

# Endothelial cell death after ionising radiation does not affect tumour vasculature functionality in murine tumour models

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## BACKGROUND

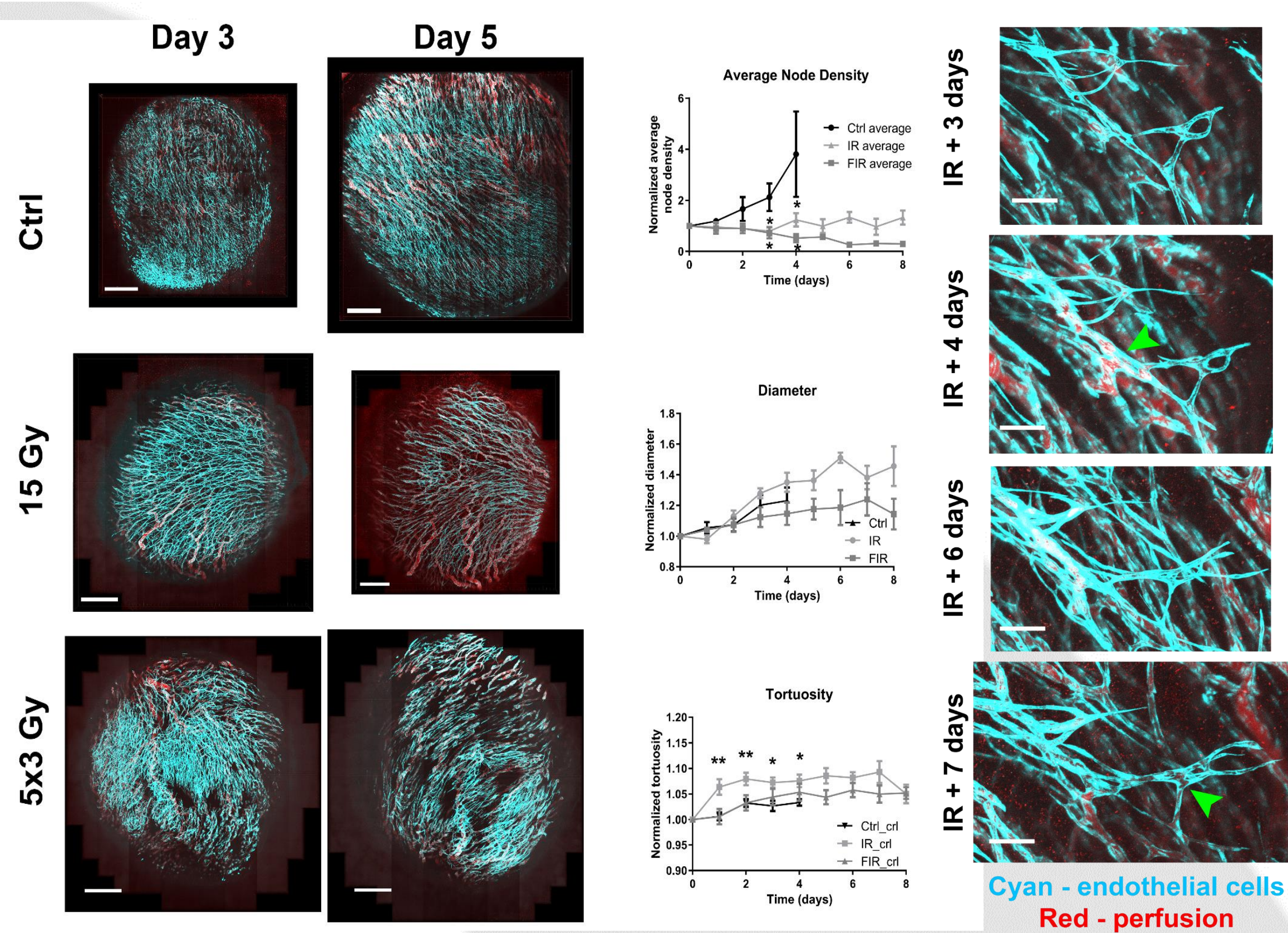
The aberrant tumour vasculature is a crucial part of the tumour microenvironment, contributing to tumour growth and response to treatment e.g. radiotherapy. Radiotherapy affects not only cancer cells, but also the tumour microenvironment, including endothelial cells, the building blocks of the tumour vasculature. However, the response to radiotherapy including the tumour vasculature is incompletely understood.

