Light-emitting Diodes as a Light Source for Intraoperative Photodynamic Therapy

Meic H. Schmidt, M.D.,
Dawn M. Bajic, B.S., Kenneth W. Reichert II, M.D.,
Todd S. Martin, A.S.E.E., Glenn A. Meyer, M.D.,
Harry T. Whelan, M.D.

Departments of Neurosurgery (MHS, KWR, GAM), Neurology (DMB, HTW), and Pediatrics (KWR, GAM, HTW), Medical College of Wisconsin, Milwaukee, Wisconsin; and Department of Engineering, Quantum Devices, Incorporated (TSM), Barneveld, Wisconsin

THE DEVELOPMENT OF more cost-effective light sources for photodynamic therapy of brain tumors would be of benefit for both research and clinical applications. In this study, the use of light-emitting diode arrays for photodynamic therapy of brain tumors with Photofrin porfimer sodium was investigated. An inflatable balloon device with a light-emitting diode (LED) tip was constructed. These LEDs are based on the new semiconductor aluminum gallium arsenide. They can emit broad-spectrum red light at high power levels with a peak wavelength of 677 nm and a bandwidth of 25 nm. The balloon was inflated with 0.1% intralipid, which served as a light-scattering medium. Measurements of light flux at several points showed a high degree of light dispersion. The spectral emission of this probe was then compared with the absorption spectrum of Photofrin. This analysis showed that the light absorbed by Photofrin with the use of the LED source was 27.5% of that absorbed with the use of the monochromatic 630-nm light. Thus, to achieve an energy light dose equivalent to that of a laser light source, the LED light output must be increased by a factor of 3.63. This need for additional energy is the difference between a 630- and 677-nm absorption of Photofrin. Using the LED probe and the laser balloon adapter, a comparison of brain stem toxicity in canines was conducted. LED and laser light showed the same signs of toxicity at equivalent light energy and Photofrin doses. The maximal tolerated dose of Photofrin was 1.6 mg/kg, using 100 J/cm^2 of light energy administered by laser or LED. This study concludes that LEDs are a suitable light source for photodynamic therapy of brain tumors with Photofrin. In addition, LEDs have the potential to be highly efficient light sources for second-generation photosensitizers with absorption wavelengths closer to the LED peak emission. (Neurosurgery 38:552–557, 1996)

Key words: Brain tumor therapy, Instrumentation, Laser, Light-emitting diodes, Light source, Photodynamic therapy, Photofrin

Photodynamic therapy (PDT) is a relatively new adjuvant treatment for brain tumors in research and clinical practice (10, 13–15, 17, 21, 23, 24, 29). The cytotoxic photodynamic effect is based on the interaction of localized photosensitizer, light, and oxygen (8). For PDT of brain tumors, the most commonly used photosensitizer is Photofrin porfimer sodium (22). Photofrin, a heterogeneous mixture of hematoporphyrin, preferentially accumulates in brain tumors (9, 12, 28, 29). The absorption spectrum of Photofrin is relatively broad, with two significant absorption peaks, a major absorption peak at 390 nm and a minor absorption peak at 630 nm (11). Traditionally, red laser light with a 630-nm wavelength has been used to activate Photofrin because of the increased tissue penetration of light at longer wavelengths. Red laser light is frequently produced by using an argon ion or KTP/YAG laser beam that is converted by a dye module to 630 nm. This conversion is inherently costly and inefficient but allows for light delivery with fiberoptics. For nonfiberoptic application of light, other light sources could potentially be useful alternatives.

In this study, we investigated the use of light-emitting diodes (LEDs) as a new light source for PDT. LEDs have frequently been used to emit low-power, broad-spectrum light of 25- to 30-nm bandwidth for photosynthesis research in

plants (1, 2, 25). LED lamps traditionally consist of an array of semiconducting LED chips. In recent years, improvements in semiconductor technology have substantially increased the light output of LED chips. A novel type of LED chip is based on the semiconductor aluminum gallium arsenide. Depending on the amount of gallium and aluminum in the LED chip, the peak wavelength can be between 630 and 940 nm with a wide bandwidth of 20 to 25 nm (2, 25). The broad emission spectrum of the LED overlaps with the absorption spectrum of photosensitizers used for PDT of brain tumors.

The objective of this study was to describe the use of LED arrays for PDT with Photofrin. The hypothesis of this investigation was that Photofrin can be activated by broad-spectrum LED light at a light energy dose equivalent to that of a 630-nm laser light source. In addition, a new light delivery device that uses LEDs as a light source was developed.

