. The system of claim 5, wherein the feedback control monitors the laser light delivered to the target site.

20 7. The system of claim 6, wherein the pulsed output is modified in response to the monitoring.

8. The system of claim 5, wherein the feedback control system includes a controller that produces a control signal.

25 9. The system of claim 8, wherein the control signal is used to adjust the pulsed output.

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10. The system of claim 1, wherein the train of pulses are optimized to confine the thermal effects of a target tissue in a medical treatment.

11. The system of claim 1, wherein the train of pulses are optimized to confine the thermal effect to the RPE without affecting the neurosensory retina of an eye.

5 12. The system of claim 1, wherein an off time of the train of pulses is of sufficient duration to provide that the target site has sufficient time to cool down from the delivery of a previous pulse before a next pulse is delivered to the target site.

10 13. The system of claim 1, wherein the resources provide the correct parameters and a trigger to the diode pump source to provide for the pulsed output having the train of pulses with on times that are optimized for confinement of thermal effects.

14. The system of claim 1, wherein the instructions include the following steps: set a starting current for the diode, set a target power from the laser, and trigger the diode to start.

15 15. The system of claim 1, wherein the pulsed output has a wavelength in the visible range suitable for a diode pumped solid state laser.

16. The system of claim 1, wherein the pulsed output has a pulse on time of 25 microseconds to 10,000 microseconds.

20 17. The system of claim 1, wherein the pulsed output has a pulse off time of 75 to 100,000 microseconds.

18. The system of claim 1, wherein the resources is configured to provide repetitive pulses at one target site.

19. The system of claim 1, wherein the solid state laser has a gain medium selected from Nd:YAG, Nd:YVO₄, Nd:YLF, Ho:YAG, Er:YAG, Yb:YAG, and Yb:YVO₄.

20. A method of treatment, comprising:

providing a diode pumped, frequency doubled solid state laser system with a pulsed output that has a train of pulses with on times optimized for confinement of thermal effects; and

5 directing a plurality of pulses to a target site, wherein a temperature rise at the target site is non-additive from pulse to pulse.

21. The method of claim 20, wherein the target site is selected from RPE, capullochoris and choroids of the eye.

22. The method of claim 20, wherein the target site has an area of about 50
10 microns to 3 mm.

23. The method of claim 20, wherein the pulsed output has a wavelength range in the visible.

24. The method of claim 20, wherein the pulsed output has a wavelength range of 520 to 615 nm.

15 25. The method of claim 20, wherein the pulsed output has a pulse on time of 25 microseconds to 10,000 microseconds.

26. The method of claim 20, wherein the pulsed output has a pulse off time of 750 to 10,000 microseconds.

27. A method of treating biological tissue by laser surgery, comprising:
20 providing a frequency doubled solid state visible laser system with a frequency doubler;
providing instructions to the laser system to create a pulsed output that has a train of pulses with on and off times that substantially confine thermal effects;
producing the pulsed output; and
25 directing the pulsed output to a target site.

28. The method of claim 27, wherein the target site is selected from RPE, capullochoris and choroids of the eye.

29. The method of claim 27, wherein a temperature rise at the target site is non-additive from pulse to pulse.

30. The method of claim 27, further comprising:
utilizing the pulsed output to provide a non-ablative effect at the target site.

5 31. The method of claim 27, wherein the pulsed output is delivered to the target site until an integral of time and energy reaches an endpoint.

32. The method of claim 27, wherein the train of pulses have a pulse width that is less than 10 milliseconds.

10 33. The method of claim 27, wherein the train of pulses has pulses greater than 25 microseconds.

34. The method of claim 27, wherein the target site is selected from RPE, capullochoris and choroids of the eye.

35. A laser treatment system, comprising:
a diode pump source coupled to a frequency doubled solid state visible laser
15 pumped by the diode pump source, the frequency double solid state visible laser
producing an pulsed output; and
a controller system responsive to a photodetector that provides instructions to
the visible laser to create a pulsed output that has a train of pulses with on and off times
that substantially confine thermal effects.

20 36. The system of claim 35, wherein the controller includes a processor that compares the photodetector signal to the target power and uses this comparison to determine the on and off times.