## AIM

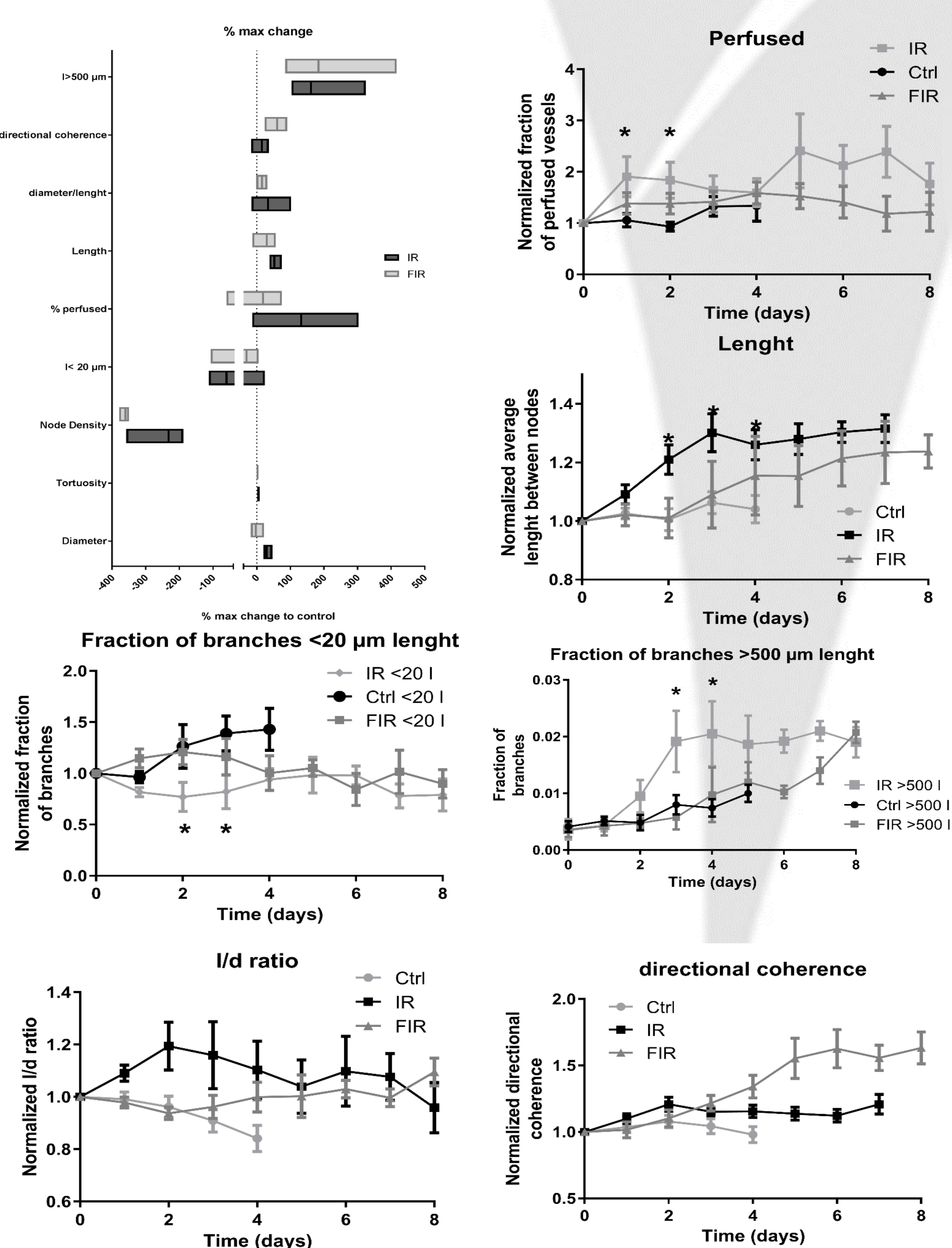
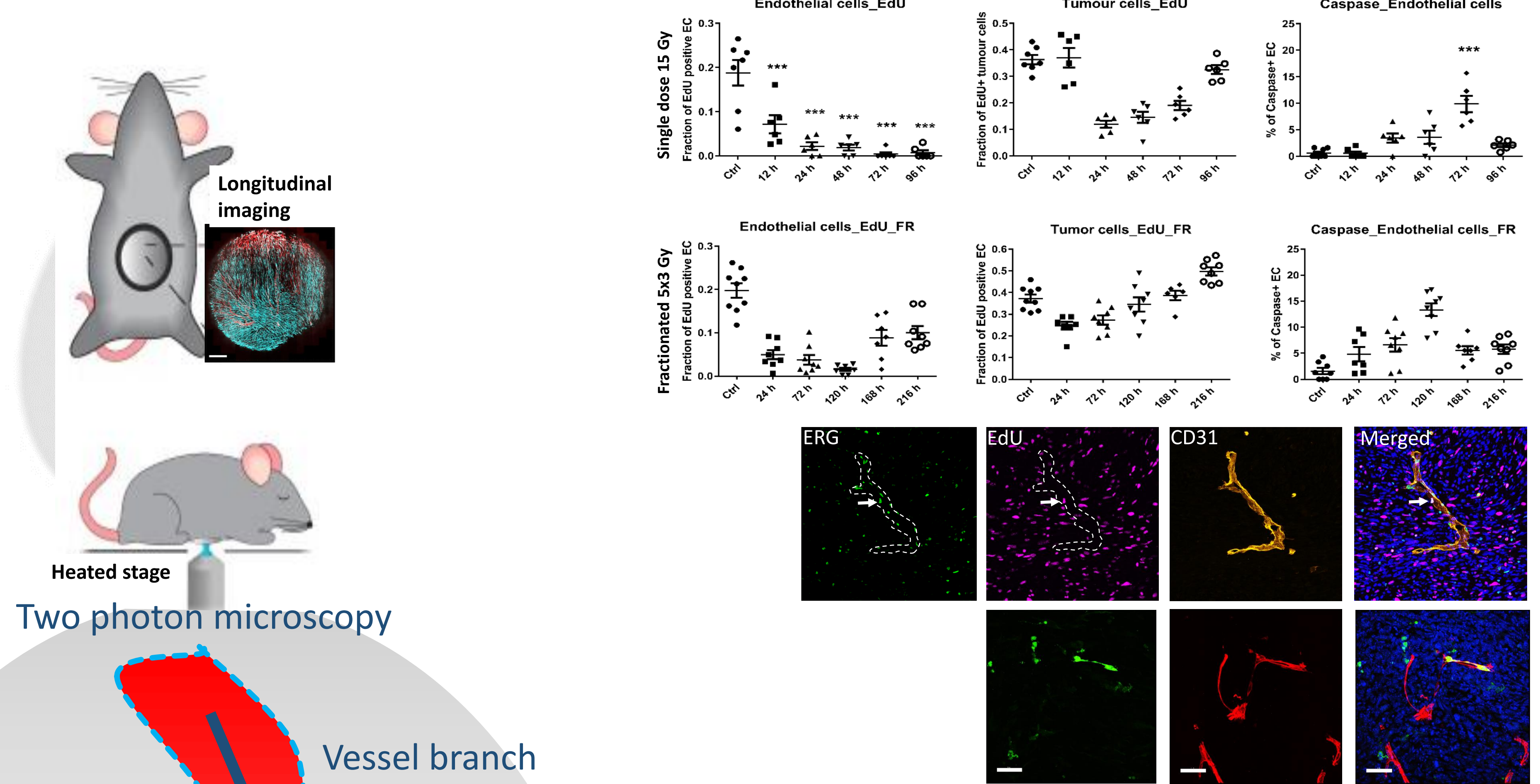
Our aim was to investigate the biological underpinnings of tumour blood vessel response to single and fractionated radiotherapy and its impact on vessel structure and function.

