A NUMERICAL MODEL FOR SIMULATING TISSUE OXYGEN PRESSURE AND DYNAMICS OF [18F]-FMISO

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Background and Objectives

- [18F]FMISO PET imaging enables visualization of hypoxia *in vivo*.
- We aim to:
  - Derive equations and simulation on a real vessel map
  - Gain ability to predict oxygen pressure and FMISO distribution in tissue with attention to blood flow in vessels
- We utilized the diffusion-convention equation to predict the FMISO behavior [1]
- We investigated the impact of actual boundary conditions in FMISO distribution
- Oxygen pressure and FMISO distribution were computed for several minutes post-injection
- This method may be utilized to predict FMISO operation in different distances of vessel

Methods

Blood flow in vessel: Flow in capillary modeling is similar to fluid flow in a channel by circular cross-section with the point that the capillary diameter is changing and permeability of its wall should be considered. The viscosity can be considered more real by using equations in [2]. The blood pressure distribution is shown in figure 1; this is used for calculation of oxygen pressure as a boundary condition.

Oxygen pressure distribution: The equation of oxygen pressure in tissue is governed by the convection – diffusion equation; therefore, the general equation can be written as:

$$\frac{\partial P_{O_2}}{\partial t} = D_{O_2}\nabla^2 P_{O_2} - \frac{M_0 P_{O_2}}{P_{O_2} + P_0} \qquad (1)$$

The first item shows the diffusing mechanism of oxygen and the second one is about consumption rate which is computed by michaslis-menten equation.M_0 is the maximum amount of oxygen consumption and at pressure of P_0 the consumption rate reaches to the half of its maximum.

FMISO concentration distribution: Diffusion-convection reaction equations for drug delivery into tumour cells were used in [3, 4, 5, 6] models that are applicable to gain FMISO concentration equation. In this work, although the dominant mechanism along with extravascular is diffusion, convection is negligible. FMISO concentration equation divides into free and bound states.

$$\frac{\partial C_f}{\partial t} = D_T\nabla^2 C_f - k(p)C_f \qquad (2)$$

$$\frac{\partial C_b}{\partial t} = K(P)C_f \qquad (3)$$

$$F_1(P) = \frac{K_{\max}P_1}{P_{O_2} + P_1} \qquad (4)$$

$$F_2(P) = \left(\frac{P_{O_2}}{P_{O_2} + P_2}\right)^K \qquad (5)$$

$F_1(P)$ is a function connecting the binding of Fmiso to oxygen pressure [7]. It is computed by utilization of maximum binding rate and at pressure of P_1 which $F_1(P)$ reaches to the half of its maximum. It should be mentioning that central area of tumour has the minimum value of oxygen and contain dead cells so, should be considered in equations. Also $F_2(P)$ is a function defines 1 and 0 for vital and dead cells in pressure respectively. By this, FMISO binds just to vital cells. Furthermore, K(P) is computed by multiplication of these two functions.

