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Uniform irradiation of irregularly shaped cavities for photodynamic therapy

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Abstract. It is difficult to achieve a uniform light distribution in irregularly shaped cavities. We have conducted a study on the use of hollow ‘integrating’ moulds for more uniform light delivery of photodynamic therapy in irregularly shaped cavities such as the oral cavity. Simple geometries such as a cubical box, a sphere, a cylinder and a ‘bottle-neck’ geometry have been investigated experimentally and the results have been compared with computed light distributions obtained using the ‘radiosity method’. A high reflection coefficient of the mould and the best uniform direct irradiance possible on the inside of the mould were found to be important determinants for achieving a uniform light distribution.

1. Introduction

Photodynamic therapy (PDT) is a promising technique to treat superficial (pre)malignant tissue. The mechanism is based on excitation of a photosensitizer, preferentially located in the microvasculature of the tumour and in the tumour cells, resulting in selective tumour destruction (Henderson and Dougherty 1992). For optimal treatment the light dose should vary as little as possible over the surface area of the tissue treated. However, especially in the oral cavity it has been found difficult to achieve such a uniform light dose for PDT of squamous cell carcinoma, or of condemned mucosa.

The light delivery method that will be discussed in this paper is based upon the use of a hollow mould which fits perfectly inside the treatment geometry. The mould consists of a material with a high diffuse reflection coefficient of 0.8–0.9. It is irradiated from the inside with an isotropic emitting (laser) light source. This produces diffusely reflected light fluences inside the mould which, due to the large number of reflection events, tend to become evenly distributed over the inside area of the mould and, hence, also over the outside area for tissue irradiation. To predict the degree of uniformity of light dose distributions in irregularly shaped cavities we combine the concept of integrating sphere theory and the ‘radiosity method’, which originates from thermal radiation heat transfer. We show that reasonably uniform irradiation is feasible in elementary geometries such as a cubical box, a cylinder, a sphere (irradiated off centre) and a ‘bottle-neck’ geometry.

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2. Material and methods

2.1. The integrating sphere

Consider an integrating sphere, of area A (m^2), with a light source inside which emits light with total power P_0 (W) and non-uniform spatial irradiance distribution $E_0(\mathbf{r})$ (W m^{-2}), where $\mathbf{r}$ denotes the position vector on the integrating sphere area. The integrating sphere subsequently produces a sequence of uniform light distributions over the surface area due to multiple reflections which can add up to several times the irradiance $E_0(\mathbf{r})$ (see e.g. the appendix of van Gemert *et al* 1987). Using ρ as the diffuse reflection coefficient of the integrating sphere surface, the total irradiance distribution inside the sphere is

$$E(\mathbf{r}) = E_0(\mathbf{r}) + (P_0/A)(\rho + \rho^2 + \rho^3 + \dots + \rho^n + \dots) = E_0(\mathbf{r}) + (P_0/A)\rho/(1 - \rho). \quad (1)$$

From (1) it follows that the overall spatial distribution of the irradiance in an integrating sphere is more uniform when ρ is closer to one, as this results in a larger contribution of the diffuse reflections, the second term on the right-hand side of (1), relative to the incident irradiance, the first term on the right-hand side of (1).

In this paper we show that this effect, which is exact for a sphere, is also valid to a certain extent for non-spherical cavities.

2.2. The radiosity method

A numerical analysis of the integrating effect can be performed using the ‘radiosity method’, which has its origin in thermal radiation heat transfer (Hottel and Sarofim 1967) and has found successful application in illumination engineering and computer graphics (Goral *et al* 1984). Radiosity is defined as the total power per unit surface area (W m^{-2}) departing from that surface, i.e. it is the sum of reflected and emitted power from the surface. In this study no surface emission is considered, the radiosity represents the reflected power per unit area.

The radiosity method requires a subdivision of the total reflecting surface into smaller surface elements. Because of multiple diffuse reflections in the cavity all these surface elements exchange power. A surface-to-surface power transfer factor is defined by the configuration factor C_{ji} which denotes the fraction of power originating from surface element j which is received by surface element i . The surface area of element i is denoted by A_i .

Analogous to the light distribution inside an integrating sphere (1) a series can be defined for the light distribution inside a cavity of arbitrary shape. For each surface element i we define $b_i^{(0)}$, as the initial radiosity contribution, caused by the reflected direct incident light from the source. Vector $\mathbf{b}^{(0)}$, $(b_1^{(0)}, b_2^{(0)}, \dots, b_N^{(0)})$, denotes the distribution of initial radiosity of the entire geometry which consists of N surface elements.