MATERIALS AND METHODS

LED probe for in vivo study

To deliver LED light in vivo and compare it with the light of a conventional laser balloon adapter, a LED probe was constructed (*Fig. 1*). The LED probe consists of a 10-cm hollow steel tube that has 144 LED chips arranged in a cylinder at the tip. The core of the tube contains three channels. One channel contains insulated wires that provide electricity for the LED tip. The other channel is filled with sterile water as a cooling fluid, which is circulated around the tip. An additional port provides access for the 0.1% intralipid fluid to inflate the latex balloon at the tip. The pump for the cooling fluid and the power supply are in a portable base unit. The power output of the LED tip is adjusted via a potentiometer at the base unit, which increases the current flow. The temperature at the tip was continuously monitored and kept below 37°C at all times.

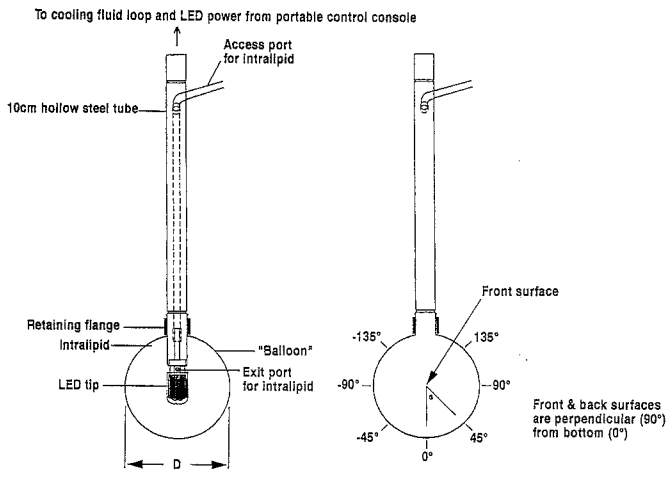

FIGURE 1. The LED balloon applicator in a schematic overview.

Spectral analysis of Photofrin and the LED

A spectral comparison of the LED probe and Photofrin (QuadraLogic Technologies, Vancouver, B.C., Canada) was performed. We obtained the absorption spectrum of Photofrin by dissolving Photofrin in a phosphate solution. The percent absorption was determined using 630-nm absorption as a reference point (100%). The emission spectrum of the LED probe was measured with a spectrophotometer. The peak emission of 677 nm was used as a reference point. The final curve (LED/Photofrin) was obtained by multiplying the percent of Photofrin absorption with the percent of LED emission.

Light measurements

The balloon of the LED probe was inflated with a 0.1% intralipid solution. The balloon diameter ranged from 2 to 5 cm. The tip of the LED probe was placed in the center of the balloon. The total power output was 1.0 W at the tip and was kept constant for all measurements. A light-detecting probe (Cuda Products Corp., Jacksonville, FL) was then used to measure the light irradiance at several points on the balloon surface. The light-detecting probe consisted of an optical fiber with a 3-mm diameter. Measurement points were selected at the front and back of and at 45, 90, 135, 0, −45, −90, and −135 degrees around the LED probe axis. The light measured by the detecting probe was transmitted via an optical fiber to an integrating sphere (Model 2525; Graseby Optronics, Orlando, FL), which contained a sensor head (Model 247; Graseby Optronics). The sensor head was coupled to a single-channel optometer (System S370; Graseby Optronics).

Photodynamic studies in vivo

Adult mongrel dogs weighing approximately 20 kg were used for in vivo PDT. All animals were intubated and placed under general anesthesia using a mixture of halothane and nitrous oxide. The head of each canine was securely fixed to a head frame and maximally flexed. Using a posterior approach, we exposed the suboccipital bone and the C1 vertebra. A wide craniectomy was performed using a power drill. A Y-shaped dural incision exposed the cerebellum, the lower brain stem, and the upper cervical spinal cord. The balloon applicator with a diameter of 2 cm was placed into the posterior fossa on the brain stem. Self-retaining retractors were used to secure the balloon applicator to prevent excessive pressure on the brain stem. All dogs (except for light-only controls) received Photofrin 24 hours before light exposure in increasing doses starting from 0.75 mg/kg. The maximum tolerated dose (MTD) was defined as the dose given to the group of canines that preceded the group with a 50% neurotoxicity rate. Group 1 received laser light and Photofrin. Group 2 received LED light and Photofrin. Each group had

light-only controls. The LED balloon adapter was adjusted to deliver 363 J/cm^2 for all animals receiving LED light. The laser light was produced by an Aurora/M laser system (Lasersonics, Inc., Santa Clara, CA), which was tuned to a 630-nm wavelength.

