Combining Computer Simulations and Imaging in Cancer Research

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Background

In the early 1970s Dr. Judah Folkman proposed treating tumours by targeting their supplying blood vessels and starving them of nutrients. This was followed by decades of research leading to the approval of the first 'anti-angiogenic' therapy, Bevacizumab, in 2004 [1].

Painful lessons on the complexity of the interactions between growing tumours and their supplying blood vessels have since been learned. In some cases anti-angiogenic therapies made outcomes worse, by making starving tumours more aggressive. In other cases they had synergistic interactions with conventional radio- and chemo-therapy, for reasons that are still not known [1].

There is still much we do not know regarding if, how and when we should target blood vessels to treat tumours. Answering these questions is of great importance to both the pharmaceutical industry and clinical research.

Our goal is to combine state-of-the-art computer simulations and high resolution, 3D imaging to answer pressing questions on the interactions between growing tumours and their supplying blood vessels.

We present three examples of our research here.

Mechanisms of Anti-Angiogenic Drug Action

The corneal micropocket assay is used to screen candidate anti-angiogenic drugs. It allows visual inspection of the effects the drugs have on blood vessel formation. We have developed an anatomically representative computer simulation of the drug effects [6].

Micro-Rheology in Tumour Blood Vessels

Oxygen in blood vessels is carried by red blood cells. When predicting oxygen delivery it is important to know the amount of red cells in each vessel. When blood vessels have diameters on the order of individual red cells, we can’t use conventional fluid dynamics equations to predict flows, but rely instead on empirical rules. These rules are based on experiments in healthy animals and glass tubes [8]. We are investigating whether they still hold in structurally abberant tumour blood vessels.

Tumour Blood Vessels And Radiotherapy Response

Radiotherapy effectiveness depends on oxygen availability in the tumour, which in turns depend on the supplying blood vessel network. We studied how the 3D structure of tumour vessel networks affects radiotherapy response.

We predicted that previous mathematical models were over-estimating the sensitivity of radiotherapy response to spatial heterogeneity in vessel spacing [2]. We are now studying biological networks post-administration of anti-angiogenics.

Experiment

Images provided by Roche Pharmaceuticals [7]. 300 ng Vascular Endothelial Growth Factor (VEGF) in mouse.

Simulations

Agent based model of vessel growth with VEGF transport on an anatomical geometry.

The simulation facilitates experiment design based on parameter sensitivity and uncertainty quantification studies, reducing reliance on animal testing. In the long term we envisage its use in virtual high throughput drug screening.

Find Out More...

We have developed a significant amount of high performance simulation software in these studies. We have released it for free and without restriction for use by academia and industry. Further details, including interactive demos and tutorials, are available here [6]: https://jmgrogan.github.io/MicrveselChaste/. Email: grogan@maths.ox.ac.uk.

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