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Comparison of Laser Beam Intensity Profiles Produced by Photodynamic Therapy (PDT) and Transpupillary Thermotherapy (TTT) Lasers

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Background and Objectives: For photodynamic therapy (PDT) or transpupillary thermotherapy (TTT) lasers, long irradiation time (typically 1 minute or longer) is used and a large area of retina is treated. Consequently, the power stability but also the light distribution within the laser beam plays a major role. This study aimed to evaluate beam intensity profiles produced by several PDT and TTT lasers.
Study Design/Materials and Methods: A beam profile analyzer (Cohu 4812 camera connected to a LPA-300PC, Spiricon, Logan, UT) was used to compare the beam profiles of PDT lasers: OPAL™ (Lumenis, USA); ACTIVIS™ (Quantel Medical, France), VISULAS™ (Zeiss, Germany). Spots of 2, 3, 4, and 5 mm were tested with each laser. Similarly, TTT lasers: OCULIGHT SLx™ (Iridex, CA) and IRIDIS ™ (Quantel Medical, France) were evaluated with 2 and 3 mm spot diameter and power ranging from 200 to 1,000 mW.
Results: PDT lasers: OPAL had a “top hat” and homogeneous profile whatever the spot size. Numerous micro-spikes and micro-nadirs of power were observed with the ACTIVIS and the VISULAS. TTT lasers: for the IRIDIS the beam shape was rather gaussian, but the homogeneity was reduced by micro-spikes of power. With the OCULIGHT Slx the beam shape was rather top hat and only few micro-spikes or micro-nadirs of power could be disclosed.
Discussion: The literature tends to prove that the shape and homogeneity of the beam profile could play a role on the efficacy of the treatment.
Conclusion: Since PDT and TTT lasers display different beam profiles, this parameter should be carefully evaluated when performing clinical evaluations of PDT or TTT treatments.

Key words: laser; photodynamic therapy; transpupillary thermotherapy; image analysis; age-related macular degeneration

INTRODUCTION

In ophthalmology, photocoagulation with a small (100–200 μm), intense, laser spot according to the Macular Photocoagulation Study (MPS) reports, was for decades the only way to treat extra or juxtafoveal choroidal neovascularization of age related macular degeneration (ARMD). Recently, photodynamic therapy (PDT) and transpupillary thermotherapy (TTT) have brought to routine clinical practice the use of larger spots (2–6.4 mm) with low irradiance for the treatment of choroidal neovascularization extended to the subfoveal zone. Photodynamic therapy has been validated by the reports of the treatment of age-related macular degeneration with photodynamic therapy (TAP) study [1,2]. For this method, the aim of the laser is to excite a photosensitizer without thermal effect. Nowadays, transpupillary thermotherapy has not been validated by a randomized multicentric study. For this method, the aim of the laser is to induce a limited heating of the choroid without reaching the photocoagulation threshold [3,4].

Ophthalmologists are used to check the focus and the power of their lasers, but when a photocoagulation is performed with a small intense “MPS like” pulse, since the heating rises far above the photocoagulation threshold even an imperfect control of power can allow to treat appropriately the patients. For such applications, the profile of the laser beam does not seem of utmost importance.

On the contrary, for PDT or TTT, long irradiation time (1 minutes or longer) and larger spots (2–6.4 mm) are used. Especially, the low irradiance used for these techniques uncovers the irregularities of light distribution within the large treated area. Consequently, power stability but also the profile of the laser beam is thought to play a role. The laser power can be easily checked with a power meter. However, laser beam distribution is the result of many parameters, starting with the basic design of the laser cavity, the type and orientation of the lasing material, the type and design of the photonic energy source used to drive the lasing material, the power supply and the optics used to deliver the energy to the tissue [5]. With so many parameters affecting the quality and reliability of a laser,

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it has become increasingly important to quantify the beam profile. However, the light beam distribution is not controlled by the ophthalmologists.

Before electronic methods for laser beam diagnostics were developed, beam profiling was often limited to optical approximations, such as reflected beams on flat surfaces, burn papers, acrylic mode burns, or fluorescent imaging. Many of these methods are still in use, even though they are unreliable, operator-dependent, and non-quantitative. Since beam imaging systems are now available, this study aimed to compare the beam intensity profiles of the main PDT and TTT lasers available and discuss the influence of factors related to the laser in the efficacy of these methods of treatments.