RESULTS

Spectral comparison results

The spectral analysis graphs are illustrated in *Figure 2*. *Curve A* represents Photofrin absorption relative to 630 nm. It can be appreciated that at 677 nm, Photofrin light absorption is only 25% of that at 630 nm. *Curve B* shows the emission spectrum of the LED probe relative to 677 nm, its peak wavelength. The final curve, *C*, is derived by multiplication of the relative 677-nm LED spectral emission and the relative 630-nm Photofrin absorption across the entire spectrum. Calculation of the total LED absorption relative to a 630-nm laser source is performed by comparison of the integration of the LED emission spectrum with the integration of the LED/Photofrin absorption spectrum. This calculation yielded a 27.5% total absorption of the 677-nm LED spectrum, as compared with the 630-nm LED spectrum. The results of these calculations indicate that 3.63 times more joules of energy from a 677-nm LED source would be required to generate an equivalent absorption result, as compared with a 630-nm monochromatic light source. This need for additional energy is the difference of absorption between 630 and 677 nm for Photofrin.

Light uniformity

The lipid-filled balloon was able to uniformly scatter the LED light. The measurements of light used with the detecting probe are shown in *Table 1*. The average light irradiation was within 20% of the average light output. In addition, it seems that the degree of uniformity remained constant with the increasing diameter of the balloon.

TABLE 1. Light Irradiance of Light-emitting Diode Probe (mW)

	Balloon Diameter			
	2 cm	3 cm	4 cm	5 cm
Front	1.441	0.638	0.460	0.256
Back	1.751	0.958	0.491	0.280
135 degrees	1.213	0.595	0.365	0.242
90 degrees	1.521	0.719	0.454	0.271
45 degrees	1.425	0.740	0.425	0.225
0 degrees	1.703	0.843	0.430	0.198
−45 degrees	1.675	0.800	0.491	0.249
−90 degrees	1.725	0.921	0.559	0.261
−135 degrees	1.217	0.620	0.432	0.249
Mean	1.525	0.7595	0.456	0.247
Minimum (%)	20.4	21.7	19.9	19.8
Maximum (%)	14.8	26.1	22.6	13.4

TABLE 2. Summary of Canine Brain Stem Toxicity Study[a]

	Number of Dogs	Clinical Toxicity	MRI
Laser and Photofrin			
Light only	2	none	nl
0.75	6	none	nl
1.2	3	none	nl
1.6	1	none	nl
2.0	2	transient	nl
3.0	1	death	–
LED and Photofrin			
Light only	1	none	nl
1.6	3	none	nl
2.0	2	transient	nl
3.0	0		

[a] **MRI, magnetic resonance imaging; LED, light-emitting diode; –, not applicable.**

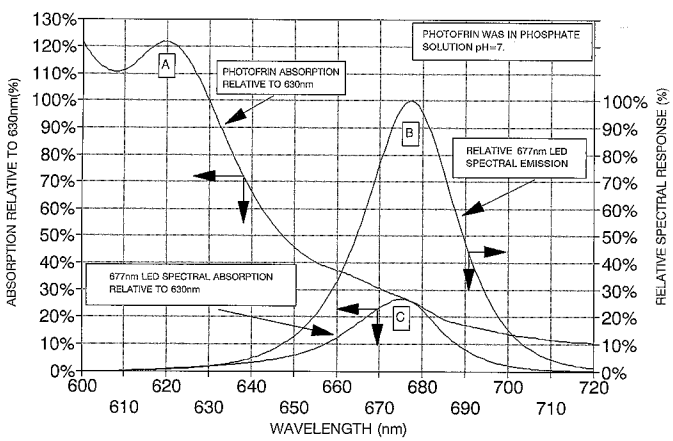

FIGURE 2. Spectral comparison of LED and Photofrin. Photofrin absorption of 677-nm LED relative to 630-nm absorption line. *A*, Photofrin absorption curve relative to 630 nm. *B*, spectral emission of the LED. *C*, integration of the LED spectral emission and the Photofrin absorption.

