



Radiation treatment monitoring using multifunctional imaging in prostate tumour xenografts

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AIM

→ To assess the effect of radiation treatment on the tumour vasculature and its downstream effects on hypoxia and choline metabolism

→ To determine the relationship between metabolic and microvascular parameters that reflects tumour microenvironment

→ PET/CT & DCE-US

non-invasive functional imaging techniques



PET/CT

→ Cancer and normal tissues differentiation according to differences in the phenotype

→ Dedicated tracer (locally produced)

→ ¹⁸F-Fluorine-Fluoromisonidazole (¹⁸F-FMISO)

→ ¹⁸F-Fluorocholine (¹⁸F-FCH)

→ Semi-quantitative parameter - Standard Uptake Value (SUV)

$$SUV = \frac{C_{PET}(T)}{ID / BW}$$

$C_{PET}(T)$ the measured activity in tissue and ID injected dose

DCE-US

→ Bolus-tracking techniques - evolution of the signal intensity in time after modifying the tissue using a contrast agent

→ 50 µl Micromarker [Fujifilm Visualsonics, Toronto, Canada]

→ Complemented by pharmacokinetic quantification

→ Brix model [Brix et al. J Comput Assist Tomogr 1991;15:621]

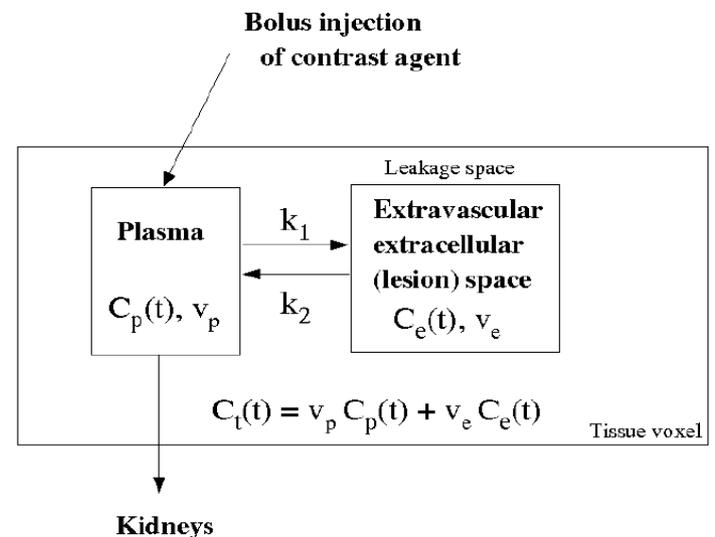
Intra-tumour vascularity at voxel level

k_{el} – Rate of clearance of CA from plasma

k_{ep} – Rate constant between ESS and plasma

A – Amplitude parameter related to the size of the ESS

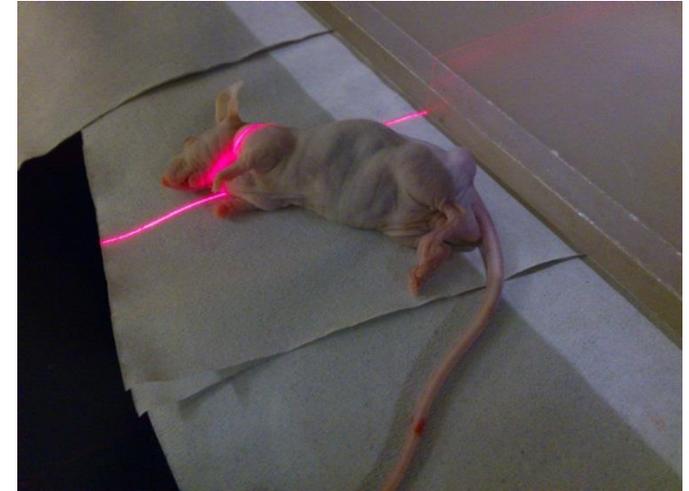
Ak_{ep} – Related to transcapillary transport





Material & Methods

- *In vivo* - Male, sexually mature BALB/c nude mice (30-35 g / 6-8 weeks old)
- Murine tumour model CWR22 – human androgen-dependent prostate cancer
- Tumour generated by subcutaneous implantation of tumour tissue (flank)