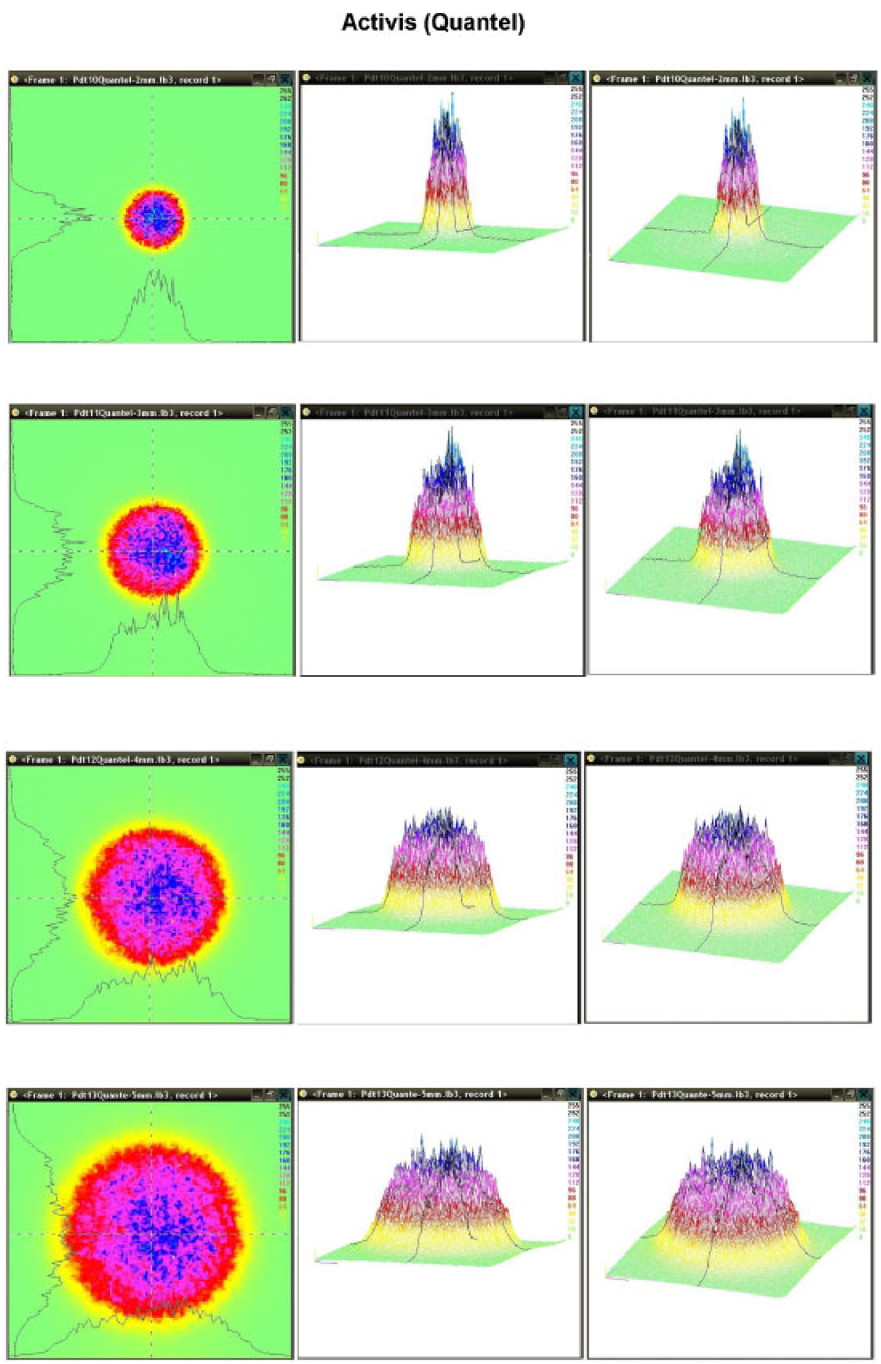

Fig. 1. Photodynamic therapy (PDT) laser (2, 3, 4, 5 mm, 50 J/cm^2). Beam profiles obtained with ACTIVIS laser. [Figure can be viewed in color online via www.interscience.wiley.com.]