Surface element j , radiosity $b_j^{(0)}$, emits power $A_j b_j^{(0)}$ diffusely of which $C_{ji} A_j b_j^{(0)}$ reaches element i . The reflection on element i , $\rho C_{ji} A_j b_j^{(0)}$, contributes $\rho C_{ji} (A_j/A_i) b_j^{(0)}$ to the radiosity of element i . Due to the initial power reflected by all $(N - 1)$ other surface elements, surface element i receives an additional contribution denoted by $b_i^{(1)}$ to its initial radiosity $b_i^{(0)}$; we have

$$b_i^{(1)} = \rho \sum_{j=1}^N C_{ji} \frac{A_j}{A_i} b_j^{(0)}. \quad (2)$$

In matrix notation, for all N surface elements (2) becomes

$$\mathbf{b}^{(1)} = \rho \mathbf{C} \mathbf{M} \mathbf{b}^{(0)} \quad (3)$$

where vector $\mathbf{b}^{(1)}$ is defined analogous to $\mathbf{b}^{(0)}$, and matrix $\mathbf{C} \mathbf{M}$ consists of elements $C_{ji} A_j/A_i$.

The second diffuse reflection yields an additional radiosity component $b_i^{(2)}$ given by

$$b_i^{(2)} = \rho \sum_{j=1}^N C_{ji} \frac{A_j}{A_i} b_j^{(1)} \quad (4)$$

or, in matrix notation, using (3),

$$\mathbf{b}^{(2)} = \rho \mathbf{C} \mathbf{M} \mathbf{b}^{(1)} = \rho^2 \mathbf{C} \mathbf{M}^2 \mathbf{b}^{(0)}. \quad (5)$$

The n th diffuse reflection yields

$$b_i^{(n)} = \rho \sum_{j=1}^N C_{ji} \frac{A_j}{A_i} b_j^{(n-1)} \quad (6)$$

which becomes

$$\mathbf{b}^{(n)} = \rho \mathbf{C} \mathbf{M} \mathbf{b}^{(n-1)}. \quad (7)$$

Finally, using B_i to represent the overall radiosity of surface element i , due to an infinite number of diffuse reflections ($n = 0 - \infty$) inside the cavity, we have

$$B_i = \sum_{n=0}^{\infty} b_i^{(n)}. \quad (8)$$

We define vector $\mathbf{B}$, ($B_1, B_2, \dots, B_N$), for the overall radiosity of all surface elements $i = 1, \dots, N$

$$\mathbf{B} = \sum_{n=0}^{\infty} \mathbf{b}^{(n)}. \quad (9)$$

This leads to the final result

$$\mathbf{B} = \mathbf{b}^{(0)} + \rho \mathbf{C} \mathbf{M} \mathbf{b}^{(0)} + \rho^2 \mathbf{C} \mathbf{M}^2 \mathbf{b}^{(0)} + \dots + \rho^n \mathbf{C} \mathbf{M}^n \mathbf{b}^{(0)} + \dots \quad (10)$$

This result for an irregular, generally shaped cavity has the same mathematical structure as (1) for an integrating sphere.

When the direct irradiance, the diffuse reflection coefficient and the configuration factors between all surface elements are known, the initial radiosity $\mathbf{b}^{(0)}$ and the subsequent terms of (10) can be obtained by matrix multiplication. In this paper computations were performed for diffuse reflection coefficients ranging from 0 to 0.99. Assuming that the wall of the mould is non-absorbing, the therapeutic light dose incident on the tissue (outside the mould) is proportional to the radiosity inside the mould.

To illustrate the mechanism of multiple diffuse reflections, consider a cubical box consisting of six equal areas A–F (figure 1), which is irradiated from the inside in such a way that the initial radiosity due to the first reflection is 1 on sides B–E, 0.1 on side A and 1.9 on side F (implying that the source is close to F). Hence, the elements of vector $\mathbf{b}^{(0)}$ are [0.1, 1, 1, 1, 1, 1.9].