PDT in vivo

The results of PDT in canines are summarized in *Table 2*. The MTD for Group 1, which received the LED/Photofrin combination, was 1.6 mg/kg. The same MTD was obtained in Group 2, which received the laser/Photofrin combination. Light only, whether laser or LED, did not cause any significant neurological deficits at the power levels used. At doses higher than 2.0 mg/kg Photofrin, no dog survived longer than 4 hours after PDT. Death was secondary to respiratory arrest from brain stem damage. At doses of 2.0 mg/kg Photofrin, neurological deficits were transient. Hind leg weakness and head tilt were noted for a period of 1 week but then completely resolved. The magnetic resonance imaging scans revealed no significant lesions in animals that survived the treatment.

DISCUSSION

Photofrin is the most frequently used photosensitizer in experimental and clinical studies for brain tumors (21). This mixture of hematoporphyrin compounds exhibits a broad spectrum of absorption with several distinct absorption peaks. Traditionally, the art of energizing Photofrin required using a 630-nm laser as the light source. The reasons for choosing this wavelength are twofold. Photofrin has a minor absorption peak in the red region of its absorption spectrum. In addition, in brain tissue, light penetration is deeper with increasing wavelength (3, 4, 20). Argon ion and KTP/YAG dye lasers have been able to provide 630-nm wavelength light with narrow bandwidth at power levels sufficient to activate Photofrin. Nevertheless, narrow bandwidth light is not necessary to activate Photofrin.

Developing new light sources and light delivery devices is critically important for PDT. In this study, a LED probe with an inflatable tip was constructed and compared with the laser balloon adapter. The concept of using a fluid-filled balloon to photoilluminate a tumor cavity after maximal resection was originally presented by Muller and Wilson (18–21) and Wilson et al. (30). They developed a laser balloon adapter in which the red laser light is delivered via a fiberoptic to the center of a fluid-filled balloon. The fluid inside the balloon serves as a light-scattering medium. In addition, the inflated balloon prevents the collapse of the resection cavity, which potentially could preclude light from reaching residual tumor cells. The LED probe is similar in that a fluid-filled balloon is used as a light-scattering medium. In contrast, the LED probe does not require a fiberoptic for light delivery. Fiberoptics create a substantial loss of power between the laser light source and the target tissue; the power loss can be as great as 50%. The red light of the LED probe is produced at the tip in the center of the balloon. Thus, there is no loss in power as for fiberoptic transmission. This makes LED a more efficient red light source.

The light output of the laser balloon adapter is directed forward as the laser light exits the optical fiber and then is scattered by the intralipid balloon fluid (30). In contrast, the LED tip is cylindrical and, combined with the intralipid in the balloon, provides reasonable spherical uniformity of light distribution. Light flux measurements showed that the LED light output with the inflated intralipid-filled balloon is within 20% of the average power output. This compares favorably with the light distribution of the laser balloon adapter (30).

Another difference between the laser balloon adapter and the LED probe is their emission spectra. The laser produces 630-nm light of narrow bandwidth (1–2 nm). The LED, in contrast, produces a red light of broad spectrum with a peak wavelength of 677 nm and a bandwidth of 25 nm. The spectral comparison of the LED with the absorption spectrum shows that a significant amount of the spectral emission of the LED is available for absorption by Photofrin. Specifically, 27.5% of the LED spectral output is absorbed, as compared with a 630-nm light source. This difference in absorption results in a decrease of absorbed energy for photodynamic effect. The LED power output can be easily increased to provide an equivalent energy. Thus, the data indicate that Photofrin can absorb light of multiple wavelengths at a light energy dose equivalent to that of 630-nm monochromatic laser light. Because the photodynamic effect depends on the light energy dose and not directly on the wavelength, an equivalent photodynamic effect is expected (5, 6, 8). Our in vivo brain stem toxicity study confirmed the hypothesis. The MTD of Photofrin was 1.6 mg/kg, using 100 J/cm^2 of light energy. LED and laser light showed the same signs of toxicity at equivalent light energy and Photofrin doses. This indicates that equivalent light energy doses, as determined by spectral comparison of laser light and LED light, have similar photodynamic effects. In addition, the broad-spectrum light provides the opportunity for Photofrin to absorb light at longer wavelengths. Thus, LED light can potentially activate Photofrin in deeper tissues as compared with monochromatic 630-nm laser light.

