A study of reoxygenation of cancer cells after application of radiation using a diffusion model

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BACKGROUND

Reoxygenation is one of the four R's of Radiobiology. The presence or lack of oxygen within a tumor can have a marked impact on the effect of radiation on the tumor.

After the passage of radiation, the majority of cells that remain will be in a hypoxic state as those that were aerated have a higher probability of cell kill. In addition to killing tumor cells, the passage of radiation could also damage the vasculature within the tumor used to transport oxygen to the remaining cells.

The diffusion of the partial oxygen pressure (pO2) within a tumor region can be modeled with a two dimensional diffusion equation:

$$\frac{\partial p}{\partial t} = D\left[\frac{\partial^2 p}{\partial x^2} + \frac{\partial^2 p}{\partial y^2}\right] + F(t) - \dot{q}$$

Where p is the partial oxygen pressure in mmHg, D is the diffusion coefficient of oxygen, *F(t)* is the incoming oxygen pressure from surrounding blood vessels, and $\dot{q}$ is the rate of oxygen consumption of the tumor cell.

OBJECTIVES

- Simulate the diffusion of oxygen within a simulated tumor region using periodic boundary conditions both before and after the application of radiation.
- Model reoxygenation of the tumor region when incident radiation destroys a region of cells and possibly destroys a supplying blood vessel.

MATERIALS & METHODS

- A 400x400 micron tumor region was simulated assuming tumor cells that were 20x20 microns.
- Blood vessels running perpendicular to the tumor region at the corners were used to supply oxygen.
- Each tumor cell consumed oxygen at a constant rate if alive, or zero oxygen if dead.
- The following combinations were simulated:
  - Input pressure of 100 mmHg or 40 mmHg.
  - Application of 0.65, 1.8, 3.6, or 6.7 Gy radiation
  - Whether one corner vessel in the radiation region was destroyed or not.
- An alternating direction implicit Crank-Nicolson method in MATLAB™ was used to solve the equation.

RESULTS

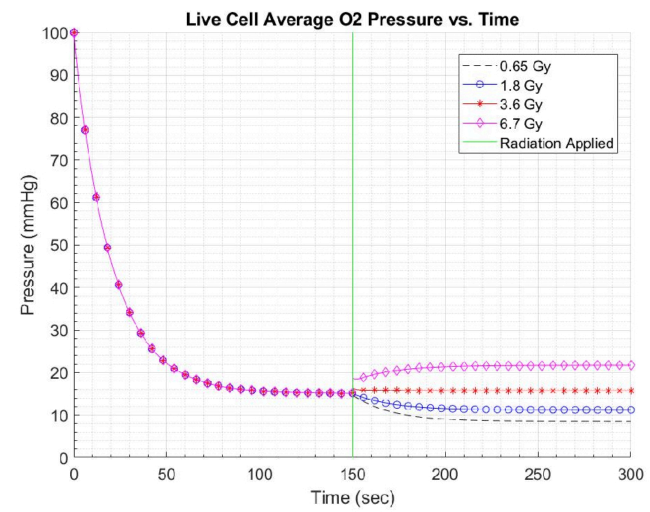

Figure 1: Average partial oxygen pressure (pO2) within live cells before and after varying doses of radiation. Input pressure from blood vessels is 100 mmHg (arterial pressure); one blood vessel is destroyed during radiation. Average pO2 in live cells drops for radiation doses 0.65 and 1.8 Gy and remains the same or rises for doses of 3.6 and 6.7 Gy, respectively.