For this geometry there are two different configuration factors, C_{OS} (opposite side from E to C, A to F, B to D) and C_{CS} (connected side from A to C, A to B, F to E, E to A, etc). They have the values $C_{OS} = 0.199\,824\,9$ and $C_{CS} = 0.200\,043\,8$ (Siegel and Howell 1992). Matrix $\mathbf{C} \mathbf{M}$ is for this case:

$$\mathbf{C} \mathbf{M} = \begin{bmatrix} 0 & C_{CS} & C_{CS} & C_{CS} & C_{CS} & C_{OS} \\ C_{CS} & 0 & C_{CS} & C_{OS} & C_{CS} & C_{CS} \\ C_{CS} & C_{CS} & 0 & C_{CS} & C_{OS} & C_{CS} \\ C_{CS} & C_{OS} & C_{CS} & 0 & C_{CS} & C_{CS} \\ C_{CS} & C_{CS} & C_{OS} & C_{CS} & 0 & C_{CS} \\ C_{OS} & C_{CS} & C_{CS} & C_{CS} & C_{CS} & 0 \end{bmatrix}. \quad (11)$$

Figure 1. The cubical box. The different sides of the box are denoted by A–F.

The radiosity contributions for each reflection, the subsequent terms of (10), are summarized in table 1 for all six sides. The reflection coefficient is taken as $\rho = 0.95$.

Table 1.

Radiosity contribution	Radiosity on A	Radiosity on B–E	Radiosity on F
Reflection of direct incidence	0.1000	1.0000	1.9000
2nd reflection	1.1209	0.9500	0.7791
3rd reflection	0.8701	0.9025	0.9349
4th reflection	0.8636	0.8574	0.8512
5th reflection	0.8133	0.8145	0.8157
6th reflection	0.7353	0.7351	0.7349
7th reflection	0.6983	0.6983	0.6983
Etc	...	...	...
Total radiosity	19.2437	20	20.7563

In this example the radiosity contribution from direct incidence shows a ratio of 19 between maximum and minimum. This ratio is only 1.079 when multiple reflections are included. This illustrates the improvement in uniformity of a light distribution achieved using an ‘integrating mould’.

2.3. Experimental details

In order to manufacture a cubical box ($10 \times 10 \times 10 \text{ cm}^3$) and a cylinder (length 30 cm, diameter 5.1 cm), PMMA (polymethylmethacrylate) for the box and PVC (polyvinylchloride) for the cylinder were coated with a 0.3 mm thick layer of barium sulphate. The diffuse reflection coefficient of this material was measured as 0.89 ± 0.04 using an integrating sphere set-up. Spheres (diameter, 4.1 cm; wall thickness, 2.0 mm) were made of PMMA holding light scattering barium sulphate particles. The reflection coefficient of this material was measured as 0.83 ± 0.04 . Also other light scattering particles were tested: titanium oxide and calcium carbonate, but their performance was inferior to that of barium sulphate. The results obtained using these materials will not be presented here.

Experiments and computations were performed on the following geometries (figure 2):

- (i) a cubical box irradiated with an isotropic light source placed in the centre of the box;

Figure 2. The geometries used in this study. (1) *Cubical box*: dimensions, $10 \times 10 \times 10 \text{ cm}^3$; 11 measurement points on one side of the box, numbered from 0 to 10; an isotropic light source in the centre of the box. (2) *Cylinder*: length, 30 cm; diameter, 5.1 cm; 11 equidistant measurement points over the length of the cylinder; isotropic light source on the central axis 3 cm from the left side. (3) *Sphere*: diameter, 4.1 cm; wall thickness, 2.0 mm; 16 circumferential measurement points at $10\text{--}160^\circ$; isotropic light source off centre by 1 cm (half the radius). (4) *Bottle-neck*: this geometry is used for computations only; diameter of the spheres, 15.2 cm; diameter of the connecting cylinder, 3.15 cm; two lengths of the connecting cylinder were studied, 10 cm and 20 cm. An isotropic light source is centred in the left sphere. Indications D_1 and D_2 denote the points used for the maximum to minimum irradiance ratio of the two spheres (see figure 8).

(ii) a cylinder irradiated with an isotropic light source placed on the axis at one tenth of the length;

(iii) a sphere irradiated with an isotropic light source located off centre at a distance of half the radius from the centre;

(iv) a 'bottle-neck' geometry with an isotropic light source in one of the spheres (computation only).

