Oxygenation in tumour cells

November 8, 2019

Because tumours expand in an uncontrolled manner, they tend to outgrow their blood supply, but as the oxygen level in the cells drop, the cells will signal for more, which stimulates the formation of blood vessels in a chaotic way, using material from nearby vessels (angiogenesis).

This results in inadequate vascularisation with highly permeable vessels, causing the natural fluid transport to malfunction. In addition, the lymphatic drain is not expanded in proportion, causing the intratumoural pressure to increase, making it more difficult for oxygen and pharmaceutics to enter the tissue.

Further, the oxygen consumption of a cell is dependent on the supply, often modeled by michaelis-menten kinetics. When the oxygen level decreases, the cells reduce their proliferation rate. If the oxygen supply disappears completely, the cell eventually dies, but with only very low oxygen supply the cells may become quiescent, making them virtually unresponsive to radiation.

The effect of irradiation in the cells depend on the oxygenation both because of the proliferation rate of the cells (since the are more sensitive during division because the DNA molecule is split) and because the presence of oxygen helps fixating radiation induced damages, inhibiting cell repair processes by binding (as free radicals) to the site of the damage. In total, the biological effect of the radiation may differ three times due to oxygen differences.

Schematically one can say that radiation kills oxygenated cells, normally near the tumour surface. By fracionating the irradiation, the tumour shrinks, causing the "new" surface to oxygenate and in the end, hopefully the entire tumour.

The goal of radiation therapy is to kill the entire tumour and nothing else. In order to do this, enough radiation must be used, but not more. Because the oxygenation status usually is unknown, the radiation dose may not be very accurately determined. Being able to estimate the oxygen level in the tumour we could deliver a carefully determined radiation dose to each part of the tumour.

The tumour may be considered a volume, containing extracellular fluid. In this fluid, there are cells (the distance between these may vary depending on tumour type size etc.). The tumours are consuming oxygen in proportion to supply. The oxygen comes from vessels at the tumour surface, where the concentration be be

considered constant. The tumour itself is poorly vascularised, the oxygen level in these vessels is rather low and the flow is slow. There is a trade-off between the amount of oxygen bound to hemoglobin and freely available in the blood (governed by the law of mass action). The free oxygen is able to diffuse into the extracellular fluid and then enter the cells.

How may the steady-state oxygen distribution throughout the tumour be estimated depending on tumour size, oxygen level in the vessels, oxygen demand by the cells, intratumoural pressure, tumour vascular fraction and cell density?