25 37. The system of claim 35, wherein the controller includes a high speed circuit that compares the photodetector signal to the target power and uses this comparison to determine the on and off time of each pulse.

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38. The system of claim 35, wherein the controller includes a high speed circuit and a processor that compares the photodetector signal to the target power and uses this comparison to determine the on and off times.

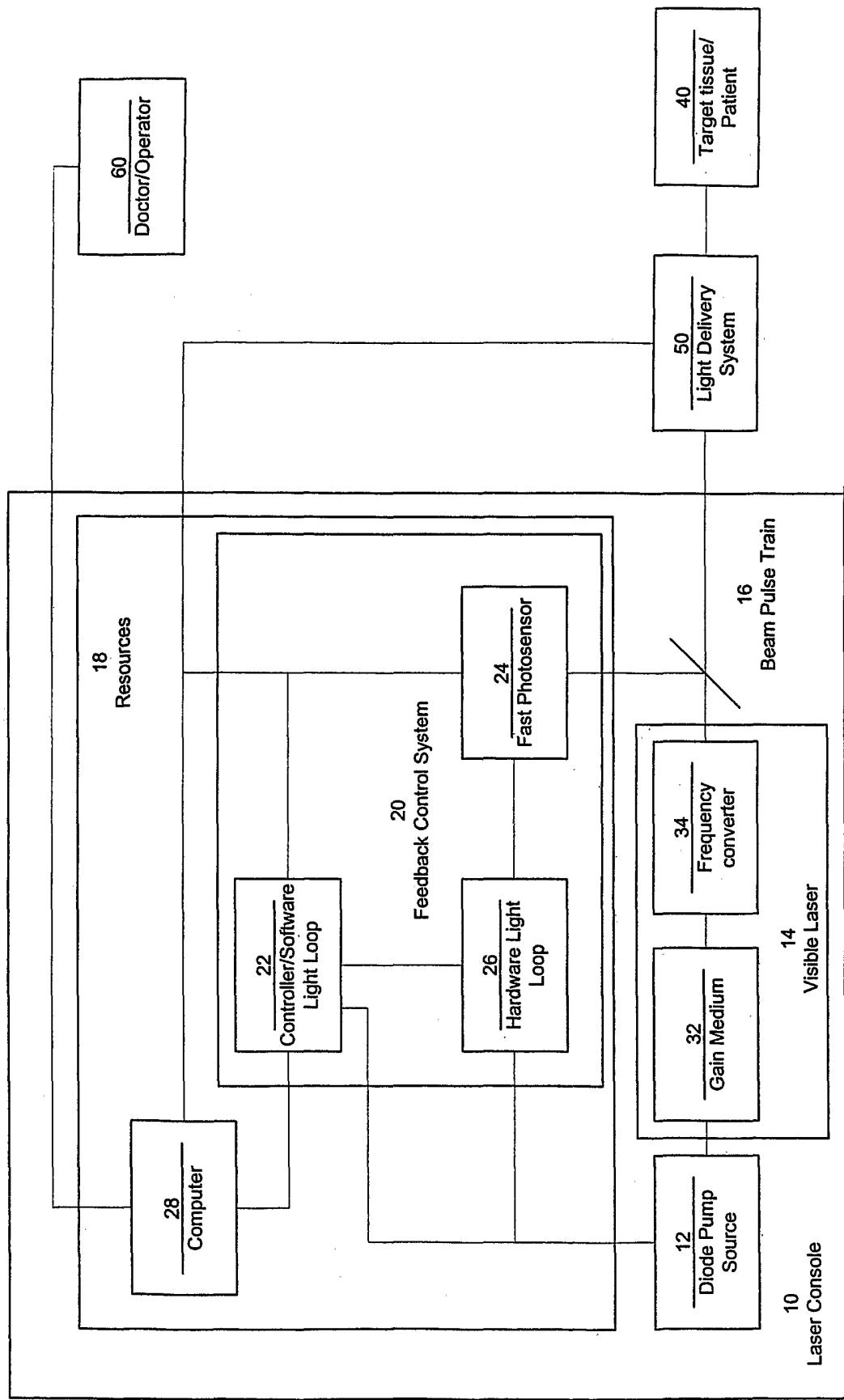


FIGURE 1. Block Diagram of the Invention