The light source used was a 10 mW HeNe laser at 633 nm, coupled into a $400 \mu\text{m}$ fibre having a small sphere (diameter 1.0 mm) at its distal end acting as an isotropic light source. The angular light distribution is shown in figure 3. The fluence inside the cavities was measured using a second 'isotropic' sphere as detector (Marijnissen and Star 1987) where the photon current was converted into an electric voltage by a photomultiplier set-up. Uncertainties of the measurement as seen in figures 4–6 are caused by errors in fibre positioning and variations in system readout.

Radiosity values of the various geometries were computed using small surface elements. The geometries were subdivided as follows: box, each side subdivided into 49 squares; cylinder, subdivided into 80 rings along the central axis; sphere, subdivided into 50 rings. The bottle-neck geometry was composed of elements used in the computations for the sphere and the cylinder. Iteration was ended when radiosity values remained constant within 0.1%.

Figure 3. The measured angular distribution ($^{\circ}$) of the isotropic light source used in our experiments. The dotted line shows the approximation used for the computations in figure 6.

Figure 4. Normalized light distribution (W m^{-2}) in the cubical box at the 11 points indicated in figure 2. The box is irradiated by a central isotropic light source. Experimental results ($\cdot$), with a reflection coefficient of 0.89 ± 0.04 , are compared with computed results for moulds with reflection coefficients of 0.00, 0.50, 0.79, 0.85 (lower bound of the experimental value, bold), 0.93 (upper bound, bold) and 0.99.

The light distribution of the various geometries will be represented according to the locations indicated in figure 2. The computed radiosities are proportional to the measured

Figure 5. Normalized light distribution (W m^{-2}) in the cylinder. The cylinder is irradiated by an isotropic light source on the axis 3 cm from the left wall (figure 2). Experimental results ($\cdot$), with a reflection coefficient of 0.89 ± 0.04 , are compared with computed results for moulds with reflection coefficients of 0.00, 0.50, 0.70, 0.85 (lower limit of the experimental value, bold), 0.93 (upper limit, bold) and 0.99.

fluences, implying that measured and computed curves can directly be compared using normalization to maximum values.

3. Results

3.1. Cubical box

Figure 4 shows the computed light distributions for various wall reflection coefficients. The measured values for $\rho = 0.89 \pm 0.04$ are also shown. The measured results are slightly higher than the computed values for $\rho = 0.85$ and 0.93, the lower and upper bounds of the measured reflection coefficient. The improvement in dose uniformity achieved by using a mould of 93% diffuse reflection is a decrease in the maximum to minimum ratio from 5.92 for direct irradiation to nearly 1.2.

3.2. Cylinder

Figure 5 shows the computed light distributions for various wall reflection coefficients. The measured values for $\rho = 0.89 \pm 0.04$ are also shown. Again, the measured results are slightly higher than the computed values for $\rho = 0.85$ and 0.93, the lower and upper bounds of the measured reflection coefficient.

Figure 6. Normalized light distribution (W m^{-2}) in the sphere. The sphere is irradiated by an off-centre isotropic light source (figure 2). Experimental results ($\cdot$), with a reflection coefficient of 0.83 ± 0.04 , are compared with computed results for moulds with reflection coefficients of 0.00, 0.50, 0.79 (lower limit of the experimental value, bold), 0.87 (upper limit, bold), 0.93 and 0.99. Computed results using an ideal isotropic light source (---) and an experimental isotropic light source (—) with the angular distribution as in figure 3 are shown.

3.3. Sphere

Figure 6 shows the computed light distributions for various wall reflection coefficients. The measured values for a wall reflectivity of 0.83 ± 0.04 are indicated. Computed results are given for irradiation with an (ideal) isotropic source and an experimental isotropic source with an angular distribution as shown in figure 3, which was used for the experiments. Our measurements correspond to the computed results for $\rho = 0.79$, the lower bound of the measured reflection coefficient.

3.4. The radiosity contribution of each reflection

For the cylinder the radiosity contribution of each reflection, normalized to its maximum value, is shown in figure 7. Note the important fact that each successive radiosity contribution is more uniform than its precursor. For the cylinder it is observed that the 57th has an added radiosity which is uniform within 10%. We mention that for the cubical box this is already observed for the third reflection.