MATERIALS AND METHODS

Beam Profile Analyzer

A Spiricon beam profile analyzer (Logan, UT) was used to measure the spatial intensity of the beam and to display the beam spatial distribution in two or three dimensions. This system was composed of COHU 4812 camera (maximum resolution 632 × 480, area: 8.7 × 6.6, maximum viewable beam 6.4 mm, element pitch 11.5 × 13.5 μm, spectral response 190-1,310 nm, update rate: 30 Hz) connected to a LPA-300PC 8 bit digitizer. Since the camera was highly sensitive, absorptive neutral-density (ND) filters were used to attenuate the laser intensity (Melles Griot, Voisins Le Bretonneux, France). These ND filters provide spectrally uniform attenuation over the wavelength range from 0.4 to 1 μm. For each measurement, four images of the laser beam were recorded and stored on hard disk. These data were analyzed off-line and graphic representations of beam

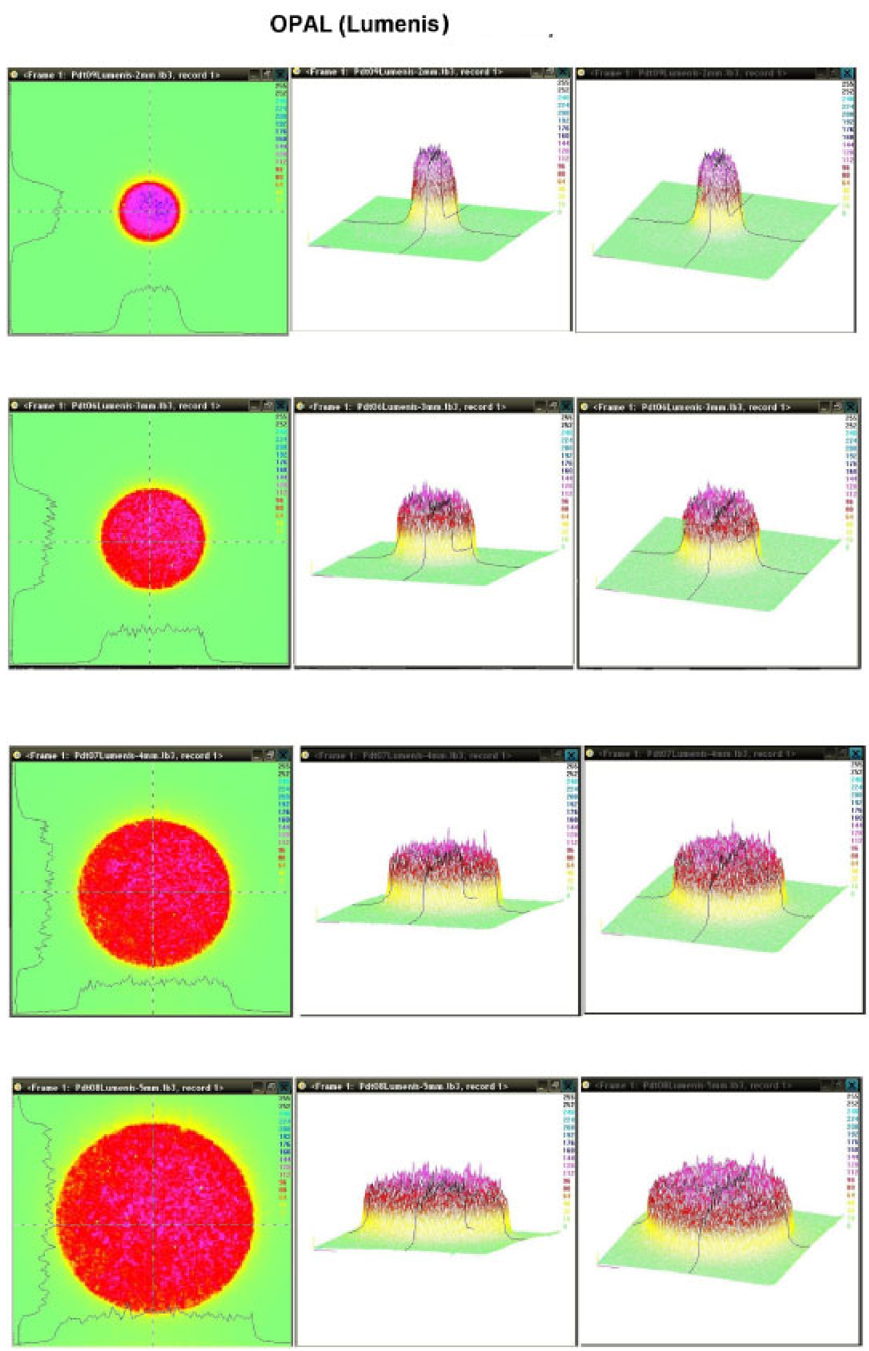

Fig. 2. PDT laser (2, 3, 4, 5 mm, 50 J/cm^2). Beam profiles obtained with OPAL laser. [Figure can be viewed in color online via www.interscience.wiley.com.]

profiles were obtained. Stability and spatial distribution as a function of diameter and laser power were particularly studied.