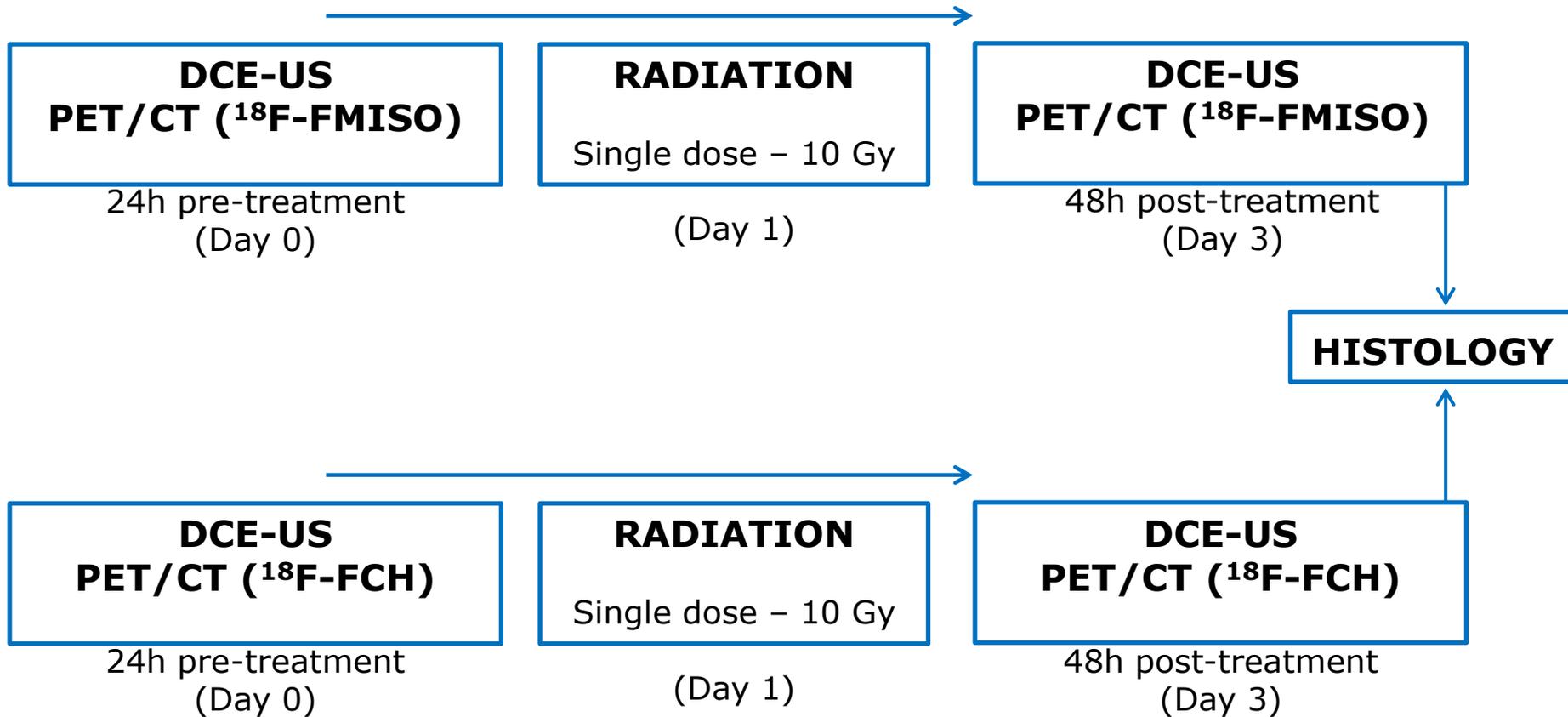


Radiation treatment

- Department of Oncology and Medical Physics at Haukeland University Hospital
- Varian Linac 600C (6 MV x-rays)
- Dose 10 Gy



