Illumination devices for photodynamic therapy of the oral cavity

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Abstract: Three compact and efficient designs are proposed to deliver an average irradiance of 50 mW/cm² with spatial uniformity well above 90% over a 25 mm² target area for photodynamic therapy of the oral cavity. The main goal is to produce uniform illumination on the target while limiting irradiation of healthy tissue, thus overcoming the need of shielding the entire oral cavity and greatly simplifying the treatment protocol. The first design proposed consists of a cylindrical diffusing fiber placed in a tailored reflector derived from the edge-ray theorem with dimensions 5.5 × 7.2 × 10 mm³; the second device combines a fiber illuminator and a lightpipe with dimensions 6.8 × 6.8 × 50 mm³; the third design, inspired by the tailored reflector, is based on a cylindrical diffusing fiber and a cylinder reflector with dimensions 5 × 10 × 11 mm³. A prototype for the cylinder reflector was built that provided the required illumination for photodynamic therapy of the oral cavity, producing a spatial uniformity on the target above 94% and an average irradiance of 51 mW/cm² for an input power of 70 mW.

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References and links

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1. Background

Photodynamic therapy (PDT) is a minimally invasive cancer treatment that attacks tumor tissue with photosensitizing drugs activated by light in the presence of oxygen. Some advantages of PDT over traditional techniques include preservation of functionality, excellent cosmetic results, good acceptance by patients, possibility to repeat the treatment and low invasiveness. In 2001, Temoporfin (Foscan)-PDT was approved in the European Union,
Norway, and Iceland for the palliative treatment of advanced head and neck cancer [1]. PDT with several photosensitizers has been successfully demonstrated in clinical trials for oral cavity cancer and pre-cancer, in which light is delivered to the oral cavity with a cylindrical diffusing fiber or with a lens terminated fiber [2]. In oral cavity applications, the photosensitizing drug is delivered systemically to the patient and may not localize with sufficient selectivity in the tumor tissue [3], thus shielding of the oral cavity is needed to ensure that only the cancerous lesion is exposed to the cytotoxic action of PDT. If healthy tissue is irradiated during the treatment, inflammation, pain, swelling, burns and scarring may occur [4]; in some cases, the teeth may also become loose [5]. For these reasons, shielding of the oral cavity is essential; reproducibility and uniformity of light dosimetry are also desired to improve the outcome of the treatment.

The design of an optical device to illuminate uniformly the target lesion without having to shield the whole oral cavity is extremely appealing. Guided by illumination theory, we identify several successful geometries to produce an average irradiance of at least 50 mW/cm² with spatial nonuniformities well below 10% over a square target area of 25 mm². These designs are scalable to permit irradiation of larger areas, and the theoretical approach is readily adaptable to curved surfaces.

2. Design

We explored different geometries to design a compact illumination device for delivery of PDT in the oral cavity. The first two designs, derived from illumination theory, inspired a third design based on a much simpler shape. We assessed the performance of each design by evaluating the average irradiance produced on the target area and the corresponding spatial nonuniformities defined as the average deviation of the irradiance (the ratio between the standard deviation of the irradiance and the average irradiance).

2.1 Tailored reflector

The first design is based on a cylindrically diffusing fiber source with a length of 1 cm and a diameter of 1 mm, of the kind that is currently used for PDT applications, which is placed inside a 1 cm long tailored reflector. The shape of the reflector, shown in Fig. 1, was derived from the edge-ray theorem [6,7] to direct the light emitted by the fiber within a 24-degree angle onto the target area, placed 1 mm away from the exit aperture of the reflector.

![Tailored reflector shape derived from the edge-ray theorem.](image)

We chose a gap of only 0.1 mm between the fiber (represented as a circle) and the reflector apex to reduce the size of the device needed to obtain good uniformity. Sample rays exiting the device with an angle of 24 degrees are shown.

The resulting device was compact, with a size of 5.5 mm × 7.2 mm × 10 mm, and suited for use in the oral cavity; it is shown in Fig. 2a. We considered a total power emitted by the cylindrical diffusing fiber of 100 mW, providing 100 mW per cm of diffuser, which is a
typical value used in clinical PDT. We modeled the fiber as a Lambertian emitter with a surface reflectance of 60%. We assumed the reflector to have an average reflectivity of 90% with 1° Gaussian scattering. The resulting irradiance produced on an area of 6 mm × 6 mm is shown in Fig. 2b.