PDT Lasers

Three PDT lasers were evaluated: (i) OPAL (Lumenis, Santa Calara); (ii) ACTIVIS (Quantel Medical, Clermont–Ferrand); and (iii) VISULAS (Zeiss, Aalen, Germany). This evaluation was performed using the conventional clinical parameters: irradiation time: 83 seconds, fluence: 50 J/cm^2 kept constant for the four different beam diameters: 2, 3, 4, and 5 mm, giving respectively a power of 19, 43, 76, and 118 mW. For each laser, the specific slit lamp adapter provided by the company was used. OPAL and ACTIVIS lasers were connected to a Haag Streit slit lamp (Haag-Streit GmbH, Wedel, Germany). The VISULAS laser was connected to Zeiss slit lamp SL120 (Zeiss, Aalen, Germany). The beam profile analyzer camera was placed in front of the slit lamp and the distance was adjusted in order to deliver the predetermined spot size.

TTT Lasers

The OCULIGHT SLx (Iridex, Mountain View, CA) and the IRIDIS (Quantel Medical, Clermont Ferrand, France)

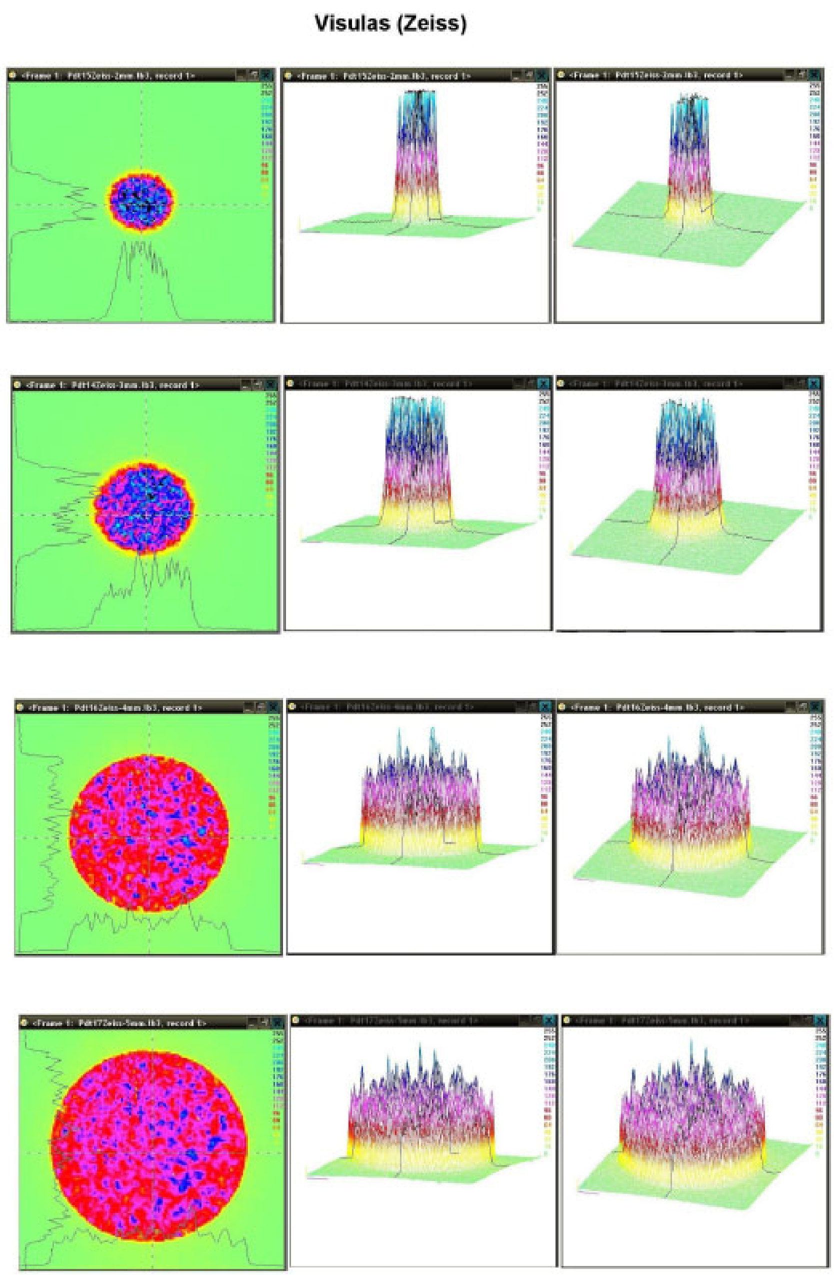

Fig. 3. PDT laser (2, 3, 4, 5 mm, 50 J/cm^2). Beam profiles obtained with VISULAS laser. [Figure can be viewed in color online via www.interscience.wiley.com.]

were used with the slit adapter provided by each manufacturer. For this study, the lasers were connected to a Haag Streit slit lamp (Haag-Streit GmbH, Wedel, Germany). The beam profile analyzer camera was placed in front of the slit lamp and the distance was adjusted in order to deliver a 2 and a 3 mm spot size. For TTT, since the power is tuned usually by the ophthalmologist, power ranging from 400 to 1,200 mW were evaluated for each spot size.