Material & Methods



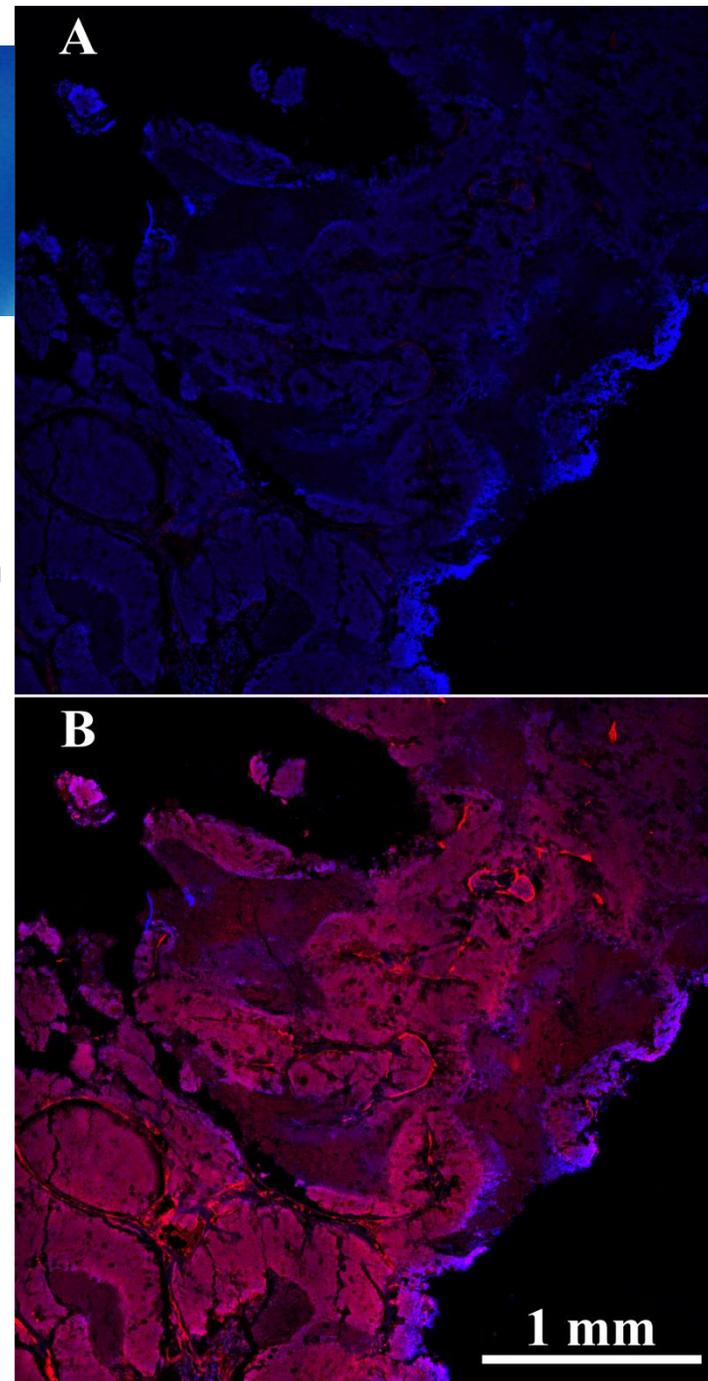
Immunohistochemical analysis

- Microvessel density (MVD)
 - CD-31 (PECAM-1 platelet endothelial cell adhesion molecule) positive structures per 0.5 mm²
- Necrosis
 - Non-stained DAPI (4',6-diamidino-2-phenylindole) regions per sampling area