## CONCLUSIONS AND FUTURE PLANS

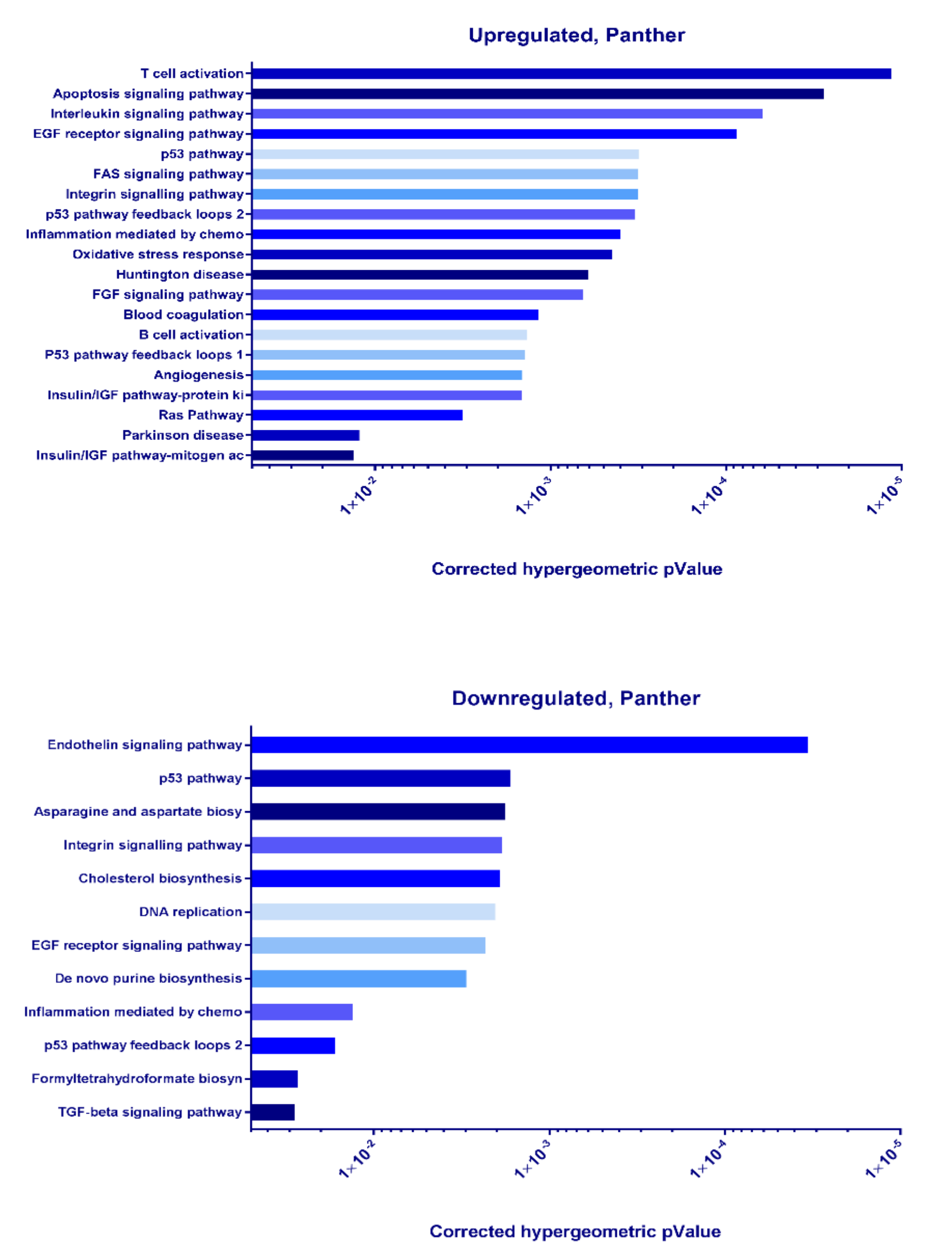
- The developed transgenic mouse model in combination with intravital microscopy and in-house image analysis increases our understanding of the tumour vasculature and its response to radiotherapy.
- Future work will focus on the underlying mechanism explaining the observed changes in vessel morphology.



**Fig 1.** Whole tumour vasculature images in (A) and an (C) establishment of a new perfused vessel in an irradiated tumour (single dose 15 Gy) followed in time. Green arrows indicate newly perfused part of the forming vessel. Irradiation of the tumours drastically decreases vascular node density (B) and decreases tortuosity. Scale bar: 1 mm (A) and 200  $\mu$ m (C).



**Fig 3.** In A) FACS and IF of proliferating and apoptotic endothelial cells after irradiation (single dose 15 Gy and fractionated irradiation of 5x3 Gy). White arrows, proliferating endothelial cells. Markers for endothelial cells CD31 and ERG, marker for proliferation EdU, Apoptosis in endothelial cells after irradiation (15 Gy and fractionated irradiation 5x3 Gy) Scale bar 30  $\mu$ m.



**Fig 4.** RNAseq data from tumour endothelial cells (FACS sorting of 100 tumour endothelial cells). Upregulation and downregulation of the most prominent pathways 48 hours after 15 Gy single dose irradiation. Left: Downregulation of angiogenesis markers 48 hours after 15 Gy single dose.

**Fig 2.** Different parameters obtained from two photon in vivo microscopy images. Images were segmented and analysed with a machine learning algorithm. IR – Irradiation single dose 15 Gy, FIR – Fractionated irradiation 5x3 Gy.