For the PDT and TTT lasers the shape and the homogeneity of the beam were analyzed. For each laser pulse, four frames were successively acquired to evaluate any modification of the homogeneity of the profile as a function of time. Spot homogeneity was quantified as a percentage of variation along the profile

RESULTS

Two dimension (2D) and three dimension (3D) beam profiles were obtained for each spot size. 2D display shows the general shape of the beam (top hat or gaussian) and the presence of micro-spikes or micro-nadir of power along an horizontal and a vertical line passing through the center of the beam profile. 3D representation provides a general view of the beam

PDT Lasers

Figures 1–3 display 2D and 3D profiles obtained respectively with the ACTIVIS, OPAL, and VISULAS lasers using 2, 3, 4, and 5 mm spot size. For the ACTIVIS, the beam shape is rather gaussian than top hat whatever the spot size. The spikes of power are numerous enough to reduce the general homogeneity of the beam profile. For the OPAL laser, the shape is quite top hat especially for the spots larger than 2 mm. Few spikes of power can be disclosed whatever the size of the spot. For the VISULAS, the beam shape is quite top hat whatever the spot size.

Table 1 reports the percentage of variation of the light along a vertical line passing through the center of the beam profile. The better stability was obtained with the OPAL laser with respectively 4.1% (2 mm), 7.7% (3 mm), 11.1% (4 mm), and 8.9% (5 mm). ACTIVIS laser stability is good with 4 mm spot (8.3%) and 5 mm spot (9.7%) when compared to 2 mm spot (17.1%) and 3 mm spot (13.9%). The worst results are obtained with the VISULAS laser with respectively 13.5% (2 mm), 12.1% (3 mm), 16.8% (4 mm), and 17.5% (5 mm).

Analysis of four frames recorded for each set-up showed that both lasers were stable. Figure 4 shows an average profile (four frames) recorded for each laser. Standard deviations correspond only to the electronic noise of the image sensor.

TABLE 1. Percentage of Variation of the Light Along a Vertical Line Passing Through the Center of the Beam Profile for Each Photodynamic Therapy (PDT) Laser

Laser	2 mm	3 mm	4 mm	5 mm
Activis	17.1%	13.9%	8.3%	9.7%
Opal	4.1%	7.7%	11.1%	8.9%
Visulas	13.5%	12.1%	16.8%	17.5%

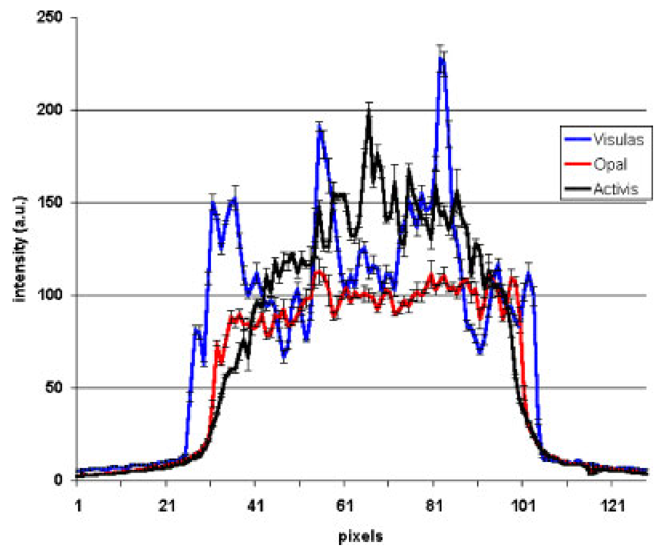

Fig. 4. Average profile (four frames) recorded for each PDT laser (2 mm spot size). [Figure can be viewed in color online via www.interscience.wiley.com.]