LEDs can also be used to activate photosensitizers other than Photofrin. Currently, several second-generation photosensitizers are under development (7). These include bacteriochlorins, substituted porphyrins, chlorins, naphthalocyanines, purpurins, phthalocyanines, and benzoporphyrin derivatives. The advantages of these second-generation photosensitizers over Photofrin include longer absorption wavelengths, higher singlet oxygen yields, and decreased skin phototoxicity. The peak absorption wavelength of benzoporphyrin derivative and some of the phthalocyanines are 690 nm and 675 nm, respectively (7, 16, 27). LEDs can produce light with corresponding peak emission wavelengths. Therefore, the LED potentially is a very efficient light source for the second generation of photosensitizers. Although laser light is available at these longer wavelengths, the use of LEDs as a light source is much more economical because they are available at a fraction of the cost of lasers. An efficient, yet cost-effective, light source, such as the LED, could greatly increase the research of and clinical interest in PDT with long wavelength photosensitizers.

Recently, the wavelength-dependent effects of benzoporphyrin derivative have been investigated (27). Phototoxicity was assessed in vitro and in vivo at several monochromatic wavelengths ranging from 678 to 700 nm. The results indicate that there was an equivalent phototoxic effect over a range of wavelength. This suggests that light sources with broad-spectrum output, such as the LED, might have equivalent efficacy.

CONCLUSION

LEDs can efficiently provide broad-spectrum red light for PDT with Photofrin. The LED balloon adapter is a new light delivery device that could be used for intracavitary PDT of brain tumors. We are currently investigating PDT with Photofrin in a canine brain tumor model using the LED probe. In addition, we are studying the use of LEDs with new photosensitizers, such as benzoporphyrin derivative and phthalocyanines, that have major absorption peaks closer to the central emission wavelength of the LED spectrum.

ACKNOWLEDGMENTS

We thank Marie Ann Lipowski for help in preparation of the manuscript. This study was supported by grants from the

National Aeronautic & Space Administration/Wisconsin Center for Space Automation and Robotics, the Children's Hospital Foundation, and the Midwest Athletes Against Childhood Cancer.

Received, May 23, 1995.
Accepted, September 28, 1995.
Reprint requests: Harry T. Whelan, M.D., Pediatric Neurology, Medical College of Wisconsin, 8701 Watertown Plank Road, MFRC 3017, Milwaukee, WI 53226.