![Fiber and Target](image)

**Fig. 2.** (a) Tailored reflector derived from the edge-ray theorem and (b) resulting irradiance produced on the target area (delimited by the square outline) 1 mm away from the reflector. The simulation was run tracing 5 million rays, giving a peak statistical error of 3%.

The average irradiance obtained on the 25 mm² target was 115 mW/cm² with an average deviation that reached the statistical noise limit of 3%. A large part of the light was lost because of the large aperture of the reflector: by adding a shield it is possible to direct light to the target while limiting irradiation of healthy cells. We studied the effect of adding a 0.2 mm-thick shield with a 90% Lambertian reflectance having an uncoated plastic window of variable size at the center. The resulting average irradiance and average deviation are shown in Fig. 3, along with the maximum deviation that was calculated as the difference between the maximum and minimum values of the irradiance on the target divided by the average irradiance.

![Graphs](image)

**Fig. 3.** (a) Average irradiance, (b) average deviation and (c) maximum deviation produced by the reflector of Fig. 4a for a window width varying from 5.1 to 20 mm and a fixed window height of 7.2 mm given by the dimension of the reflector. The goal of average deviation well below 10% drove the choice of an optimal window width of 6.5 mm.

The increase in the average deviation as the window decreased to 5.1 mm was mainly due to the reduction in irradiance caused by the edge of the shield, as is shown by the similar trend in the maximum deviation.

We identified an optimal window width of 6.5 mm from the near-peak average irradiance coupled with a first minimum in the average deviation. The device with this optimal window size and the corresponding irradiance produced on the target are shown in Fig. 4.
Fig. 4. (a) Tailored reflector with a central window with an optimal width of 6.5 mm and 
(b) the resulting irradiance produced on the target (indicated by the square outline). The 
simulation was run tracing 5 million rays, with a peak statistical error of 3%.

The average irradiance produced on the target was 130 mW/cm² with an average deviation 
that reached the peak statistical error of 3%; the uniformity is excellent and, since the 
irradiance obtained is much greater than the required 50 mW/cm², the input power could be 
reduced from 100 mW to 40 mW, enabling the use of lower power sources.

We also explored a configuration in which the window is placed laterally on the device, 
for better anatomic conformation in the oral cavity, as shown in Fig. 5.

Fig. 5. (a) Tailored reflector with a lateral window and (b) the resulting irradiance produced on 
the target (indicated by the square outline). The simulation was run tracing 5 million rays, with 
an error below 3%.

The average irradiance obtained on the target was 128 mW/cm² with an average deviation 
that reached the peak statistical error of 3%. There was a slight gradient in the irradiance 
produced by the edge of the reflector, but the spatial nonuniformities were well below 10%. 
Also for this configuration we could reduce considerably the input power to 40 mW and still 
produce the required illumination at the target.

2.2 Lightpipe

The second design we explored was a fiber illuminator coupled to a solid PMMA lightpipe 
with an overall dimension of 6.8 mm × 6.8 mm × 50 mm. The fiber had a core diameter of 
0.4 mm and a numerical aperture of 0.22. The lightpipe, shown in Fig. 6a, had a reflective 
coating and a square cross section. It consisted of an initial tapered section 2 cm long, in 
which the size of the lightpipe increased linearly from 1 mm to 6.8 mm, followed by a 3 cm 
long straight section terminated by a 45 degree mirror to direct the light laterally to the output 
window. A Lambertian diffusive film with 60% transmission was placed at the input of the 
lightpipe to increase the angular range of the light and favor a more efficient homogenization 
of the light with a shorter device. The lengths of the tapered and straight sections were 
optimized to obtain good spatial uniformity while keeping the device compact. The reflective
coating was added for two reasons: first of all, since the device is to be used in the oral cavity with the goal of limiting irradiation of healthy tissue, it is not possible to rely uniquely on total internal reflection to confine light inside the lightpipe; secondly, the diffusive film at the input of the lightpipe would cause part of the light to exceed the critical angle of the lightpipe and leak out of the lightpipe if no coating were present. We considered a power of 100 mW emitted by the fiber and a reflectivity of 90% with 1° Gaussian scattering for the lightpipe coating. The irradiance was evaluated at a distance of 1 mm from the output window and is shown in Fig. 6b.