TTT Lasers

Beam profiles were obtained for 2 and 3 mm and power tuned 400, 600, 800, 1,000, and 1,200 mW (Figs. 5 and 6). With both lasers, the shape of the beam profiles were rather top hat for 3 mm spots and rather gaussian with the 2 mm spots. For the 3 mm spots, the homogeneity of the beam profile was generally good with the OCULIGHT Slx laser and variable with the IRIDIS. Table 2 reports the percentage of variation of the light along a vertical line passing through the center of the beam profile. The better stability was obtained with the OCULIGHT Slx laser with respectively 7.6% (2 mm, 300 mW), 3.2% (3 mm, 400 mW), 1.2% (3 mm, 600 mW), 4.2 % (3 mm, 800 mW), and 2.5% (3 mm, 1,200 mW). Analysis of four frames recorded for each set-up showed that both lasers were stable (data non shown).

DISCUSSION

Laser beam quality is of great importance for low intensity irradiation performed with large spots such as with PDT or with TTT. The interest of a beam profile control has been advocated for different types of lasers [5] but to the best of our knowledge, no study has addressed this specific parameter for PDT not even for TTT. Even in the TAP I and II reports, light distribution in the treated area has not been mentioned [1,2]. The laser manufacturers recommend to regularly check the power of the lasers and usually, an automatic control of power checks the global power of the spots. However for identical irradiance, the profile of the beam can have various shapes that can considerably influence the efficacy of the treatment. The absence of variation through time on the four frames acquired for each spot size (Fig. 4) is in favor of variations due to the optical design instead of variation due the laser cavity itself. This

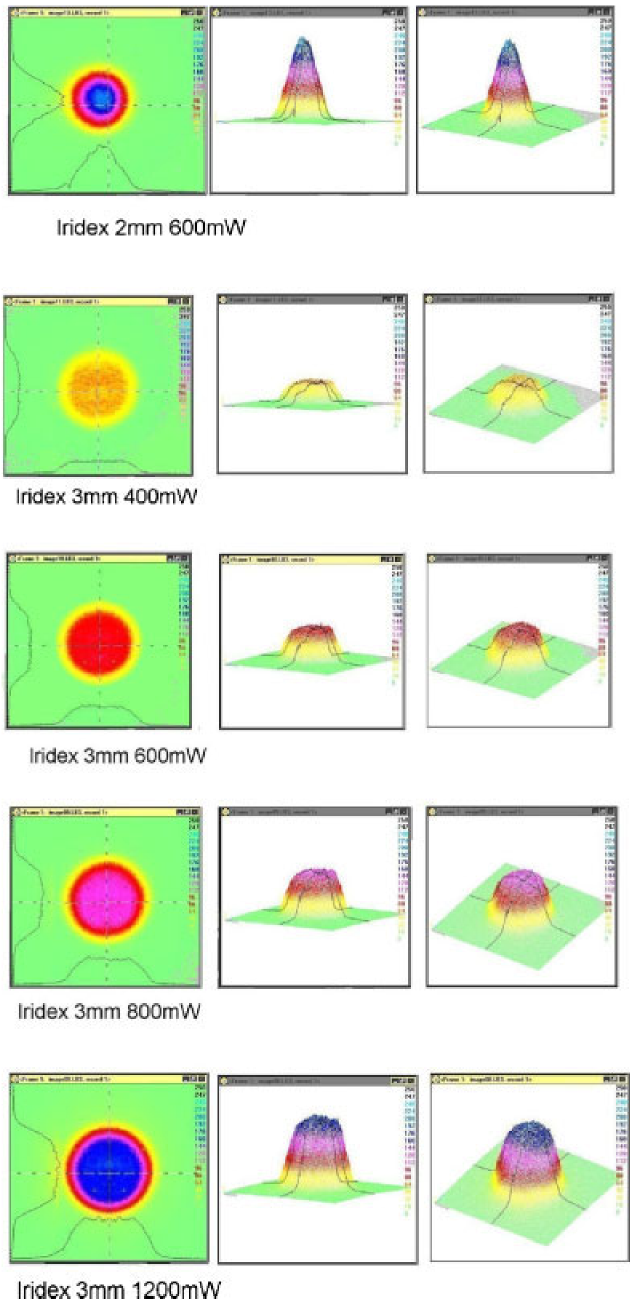

Fig. 5. Transpupillary thermotherapy (TTT) laser beam profiles obtained with the OCULIGHT SLx. [Figure can be viewed in color online via www.interscience.wiley.com.]