Results

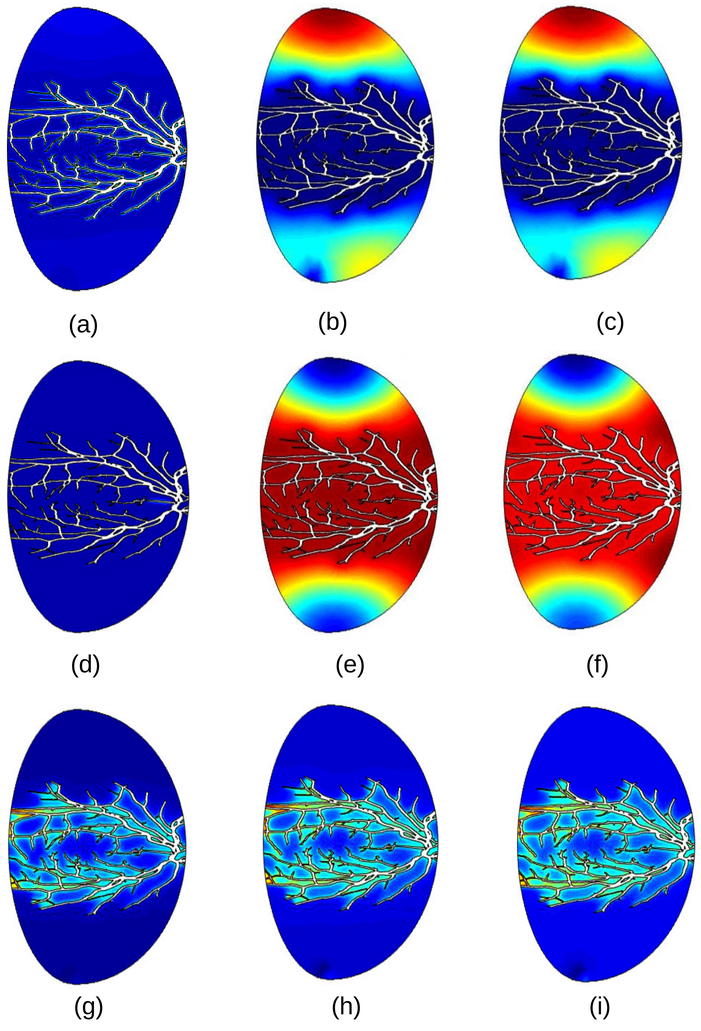

Figure 1: Simulated oxygen pressure for *t* = 120 min (a), 240 min (b), 300 min (c) and free FMISO concentration for *t* = 120 min (d), 240 min (e), 300 min (f), and bound FMISO concentration for *t* = 120 min (g), 240 min (h), 300 min (i).

The oxygen pressure is non-dimensionalized. The results are shown in figure 1 for 120, 240 and 300 minutes after injection. The oxygen pressure has high value around the inlet part of vessel, but this is just for the early time after injection then it decreases. On the other hand, FMISO distribution in the bound state have great value in far distance but by passing time as is show in figure 2 it increases to achieve a peak and then decreases. This indicates dependency to oxygen pressure. The time activity curve was calculated by averaging the FMISO concentration in every parts of domain and is shown in figure 2.

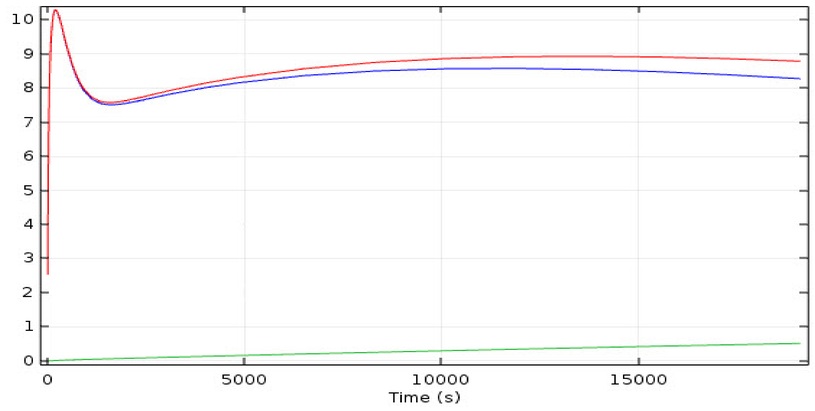

Figure 2: simulated TACs for bound, free and total FMISO concentration; green, blue and red, respectively.

Conclusions

FMISO has low speed of translating and diffusion, therefore, the time of imaging should be long. Distinctive equations was propounded for both free and bound states; subsequently, results can be analyzed separately and this provides a benefit. Every main process for simulation of FMISO uptake and repartition is regarded. The results in figure 1 indicates that the tracer accumulated in the areas which contain the minimum value of oxygen, so, there is a strong level of hypoxia. It is worth mentioning that by changing some minor material parameters, the following model can be used for various other tracers and drugs as well.

References

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