Figure 7. Normalized radiosity distribution (W m^{-2}) of each reflection in the cylinder. The isotropic light source is positioned on the central axis, 3 cm from the left wall. Note the important fact that each successive radiosity contribution is more uniform than its precursor. The 57th reflection produces an additional radiosity which is uniform within 10%. We mention that for the cubical box this is already observed for the third reflection. The numbered curves indicate the reflection of the direct incident light (0), the first following reflection (1), etc.

3.5. Uniformity of the light distribution in relation to the reflection coefficient

Figure 8 presents all computed radiosity data in terms of the ratio between maximum and minimum values for all geometries considered as a function of the reflection coefficient. It clearly shows that the light distribution tends to become more uniform for a higher reflection coefficient. We also see that for some geometries, such as the cylinder and the bottle-neck geometries, maximum to minimum ratios of less than 10 occur for a reflection coefficient of at least 0.95.

4. Discussion

The approach presented here can be used for determining basic irradiation parameters for PDT of irregular shaped cavities. In the oral cavity the computation can be simplified by using elementary geometries (box, cylinder or sphere) and by defining planes of symmetry, although the computational method has potential for more difficult geometries as well. The approach has recently resulted in the production of an applicator for PDT of a specific part of the oral cavity (unpublished).

For light propagating through a non-scattering medium the computational method may be preferred over a Monte Carlo approach (especially when multiple reflections occur).

Figure 8. Ratio of maximum to minimum irradiance found in all computed light distributions in relation to the reflection coefficient. For all these geometries a higher reflection coefficient leads to a more uniform light distribution, with a completely uniform light distribution as a limiting case of a reflection coefficient approaching unity. The numbered curves indicate the following: 1, cubical box, central isotropic light source; 2, sphere, off-centre isotropic light source; 3, sphere, off-centre isotropic light source with angular light distribution according to figure 3; 4, cylinder, isotropic light source on axis, 3 cm from left wall; 5, 6, bottle-neck geometry, with the length of the connecting cylinder respectively 10 cm and 20 cm, isotropic light source centred in left sphere.

Once all configuration factors are available for the radiosity method, the iterative process is less time consuming than current Monte Carlo programs. The radiosity program has the additional advantage that it can be used in an interactive way; the position of the light sources for instance—which does not influence the configuration factors—can be varied to optimize the light distribution. In contrast, Monte Carlo programs would have to start a completely new run for a new position of the light sources.

Our approach to irradiate irregularly shaped cavities using a hollow integrating mould indicates that the uniformity of the direct incidence and the reflection coefficient of the mould are the main factors in creating a light distribution competent for PDT treatment. From figure 8 we observe that when geometries have a fairly non-uniform direct irradiance distribution it is difficult to achieve a uniform light distribution using the multiple reflections from an integrating mould. For the cylinder and the bottle-neck geometries, both with a very unsuitable location chosen for the isotropic light source, the mould needs a high reflection coefficient of at least 0.95. On symmetry grounds, it is easy to deduce from figure 5 what the light distribution would be if another isotropic source were placed at 3 cm from the right side. This would improve the light distribution considerably, decreasing the maximum to minimum ratio from 7.32 to 1.98 for a 93% reflecting mould.

Although creating a uniform light distribution is more difficult in some geometries than in others, figure 7 shows that in the process of multiple reflections each subsequent reflection produces a more uniform distribution. Hence it is to be expected that an integrating effect in a diffusely reflecting geometry will always improve the uniformity of the resulting light distribution. This was reported earlier by Allerdice *et al* (1993), from clinical experience, and in conference proceedings by Beyer *et al* (1990) and Dwyer *et al* (1995). However, although the latter authors developed ideas similar to those reported in this work, they neither mentioned the use of the radiosity method for theoretical and interactive predictions of the resulting light dose distribution, nor did they give a theoretical explanation of the mechanism involved to achieve a uniform irradiation condition.

In this study the mould was assumed to be non-absorbing. However, the power which is absorbed by the mould can be a substantial percentage of the input power. For instance, when the material is 96% reflecting and 2% absorbing, 50% of the input power will be lost by absorption. Using low irradiation levels as in PDT, this will not lead to a disturbing temperature rise of the material of the mould and hence of the tissue to be treated.

In conclusion, we have shown that the use of integrating moulds is promising for achieving uniform irradiation conditions of irregularly shaped cavities. For optimal performance it is recommended that the direct irradiance should be as uniform as possible, for example by applying multiple sources, and that the integrating mould is made of a material with a high reflection coefficient and low absorbance.

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