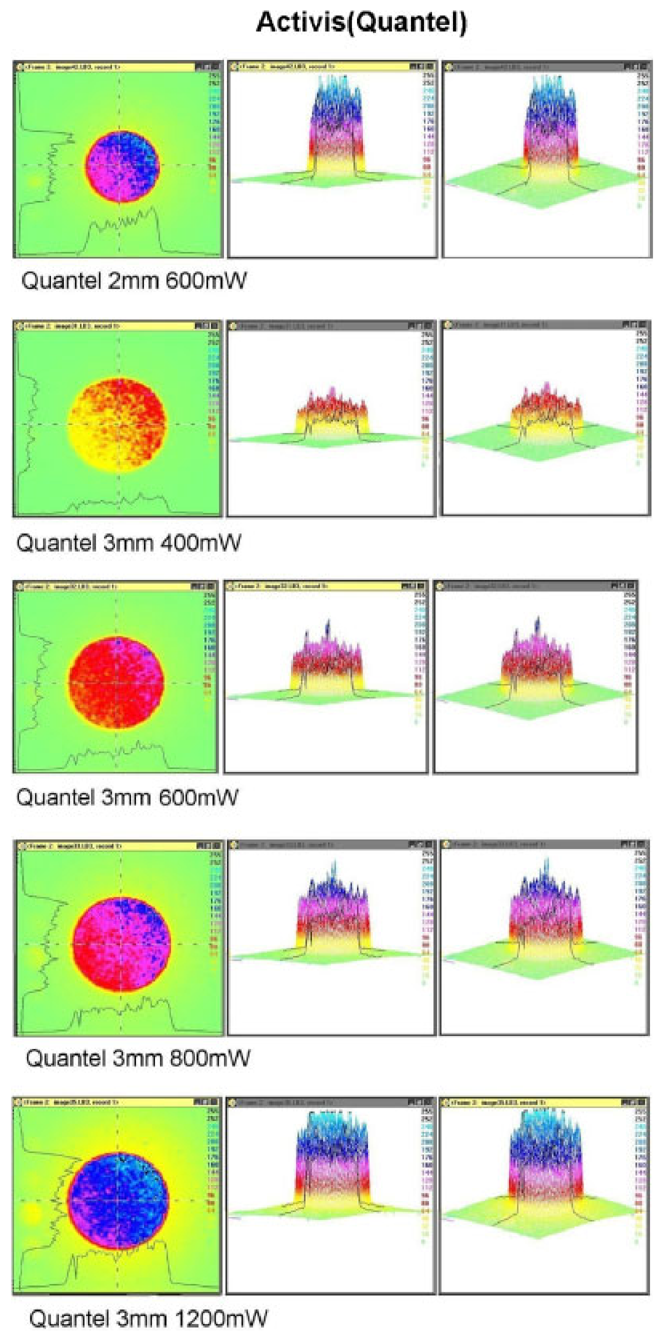

Fig. 6. TTT laser Beam profiles obtained with the IRIDIS. [Figure can be viewed in color online via www.interscience.wiley.com.]

in vitro study has not compared functional nor angiographic results obtained with different PDT or TTT lasers. However, the micro-spikes or micro-nadirs of power shown here induce variations of local irradiance that could have clinical implications.

PDT is based on the administration of a photosensitizer (Visudyne®) and the 690 nm CW laser irradiation applied for 83 seconds is only used to trigger the formation of free radicals producing a vascular damage. As some authors have recently pointed out, the efficacy of PDT for the treatment of choroidal neovascularization is more modest than previously thought [6]. Schematically, this can be attributed to either one or the two main compounds of the technique that is, “the drug” and or “the laser.” The irregularities displayed on Figures 1–3 could question the role of the laser.

Focusing alterations that can occur with the ACTIVIS or with the VISULAS could possibly bring an explanation

TABLE 2. Percentage of Variation of the Light Along a Vertical Line Passing Through the Center of the Beam Profile for Each Transpupillary Thermotherapy (TTT) Laser

Laser	2 mm (600 mW)	3 mm (400 mW)	3 mm (600 mW)	3 mm (800 mW)	3 mm (1,200 mW)
Iridis	11.3%	19.2%	18.0%	12.3%	5.3%
Oculight	7.6%	3.2%	1.2%	4.2%	2.5%

to variable response after a PDT session. Some pigment alterations have been reported in the follow up of PDT session [7,8]. Multiple and complex factors probably influence the location of a recurrence of choroidal neovascularization after laser based treatments or even after translocation surgery [9–11]. However, showing gaussian and top hat beam profiles in this study could question the role of the laser, when a recurrence of neovascularization is located at the circumference the scar of previous treatments. Lastly, very few explanations have been provided for the presence of different compounds within the PDT scars (i.e., atrophy, fibrosis, active, and inactive neovascularization) as mentioned by Coscas et al. [12,13]. Maybe, the micro-spikes and micro-nadir of power shown in this study could help to provide an explanation to this heterogeneity of the PDT scar.