REFERENCES

1. Barta DJ, Tibbitts TW, Bula RJ, Morrow RC: Evaluation of light-emitting diode characteristics for a space-based plant irradiation source. **Adv Space Res** 12:141–149, 1992.
2. Bula RJ, Morrow RC, Tibbitts TW, Barta DJ, Ignatius RW, Martin TS: Light-emitting diodes as a radiation source for plants. **Hortic Sci (Calcutta)** 26:203–205, 1991.
3. Eggert HR, Blazek V: Optical properties of human brain tissue, meninges, and brain tumors in the spectral range of 200 to 900 nm. **Neurosurgery** 21:459–464, 1987.
4. Eggert HR, Blazek V: Optical properties of normal human intracranial tissues in the spectral range of 400 to 2500 nm. **Adv Exp Med Biol** 333:47–55, 1993.
5. Fingar VH, Henderson BW: Drug and light dose dependence of photodynamic therapy: A study of tumor and normal response. **Photochem Photobiol** 46:837–841, 1987.
6. Fingar VH, Potter WR, Henderson BW: Drug and light dose dependence of photodynamic therapy: A study of cell clonogenicity and histologic changes. **Photochem Photobiol** 45:643–650, 1987.
7. Heier SK, Heier LM: Tissue sensitizers. **Gastrointest Endosc Clin N Am** 4:327–352, 1994.
8. Henderson BW, Dougherty TJ: How does photodynamic therapy work? **Photochem Photobiol** 55:145–157, 1992.
9. Hill JS, Kaye AH, Sawyer WH, Morstyn G, Megison PD, Stylli S: Selective uptake of haematoporphyrin derivative into human cerebral glioma. **Neurosurgery** 26:248–254, 1990.
10. Ji Y, Walstad D, Brown JT, Powers SK: Improved survival from intracavitary photodynamic therapy of rat glioma. **Photochem Photobiol** 56:385–390, 1992.
11. Kaye AH, Morstyn G, Apuzzo MLJ: Photoradiation therapy and its potential in the management of neurological tumours. **J Neurosurg** 69:1–14, 1988.
12. Kaye AH, Morstyn G, Ashcroft RG: The uptake and retention of haematoporphyrin derivative in an in vitro and in vivo model of glioma. **Neurosurgery** 17:883–890, 1985.
13. Kaye AH, Morstyn G, Brownbill D: Adjuvant high-dose photoradiation therapy in the treatment of cerebral glioma: A phase 1–2 study. **J Neurosurg** 67:500–505, 1987.
14. Kostron H, Weiser G, Fritsch E, Grunert V: Photodynamic therapy of malignant brain tumors: Clinical and neuropathological results. **Photochem Photobiol** 46:937–943, 1987.
15. Laws ER Jr, Cortese DA, Kinsey JH, Eagan RT, Anderson RE: Photoradiation therapy in the treatment of malignant brain tumors: A phase I (feasibility) study. **Neurosurgery** 9:672–678, 1981.
16. Leach MW, Khoshyomn S, Bringus J, Autry SA, Boggan JE: Normal brain tissue response to photodynamic therapy using aluminum phthalocyanine tetrasulfonate in the rat. **Photochem Photobiol** 57:842–845, 1993.
17. Lindsay EA, Berenbaum MC, Bonnett R, Thomas DG: Photodynamic therapy of a mouse glioma: Intracranial tumours are resistant while subcutaneous tumours are sensitive. **Br J Cancer** 63: 242–246, 1991.
18. Muller PJ, Wilson BC: Photodynamic therapy: Cavitary photoillumination of malignant cerebral tumours using a laser coupled inflatable balloon. **Can J Neurol Sci** 12:371–373, 1985.
19. Muller PJ, Wilson BC: An update on the penetration depth of 630 nm light in normal and malignant human brain tissue in vivo. **Phys Med Biol** 31:1295–1297, 1986.
20. Muller PJ, Wilson BC: Photodynamic therapy of malignant primary brain tumours: Clinical effects, post-operative ICP, and light penetration of the brain. **Photochem Photobiol** 46:929–935, 1987.
21. Muller PJ, Wilson BC: Photodynamic therapy of malignant brain tumours. **Can J Neurol Sci** 17:193–198, 1990.
22. Origitano TC, Caron MJ, Reichman OH: Photodynamic therapy for intracranial neoplasms: Literature review and institutional experience. **Mol Chem Neuropathol** 21:337–352, 1994.
23. Powers SK, Cush SS, Walstad DL, Kwock L: Stereotactic intratumoral photodynamic therapy for recurrent malignant brain tumors. **Neurosurgery** 29:688–695, 1991.
24. Schmidt MH: Intraoperative photodynamic therapy in a posterior fossa brain tumor model. Medical College of Wisconsin, 1994 (dissertation).
25. Tennessen DJ, Singsaas EL, Sharkey TD: Light-emitting diodes as a light source for photosynthesis research. **Photosynth Res** 39:85–92, 1994.
26. van Lier JE, Spikes JD: The chemistry, photophysics and photosensitizing properties of phthalocyanines. **Ciba Found Symp** 146: 17–27, 1989.
27. Waterfield EM, Renke ME, Smits CB, Gervais MD, Bower RD, Stonefield MS, Levy JG: Wavelength-dependent effects of benzoporphyrin derivative monoacid ring A in vivo and in vitro. **Photochem Photobiol** 60:383–387, 1994.
28. Whelan HT, Kras LH, Ozkar K, Bajic DM, Schmidt MH, Liu Y, Trembath LA, Uzum F, Meyer GA, Segura AD, Collier D: Selective incorporation of ^{111}In-labeled Photofrin by glioma tissue in vivo. **J Neurooncol** 22:7–13, 1994.
29. Whelan HT, Schmidt MH, Segura AD, McAuliffe TL, Bajic DM, Murray KJ, Moulder JE, Strother DR, Thomas JP, Meyer GA: The role of photodynamic therapy in posterior fossa brain tumors: A pre-clinical study in a canine glioma model. **J Neurosurg** 79:562–568, 1993.
30. Wilson BC, Muller PJ, Yanch JC: Instrumentation and light dosimetry for intraoperative photodynamic therapy (PDT) of malignant brain tumours. **Phys Med Biol** 31:125–133, 1986.

COMMENTS

Schmidt et al. describe the development of an inflatable balloon device fitted with light-emitting diodes (LEDs), which may have application as a light source for photodynamic therapy (PDT) of brain tumors. The authors correctly observe that "the development of more cost-effective light sources for PDT of brain tumors would be of benefit for both research and clinical application."