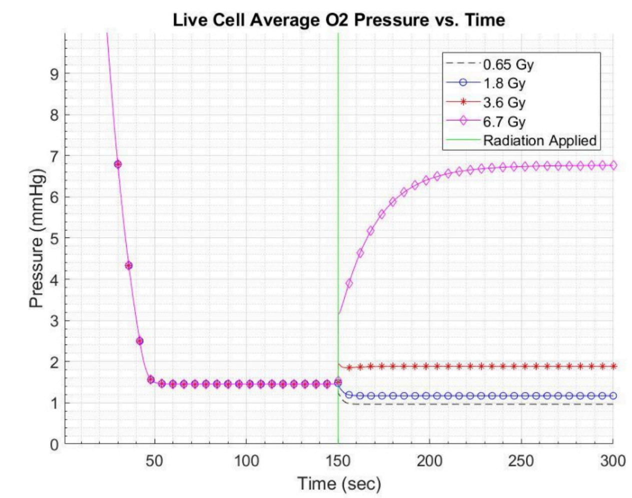

Figure 2: Average partial oxygen pressure (pO2) within live cells before and after varying doses of radiation. Input pressure from blood vessels is 40 mmHg (venous pressure); one blood vessel is destroyed during radiation. Average pO2 in live cells drops for radiation doses 0.65 and 1.8 Gy and rises for a dose of 3.6 and rises dramatically for a dose of 6.7 Gy.

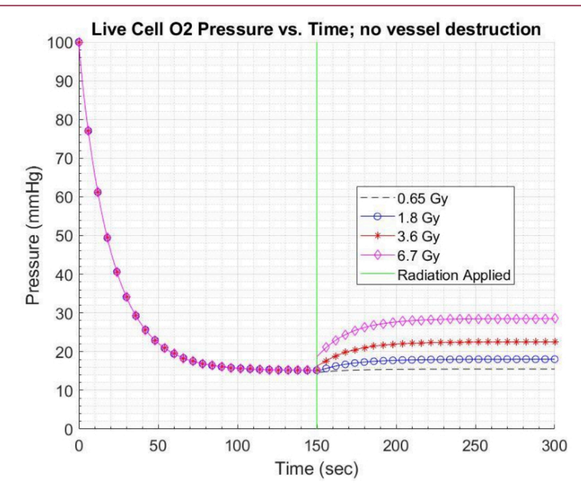

Figure 3: Average partial oxygen pressure (pO2) within live cells before and after varying doses of radiation. Input pressure from blood vessels is 100 mmHg (arterial pressure); no blood vessels are destroyed during radiation. Average pO2 in live cells remains the same or rises for all doses tested.

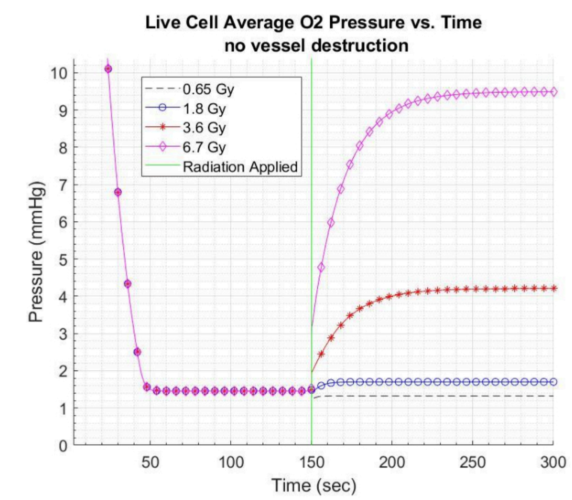

Figure 4: Average partial oxygen pressure (pO2) within live cells before and after varying doses of radiation. Input pressure from blood vessels is 40 mmHg (venous pressure); no blood vessels are destroyed during radiation. Average pO2 in live cells drops slightly for 0.65 Gy, and remains nearly constant or rises dramatically for all other applied doses.

CONCLUSIONS

- Oxygen diffuses rapidly within the tumor region, reaching an equilibrium average pressure on a time scale of minutes both before and after radiation application.
- Average pO2 within live cells drops after a low dose treatment when a blood vessel is destroyed, but rises for higher dose treatments.
- When no blood vessels are destroyed, average pO2 remains nearly the same or rises dramatically.
- Tumor cells only fall below the hypoxic threshold of 2.5 mmHg pO2 while under venous pressure for low dose treatments (0.65 and 1.8 Gy) and for medium sized treatments (3.6 Gy) when vessel destruction occurs.

REFERENCES

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