TTT uses a moderate temperature rise, under the photocoagulation threshold, induced by a 810 nm CW diode laser applied during 60 seconds on a large spot to decrease exudation related to choroidal neovascularization [14]. The therapeutic mechanisms of the method remain unknown although the implication of a choroidal hyperexpression of heat shock proteins (HSP) has been shown [3,4]. The "therapeutic temperature zone" of TTT is probably close to the photocoagulation threshold.

Overdosage with a macular burn, although rare is the most significant side effect of TTT, corresponding to a temperature rise beyond the photocoagulation threshold [15]. If an adequate focus of the laser beam is important for limiting over dosages with TTT, the data provided here draw the attention on the importance of the laser beam profile for the reliability of the technique. Based on the results shown here, the use of a 3 mm spot seems more reliable than a 2 mm spot due its better homogeneity.

In conclusion, among the parameters guiding the choice of a PDT or a TTT laser, the shape and homogeneity of the beam profile seems of more importance than previously thought. The measurement of the global power is not the only parameter to be evaluated to check the reliability and the safety of the laser. Furthermore, since PDT and TTT lasers display different beam profiles, this parameter should be carefully evaluated when performing clinical evaluations of PDT or TTT treatments.

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REFERENCES

1. TAP I. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: One-year results of 2 randomized clinical trials—TAP report. Treatment of age-related macular degeneration with photodynamic therapy (TAP) Study Group. Arch Ophthalmol 1999;117(10):1329–1345.
2. TAP II, Bressler NM. Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: Two-year results of 2 randomized clinical trials-tap report 2. Arch Ophthalmol 2001;119(2): 198–207.
3. Mainster MA, Reichel E. Transpupillary thermotherapy for age-related macular degeneration: Long-pulse photocoagulation, apoptosis, and heat shock proteins. Ophthalmic Surg Lasers 2000;31(5):359–373.
4. Desmettre T, Maurage CA, Mordon S. Heat shock protein hyperexpression on chorioretinal layers after transpupillary thermotherapy. Invest Ophthalmol Vis Sci 2001;42(12): 2976–2980.
5. Green L. On-line beam performance monitoring to improve laser reliability and performance. In: Kudryashov A, editor. Laser resonators and beam control V. San Jose, Bellingham, USA: SPIE; 2002. pp 12–23.
6. Sternberg P, Jr., Lewis H. Photodynamic therapy for age-related macular degeneration: A candid appraisal. Am J Ophthalmol 2004;137(3):483–485.
7. Postelmans L, Pasteels B, Coquelet P, El Ouardighi H, Verougstraete C, Schmidt-Erfurth U. Severe pigment epithelial alterations in the treatment area following photodynamic therapy for classic choroidal neovascularization in young females. Am J Ophthalmol 2004;138(5):803–808.
8. Wachtlin J, Behme T, Heimann H, Kellner U, Foerster MH. Concentric retinal pigment epithelium atrophy after a single photodynamic therapy. Graefes Arch Clin Exp Ophthalmol 2003;241(6):518–521.
9. Simon P, Glacet-Bernard A, Coscas G, Soubrane G. Progression of choroidal neovascularization after macular translocation in age-related macular degeneration and degenerative myopia. J Fr Ophtalmol 2002;25(7):694–700.
10. Fujii GY, de Juan E, Jr., Pieramici DJ, Humayun MS, Phillips S, Reynolds SM, et al. Inferior limited macular translocation for subfoveal choroidal neovascularization secondary to age-related macular degeneration: 1-year visual outcome and recurrence report. Am J Ophthalmol 2002; 134(1):69–74.
11. Shen WY, Lee SY, Yeo I, Lai CM, Mathur R, Tan D, et al. Predilection of the macular region to high incidence of choroidal neovascularization after intense laser photocoagulation in the monkey. Arch Ophthalmol 2004;122(3):353–360.

12. Coscas G, Coscas F, Soubrane G. Monitoring the patient after treatment: Angiographic aspects of recurrence and indications for retreatment. J Fr Ophtalmol 2004;27(1):81–92.
13. Coscas G, Coscas F, Zourdani A, Soubrane G. Optical coherent tomography and ARMD. J Fr Ophtalmol 2004; 27(9 Pt 2):3S7–3S30.
14. Reichel E, Berrocal AM, Ip M, Kroll AJ, Desai V, Duker JS, et al. Transpupillary thermotherapy of occult subfoveal choroidal neovascularization in patients with age-related macular degeneration. Ophthalmology 1999;106(10):1908–1914.
15. Benner JD, Ahuja RM, Butler JW. Macular infarction after transpupillary thermotherapy for subfoveal choroidal neovascularization in age-related macular degeneration. Am J Ophthalmol 2002;134(5):765–768.