Editor's Pick

In Silico Model of the Early Effects of Radiation Therapy on Microcirculation and the Surrounding Tissues

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Phys. Med. 2020 May;73:125-134. doi: 10.1016/j.ejmp.2020.04.006. Epub 2020 Apr 29

What was your motivation for initiating this study?

Several trials have found that the risk of late normal tissue toxicity increases after radiotherapy for patients with medical conditions or specific habits that adversely affect the stability of the vascular system (hypertension, diabetes, smoking, alcohol abuse, obesity, use of cholesterol-lowering drugs, and use of drugs for cardiac morbidity). Radiation damage to arterioles, capillaries, and venules, i.e. to the smallest and most sensitive structures of the cardiovascular system, were widely investigated in animal studies during the 1970s. Dose delivery techniques have evolved since that time and now, in the golden era of conformal radiotherapy and, indirectly, of dose escalation and hypo-fractionation, we need a robust radiobiological knowledge of functional changes in the capillary bed to avoid, depending on the irradiated region, chemical imbalances, lack of nutrients or organ impairment.

A half-century after the animal studies, we have adequate computational power to describe the capillary network by in silico simulation. To this purpose, we have presented a computational model that describes the fluid dynamics of microcirculation when the parameters of the network and the surrounding tissues are affected by radio-induced changes.

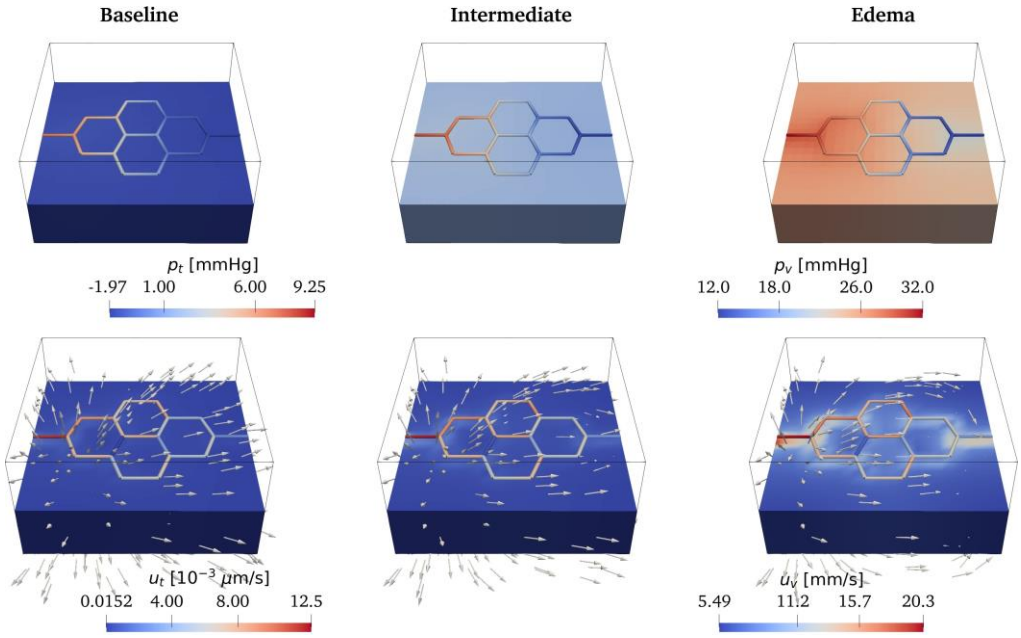

Figure 1: *Fluid dynamics variables: pressures pt[mmHg] and pv [mmHg] (top) and velocities ut[μm/s] and uv [mm/s] (bottom) for the baseline (left), intermediate (centre) and edema (right) states.*

What were the main challenges during the work?

We extended the model that had been derived in Possenti et al (https://doi.org/10.1002/cnm.3165), which described the blood flow in a microvascular network and the interstitial flow in the surrounding volume, to take into account the deformation of the vessels due to the pressure load. The main challenges of the study were to define the predominant acute effects of ionising irradiation on microcirculation, to identify the parameters affected by this perturbation and, especially, to include such variations in the simulation code to obtain a reasonable output from a qualitative point of view.

What is the most important finding of your study?

We proposed the first development of a computational mechanistic model that could be used to describe the effects of impairment of the endothelial membrane on the wall elasticity. Different scenarios were considered, starting from a healthy normal situation and then shifting to a flawed scenario, possibly describing a patient with comorbidities or a patient who had already experienced several fractions of radiotherapy.

What are the implications of this research?

The plan in this five-year project, which is funded by the Italian Foundation for Cancer Research, the AIRC Foundation (IG 21479,

P.I. Dr Tiziana Rancati), is to integrate the simulations through in vitro analysis. Indeed, to quantify the alterations that radiotherapy causes to the parameters, we aim to obtain a set of measurements from capillary networks grown in a microfluidic chip and irradiated with photons at different doses and different field geometries. Through combination of these two steps, we aim to develop a consistent computational model to describe the acute effect of ionising radiation on microcirculation and its evolution in patients during the treatment itself. The model will be validated or tuned on a cohort of 100 patients who are undergoing radiotherapy.

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Reference:
Possenti et al, International Journal for Numerical Methods in Biomedical Engineering 35(8), October 2018.
https://doi.org/10.1002/cnm.3165