Microvasculature-on-Chip: A New Tool for \textit{in vitro} Radiobiological Studies

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The therapeutic index of cancer radiotherapy remains limited by acute and chronic side effects with often severe consequences to patients. Among healthy tissues/organs exposed to ionizing radiation during treatment, the microvasculature is a central player involved in both tumour response and healthy tissue/organ radiological side-effects. However, current \textit{in vitro} vascular models based on 2D culture of endothelial cells offer only limited radiobiological insight due to their failure in recapitulating the complex 3D environment experienced by these cells within the human microvasculature. To address this issue, we demonstrate the feasibility of using a bioengineered ‘microvasculature-on-a-chip’ microfluidic model dedicated to radiobiological studies \cite{1}.

\textbf{Methods.} Human umbilical vein endothelial cells (HUVECs) were cultured in microfluidic devices to form perfusable microvascular networks, and the biological responses to x-ray ionizing radiation, including vasculature damages (e.g. cellular apoptosis and DNA double strand break and repair), inflammation effects (e.g. expressions of pro-inflammatory biomarkers) and extravasation of monocytes were systematically assessed.

\textbf{Results.} HUVECs were significantly more radioresistant in regard to structural damages (cell-cell interactions) and apoptosis when cultured in the 3D environment of the microvasculature-on-chip compared to cells cultured within 2D monolayers. In addition, faster repair of DNA damages occurred for cells in the microvasculature-on-chip than those in 2D. Post-irradiation expression of pro-inflammatory cytokines (e.g. IL-6 and IL-8) was found to peak at 24 hours and was strongly dose-dependent in the microvasculature-on-chip model. Finally, the perfusable nature of the model enabled to test the effects of radiation and inflammation of the extravasation of both tumour cells and PBMCs from the microvasculature.

\textbf{Conclusions.} It is anticipated that such vasculogenesis models will yield more accurate prediction of the response of healthy tissue to ionizing radiation than standard 2D culture models and, consequently, that they will guide the development of better radiotherapy protocols with lesser radiation-induced acute and long-term side-effects.

\textbf{References}