![Fig. 6. (a) Solid PMMA lightpipe device with reflective coating and (b) resulting irradiance (the target outline is represented by a square). The simulation was run tracing 5 million rays, with a peak statistical error of 2%.](image)

The average irradiance on the target was 77 mW/cm² with an average deviation of 4%. Since the required average irradiance is 50 mW/cm², it would be possible to reduce the input power from 100 mW to 70 mW and still meet the requirements for the PDT treatment.

### 2.3 Cylinder

Since both the tailored reflector and the lightpipe produced excellent results with an input power considerably lower than typically used in the clinic, we decided to explore the possibility of meeting the illumination requirements on the target with a much simpler device, which would be easier to manufacture. Inspired by the geometry of the tailored reflector, we studied the performance of a half cylinder reflector in which the 1 mm diameter cylindrical diffusing fiber emitting a power of 100 mW was placed in close proximity of the wall of the reflector. Such configuration and the resulting irradiance are shown in Fig. 7 for a cylinder diameter of 6 mm.

![Fig. 7. (a) 6 mm diameter half cylinder reflector with a cylindrically diffusing fiber source placed 0.1 mm from the cylinder surface. (b) Irradiance distribution produced by the reflector (the target is shown by the square outline). The simulation was performed tracing 5 million rays, with a peak statistical error of 1%.](image)

The irradiance distribution produced by the half cylinder reflector was highly nonuniform, and the hot spots produced along the edges of the cylinder fell within the target area. However, the careful choice of the size of the cylinder and the position of the fiber allowed us
to identify a more favorable situation, as is illustrated in Fig. 8 by comparing the tailored reflector derived in Section 2.1 and a cylinder reflector with a diameter of 8 mm and a separation between the reflector and the diffusing fiber of 0.1 mm.

![Fig. 8.](image)

In this case, while the irradiance distribution was still highly non uniform, the hot spots produced by the cylinder reflector fell outside the target of interest so that the region of good spatial uniformity produced at the center could be exploited by the addition of an appropriate shield 0.2 mm thick. The optimal window size for the shield was identified to be 7 mm × 5.5 mm and the resulting illumination device is shown in Fig. 9.

![Fig. 9.](image)

The average irradiance on the target was 104 mW/cm² with an average deviation of 5%. The performance obtained with this simple geometry was excellent and allowed us to meet the requirements for PDT treatment of average irradiance of 50 mW/cm² and average deviation below 10% using an input power as low as 50 mW. The overall size of the device was 5 × 10 × 11 mm³.

The lateral configuration for this reflector is shown in Fig. 10.
The average irradiance on the target was 103 mW/cm² with an average deviation of 6%. In both configurations, the cylinder reflector performed worse than the tailored reflector, producing a lower average irradiance and higher average deviation, but still well within the requirements, thus offering an excellent compromise between performance and ease of fabrication.

3. Analysis of scalability and sensitivity to misalignments

We identified the cylinder reflector as the most promising geometry in terms of manufacturability and cost for realizing a prototype. In order to evaluate the robustness of the design to misalignments of the source, we studied the effect on the irradiance produced at the target of a vertical or horizontal displacement of the diffusing fiber up to 0.4 mm. The resulting average irradiance and average deviation are shown in Fig. 11.

A vertical displacement of the fiber proved to be less critical than a horizontal displacement: a 0.4 mm vertical displacement of the fiber degraded the average deviation from 5% to only 6%, while a horizontal displacement of 0.35 mm towards the window yielded an average deviation of 9%. When the fiber is moved towards the output of the cylinder reflector, the hot spots produced along the edges of the cylinder (see Fig. 8b) move closer to the window and eventually fall on the target: this explains the increase in both average irradiance and average deviation as the fiber is displaced forward, since the hot spots of the irradiance previously blocked by the shield begin to hit the target.

