Erratum: “A comprehensive mathematical model of microscopic dose deposition in photodynamic therapy” [Med. Phys. 34, 282–293 (2007)]

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Recently, we published an improved mathematical model of photodynamic therapy (PDT) dose deposition on length scales corresponding to intercapillary distances.¹ This model describes the spatial and temporal dynamics of oxygen (³O₂) consumption and transport and microscopic singlet oxygen (¹O₂) dose deposition during PDT treatment. It also enables simulation of volume-averaged quantities like hemoglobin oxygen saturation (SO₂) and photosensitizer fluorescence photobleaching, which are accessible experimentally.

In a subsequent modeling study of the kinetics of the recovery of SO₂ following the interruption of PDT irradiation, we were troubled by what appeared to be physically unreasonable simulation results. The origin of these erroneous results was a sign error in one of the terms buried deep in the original code, which had the effect of creating a tumor microenvironment that was more hypoxic than we had specified as an initial condition. We emphasize that in our previously published article on this model, there were no errors in what was described, but the plots presented in that article were quantitatively affected by this sign error. Specifically, this error was in the numerator of Eq. (2) of Wang *et al.*,¹ which was correct in the text; the error was only in the code. In this erratum, we show the revised figures generated by using the same photophysical and physiological parameters described previously.¹ We also use this occasion to describe a few relatively minor improvements to the model.

The oxygen transport equation in the capillary is revised slightly from the original and is now written

$$(1 + S) \frac{\partial C_{\text{cap}}}{\partial t} = D_{\text{cap}} \left[\frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial C_{\text{cap}}}{\partial r} \right) \right] + D_{\text{cap}} \frac{\partial^2 C_{\text{cap}}}{\partial z^2} - V(1 + S) \frac{\partial C_{\text{cap}}}{\partial z}, 0 \leq r \leq R_c, \quad (1)$$

where

$$S = C_{\text{sat}} n C_{50}^n \frac{C_{\text{cap}}^{n-1}}{(C_{50}^n + C_{\text{cap}}^n)^2}. \quad (2)$$

Here, we include a new term, $(1 + S)$, on the left-hand side of the transport equation for the capillary [Eq. (1)], which more

correctly provides for the dynamic unloading of ³O₂ from hemoglobin.² Further, the revised code uses Michaelis–Menten kinetics to describe the rate of metabolic ³O₂ consumption not only in the calculation of the time-dependent state, as was done previously, but also in the calculation of the steady-state with axial diffusion. The equation for the tissue region remains as previously described

$$\frac{\partial C_{\text{tiss}}}{\partial t} = D_{\text{tiss}} \left[\frac{1}{r} \frac{\partial}{\partial r} \left(r \frac{\partial C_{\text{tiss}}}{\partial r} \right) \right] + D_{\text{tiss}} \frac{\partial^2 C_{\text{tiss}}}{\partial z^2} - \Gamma, \quad R_c \leq r \leq b. \quad (3)$$

The definitions and the values of the parameters were previously described.

FIG. 1. Calculated axial and radial distributions of the ³O₂ concentration $[^3\text{O}_2](r, z)$ for (a) 0 J cm⁻² and mTHPC-PDT conducted at irradiances of (b) 10 mW cm⁻² for a fluence of 50 J cm⁻², (c) 100 mW cm⁻² for a fluence of 3 J cm⁻², and (d) 100 mW cm⁻² for a fluence of 50 J cm⁻², assuming a non-uniform initial sensitizer distribution. The anoxic regions shown in Figs. 3(b)–3(d) of Wang *et al.* (Ref. 1), which do not appear in these corrected results, were due to the sign error in the code.

FIG. 2. (a) Computed $\langle \text{SO}_2 \rangle$ within the capillary vs irradiation time (s), (b) computed normalized $\langle [S_0] \rangle$ vs fluence (J cm^{-2}), and (c) computed $\langle [^1\text{O}_2] \rangle$ vs fluence (J cm^{-2}) for two fluence rates, 10 and 100 mW cm^{-2} , assuming an initially nonuniform sensitizer distribution. The initial decrease in $\langle \text{SO}_2 \rangle$ in (a) is not as significant as shown in Fig. 4(b) of Wang *et al.* (Ref. 1). Compared to Figs. 5(a) and 7(a) of our previous paper (Ref. 1), the rates of photobleaching and dose deposition for the 10 and 100 mW cm^{-2} cases in (b) and (c) are more rapid. For a given fluence, the differences in bleaching and dose deposition between these two fluence rates are now smaller.

Using the corrected code and implementing the above modifications to the model, we repeated the simulations for the case of a $130 \mu\text{m}$ intercapillary spacing. Figure 1 shows the revised computed spatial distributions of $^3\text{O}_2$ concentration, $[^3\text{O}_2](r, z)$, for (a) 0 J cm^{-2} and mTHPC-PDT conducted at irradiances of (b) 10 mW cm^{-2} for a fluence of 50 J cm^{-2} , (c) 100 mW cm^{-2} for a fluence of 3 J cm^{-2} , and (d) for a fluence of 50 J cm^{-2} , assuming a nonuniform initial

FIG. 3. Computed spatial distributions of $^1\text{O}_2$ dose, $[^1\text{O}_2](r, z)$, deposited during mTHPC-PDT at irradiances of 10 and 100 mW cm^{-2} for a fluence of 50 J cm^{-2} , assuming initially uniform [(a1) and (a2)] and nonuniform [(b1), and (b2)] sensitizer distributions. Compared to Fig. 8 of Wang *et al.* (Ref. 1), the axial gradient in $[^1\text{O}_2]$ is now significantly less severe.

sensitizer distribution 3 h after i.v. injection. The anoxic regions shown in Figs. 3(b)–3(d) of our original article,¹ which do not appear in these corrected results, were a result of the sign error in the code.

Revised numerical calculations of volume-averaged hemoglobin $^3\text{O}_2$ saturation, $\langle \text{SO}_2 \rangle$, within the capillary versus irradiation time, the normalized, volume-averaged ground state sensitizer concentration, $\langle [S_0] \rangle$, versus fluence, and the volume-averaged $^1\text{O}_2$ dose, $\langle [^1\text{O}_2] \rangle$, versus fluence for two fluence rates, 10 and 100 mW cm^{-2} , assuming nonuniform initial sensitizer distribution are shown in Figs. 2(a), 2(b), and 2(c), respectively. The initial decrease in $\langle \text{SO}_2 \rangle$ in Fig. 2(a) is not as significant as shown in Fig. 4(b) of Wang *et al.*¹ Compared to Figs. 5(a) and 7(a) of our previous article, the rates of photobleaching and dose deposition for the 10 and 100 mW cm^{-2} cases in Figs. 2(b) and 2(c) are more rapid, and for a given fluence, the differences in the extent of sensitizer degradation and dose deposition between these two fluence rate cases are smaller. The differences between these and our previous results originate from greater oxygen availability in the tumor region after correcting the sign error.

Figure 3 shows the computed spatial distributions of $^1\text{O}_2$ dose, $[^1\text{O}_2](r, z)$, deposited during mTHPC-PDT at irradiances of 10 and 100 mW cm^{-2} for a fluence of 50 J cm^{-2} , assuming initially uniform [(a1) and (a2)] and nonuniform [(b1), and (b2)] sensitizer distributions. Compared to our previously published Fig. 8,¹ the axial gradients in $[^1\text{O}_2]$ are now less severe.

The corrected MATLAB code is available, and interested readers should contact the authors for the updated version.

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²T. D. Lagerlund (personal communication).