In the clinical situation, lasers have generally been the most commonly used light sources for PDT of brain tumors, although incandescent sources have also been used with a variety of techniques to deliver the light to the tumor. Delivery techniques have included the use of a flat-cut optical fiber held in place by a retraction arm and suspended in the resec-

tion cavity filled with intralipid (1, 2), the use of an inflatable intralipid-filled balloon applicator containing an optical fiber placed in the cavity (4, 5), the stereotactic implantation of fibers (3, 6), and shining of incandescent light directly on the tumor bed. Although lasers have until now been the light sources of choice, the potential for lower-cost, more efficient LED sources offers considerable promise. The studies reported in this article combine the advantages of an aluminum gallium arsenide LED array with the intracavitary balloon device developed by Muller and Wilson (4, 5). However, the LED array has a maximum spectral output at 675 nm and a poor spectral output at 630 nm (*Fig. 2* in article). Thus, the real potential for the device described here is probably not as an irradiation source to activate either hematoporphyrin derivative or Photofrin, but rather as a source to activate the potential new "second-generation" sensitizers with peak absorption wavelengths in the range of 650 to 750 nm, which have a much longer penetration through brain and tumor. The work reported by Schmidt et al. is important, as the development of such sources is necessary before Phase III trials of PDT as an adjuvant therapy for cerebral glioma, using new sensitizers with longer wavelengths of absorption, can be undertaken.

John S. Hill
Andrew H. Kaye
Melbourne, Australia

1. Kaye AH, Hill JS: Photodynamic therapy of cerebral tumours. **Neurosurg Q** 1:233–258, 1992.
2. Kaye AH, Morstyn G, Brownbill D: Adjuvant high-dose photoradiation therapy in the treatment of cerebral glioma: A phase I/II study. **J Neurosurg** 67:500–505, 1987.
3. McCulloch GAJ, Forbes IJ, Lee See K, Cowled PA, Jacka FJ, Ward AD: Phototherapy in malignant brain tumors, in Doiron DR, Gomer CJ (eds): *Porphyrin Localization and Treatment of Tumors.* New York, Alan R. Liss, 1984, pp 709–717.
4. Muller PJ, Wilson BC: Photodynamic therapy: Cavitary illumination of malignant cerebral tumours using a laser coupled inflatable balloon. **Can J Neurol Sci** 12:371–373, 1985.
5. Muller PJ, Wilson BC: Photodynamic therapy of malignant brain tumours. **Can J Neurol Sci** 17:193–198, 1990.
6. Powers SK, Cush SS, Walstad DL, Kwock L: Stereotactic intratumoral photodynamic therapy for recurrent malignant brain tumors. **Neurosurgery** 29:688–696, 1991.

The investigators present a novel device, namely a LED array for the purpose of cavitary photoillumination for brain tumor PDT. The device creates virtually uniform surface irradiance, is volume expandable, and has a wavelength spectrum appropriate to the activation of the most popular photosensitizer in clinical use (porfimer sodium, Photofrin).

Photofrin activation increases with decreasing wavelength, but the tissue penetration of photic energy increases with increasing wavelength. Thus, the wavelength of 630 nm has been used for PDT because it is the last peak in the sensitizer's absorption spectrum. The authors showed that Photofrin light absorption with the LED device was 28% of the absorption achieved with monochromatic 630-nm light; however, the reduced absorption could be off set by increasing the total photic energy output of the LED array.

The photoillumination of brain tumor tissue by laser light has been the method of choice, because monochromatic, coherent light can be coupled to optical fibers and thus directed to the target tissue; laser applications have also allowed a relatively accurate dosimetry. Disadvantages of laser technology are the capital cost and the maintenance requirements. The introduction of effective alternate light sources will significantly enhance the application of brain tumor PDT.

Paul J. Muller
Toronto, Ontario, Canada

This article represents a simple, clean experimental design set up to study the question of whether non-laser-dependent alternative light sources can be used for photoactivation of porphyrin-based PDT. The authors have successfully designed a device that is not dependent upon expensive, technically complicated lasers. These devices also offer the opportunity to be used on a large variety of new photosensitizers that are currently coming into experimental and clinical use. Technical breakthroughs such as these will allow progress to be made in the application of innovative treatments to difficult clinical problems, such as the treatment of brain tumors.

Thomas C. Origitano
Maywood, Illinois