In summary, displacements up to 0.35 mm can be tolerated by the cylinder reflector. The vertical positioning did not appear to be critical; a horizontal displacement up to 0.35 mm still allowed us to meet the requirement of average deviation below 10%, but limiting the displacement to 0.2 mm would offer a more stable condition.
This specific device could be used to treat a field including flat lesions characteristic of early or pre-cancer up to 5 mm × 5 mm in area. For treatment fields that are greater than 5 mm × 5 mm, modifications to the design can be envisioned. In particular, a longer diffusing fiber can be employed. A 2 cm-long cylindrical diffusing fiber placed in a 2 cm-long cylinder reflector with a diameter of 6 mm and a window of 7 mm × 5.5 mm was recently shown to produce an average irradiance of 162 mW/cm² and average deviation of 3% with an input power of 200 mW (100 mW per cm of diffuser) [8]. For this device, it would also be possible to increase the width of the window from 7 to 18 mm to illuminate an area of 17 mm × 5 mm with an average irradiance of 98 mW/cm² and an average deviation of 8%. The device could be scaled to an overall size of 8 × 16 × 20 mm³ with a window of 14 mm × 11 mm and still produce the required illumination (an average irradiance of 55.1 mW/cm² with an average deviation of 10%) over an area of 13 mm × 10 mm, leaving a gap of 0.6 mm between the cylinder wall and the diffusing fiber. If desired, different geometries could be explored to produce a more compact device. The theoretical approach is readily adapted to curved treatment windows, which will likely be necessary in several locations within the oral cavity.

4. Experimental validation

A prototype for the cylinder reflector was manufactured by machining a cylinder from a block of aluminum as shown in Fig. 12.

![Fig. 12. Cylinder reflector prototype fabricated in aluminum. The diffusing fiber is inserted in the reflector through holes in the sides of the cylinder. For ease of manufacturing and testing, the size of the prototype was 5 mm x 25 mm x 11 mm. The size of a final device based on this design would be only 5 mm x 10 mm x 11 mm, as indicated.]

The light source employed for measurements was a fiber coupled laser (Model BWF-670-300-E/55370, BWTEK B & W TEK Inc.) with a central wavelength of 668 nm. The cylindrical diffusing fiber (Pioneer Optics), having a length of 1 cm and diameter of 1 mm, was positioned into the cylinder through holes in the lateral sides of the cylinder reflector. To measure the irradiance produced by the device, a pinhole with a diameter of 1 mm was placed in front of the detector (Model 818-ST, Newport) and scanned to sample the output. In order to compare the experimental results with the simulations, we measured the flux emitted by the diffusing fiber and adjusted the power in the simulations to match this value. Additionally, we modified the reflectivity in the simulations to better match the experimental results: we considered a reflectivity of 85%, 80% of which producing a near-specular component and the remaining 20% producing a diffuse component. The normalized irradiance map obtained is compared to the numerical simulation in Fig. 13.
The numerical simulations were smoothed with a Gaussian function having a width equal to the size of the pinhole used for the experiment; variations of this parameter within the tolerances of the pinhole gave a change in the simulated average deviation of less than 1%.

The cross-sections of the simulated and experimental irradiances of the unshielded cylinder are shown in Fig. 14.

An asymmetry of the experimental irradiance can be noticed in Fig. 14a that can be accounted for in the numerical simulations with a vertical displacement of the fiber inside the reflector of 0.3 mm; nonetheless the cross-sections of experimental data and numerical simulation differed by no more than 13% for the cross-section of Fig. 14a and 7% for the cross-section of Fig. 14b, with an average difference of 4% in both cases. As verified with the analysis of the sensitivity of misalignments in Section 3, we do not expect this displacement to affect significantly the uniformity of the irradiance obtained with the reflector in presence of the shield. Other factors that can explain the differences between the nominal design and the built device are non-optimal polishing of the cylinder surface and experimental non-idealities such as tilts in the detector plane and angular cutoff introduced by the combination of pinhole and detector.

The shield was fabricated by applying a diffuse reflective coating on a 0.157 mm thick vinyl coverslip leaving a central uncoated region of 7 mm × 5.5 mm. The normalized irradiance measured is shown in Fig. 15 compared with the numerical simulation in which we introduced a vertical misalignment of the fiber of 0.3 mm.
Fig. 15. (a) Simulated and (b) experimental normalized irradiances of the shielded cylinder reflector. The measurements were made every 0.5 mm along the lateral and vertical directions. The square outlines represent the outline of the target area.

The cross sections of experimental and simulated irradiances are shown in Fig. 16.

Fig. 16. Cross-sectional plots of the experimental and simulated normalized irradiances of the shielded cylinder reflector.

With a power of 70 mW from the diffusing fiber and a cylinder reflectivity of 85%, the numerical simulations predicted an average irradiance of 58 mW/cm² with an average deviation of 4%.

We estimated the irradiance on the target by calculating the ratio between the power measured by the detector and the size of the pinhole, averaging over the various measurements that were made over the target area. The average irradiance was estimated to be 51 mW/cm² for a power emitted by the diffusing fiber of 70 mW. The experimental average deviation obtained on the 25 mm² target was 6%, in excellent agreement with the 4% average deviation produced by the numerical simulations.

In the clinic, the typical power emitted by a 1 cm diffusing fiber ranges between 100 and 400 mW; a power of 70 mW allowed our prototype to meet the treatment parameters of 50 mW/cm² with average deviation well below 10%.

5. Discussion and conclusion

We proposed three devices for delivery of photodynamic therapy to the oral cavity. The main characteristics of the three designs proposed are summarized in Table 1 for an input power of 100 mW and reflectivity of 90% for reflectors and coatings. All devices provide efficient and uniform illumination with a power that is readily available in the clinic and greatly simplify the treatment procedure by limiting irradiation of healthy cells and avoiding the necessity of shielding the whole oral cavity as is currently done in clinical trials.
Table 1. Comparison of the designs

| Design          | Configuration | Dimensions of device (mm³) | Average irradiance (mW/cm²) on 25 mm² target, Goal 50 mW/cm² | Average deviation (%), Goal < 10% |
|-----------------|---------------|---------------------------|---------------------------------------------------------------|----------------------------------|
| Tailored reflector | Central window | 5.5 × 7.2 × 10            | 130                                                           | < 3                              |
|                  | Lateral window | 5.5 × 7.2 × 10            | 128                                                           | 3                                |
| Lightpipe        | -              | 6.8 × 6.8 × 50            | 77                                                            | 4                                |
| Cylinder reflector | Central window | 5 × 10 × 11              | 104                                                           | 5                                |
|                  | Lateral window | 5 × 10 × 11              | 103                                                           | 6                                |

The total flux reaching the target is 32 mW for the tailored reflector (the central window configuration), 19 mW for the lightpipe and 26 mW for the cylinder reflector (the central window configuration), with an input flux of 100 mW. We define the efficiency of an illumination device for PDT as the ratio between the flux that reaches the target and the input flux. The efficiency of the lightpipe device amounts to 19% and is mainly limited by the losses given by the diffusing film placed at the input of the lightpipe and by multiple reflections along the lightpipe; the efficiencies of the two reflector designs are reduced by the losses due to multiple reflections, which give an efficiency of 32% for the tailored reflector (in the central window configuration) and of 26% for the cylinder reflector (central window configuration).

We identified the cylinder reflector as the optimal device given its excellent performance combined with a simple design that is easy to manufacture. The cylinder reflector prototype that we fabricated demonstrated the direct clinical applicability of this device, producing an experimental average deviation below 6% and an average irradiance of 50 mW/cm² with a power of 70 mW emitted by the diffusing fiber.

We optimized all designs to obtain the best spatial uniformity with a compact device; while more efficient solutions can be devised, we developed three designs that provide the desired irradiance with the source powers currently available in PDT applications and offer a considerable improvement over the current treatment procedure for flat lesions characteristic of early and pre-cancer conditions. Specifically, devices like these offer more uniform and reproducible dosimetry and reduce or eliminate the need to shield normal tissues in the cavity. Because the illuminators would be placed in direct contact with the treatment field and immobilized there, they would not be vulnerable to patient motion. The flat surfaces amenable to treatment with planar windows include the top and bottom of the tongue, the cheek, and the gum line. Small lesions on soft, curved surfaces, such as the lateral surface of the tongue, could also be treated with devices like those presented here. Gentle compression would flatten the soft tissue against the planar treatment window. There will naturally be sites where curved treatment windows would be necessary, and we have begun to consider the design of such devices. As these devices are optimized and undergo preliminary clinical evaluation, we anticipate that clinicians may eventually have a small family of illuminators, each tailored to particular treatment field sizes and sites.

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