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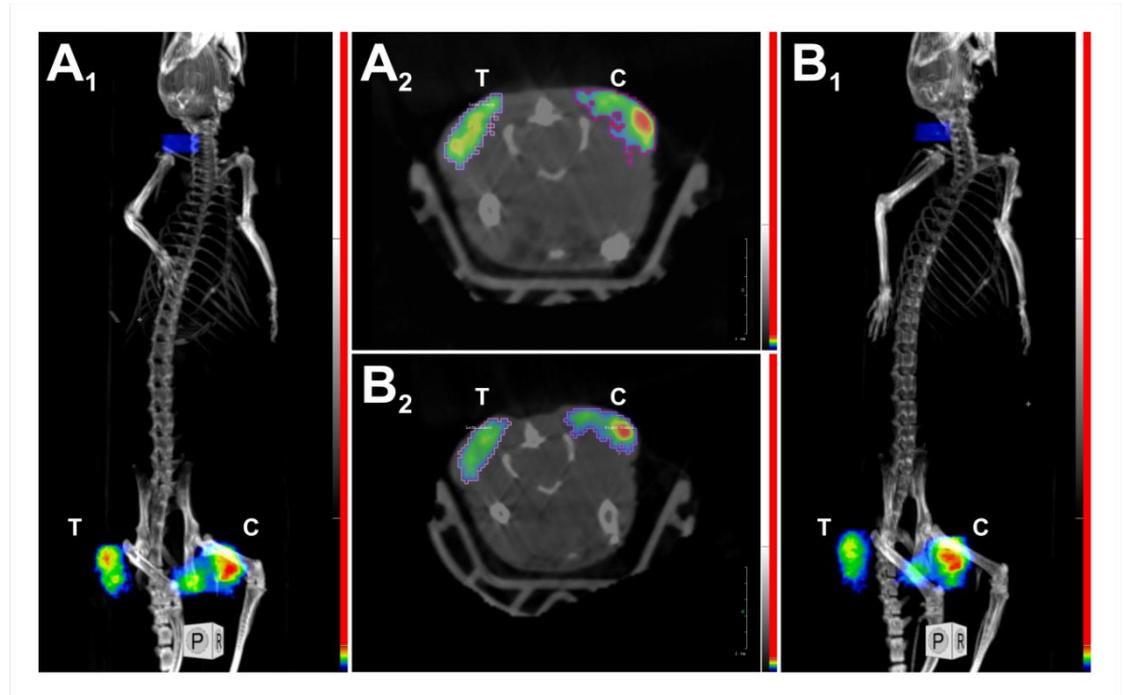
Statistical analysis

- Wilcoxon's matched-pairs test
- Kendall's Tau-b
- Bonferroni correction for multiple testing
- 5 % level of significance



^{18}F -Fluoromisonidazole (^{18}F -FMISO)

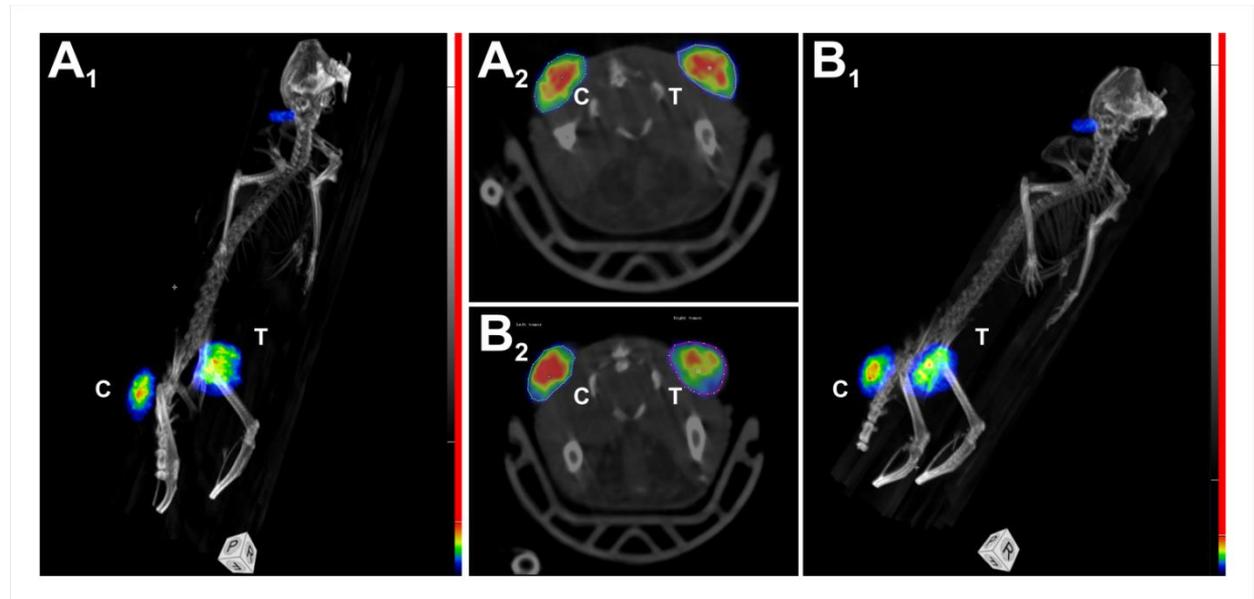
- ^{18}F -FMISO - Hypoxia marker
- 120 min between tracer injection and PET/CT acquisition
- Post-treatment
 - ↓ SUV_{mean} ($p = 0.05$)
 - ↓ SUV_{max} ($p < 0.05$)



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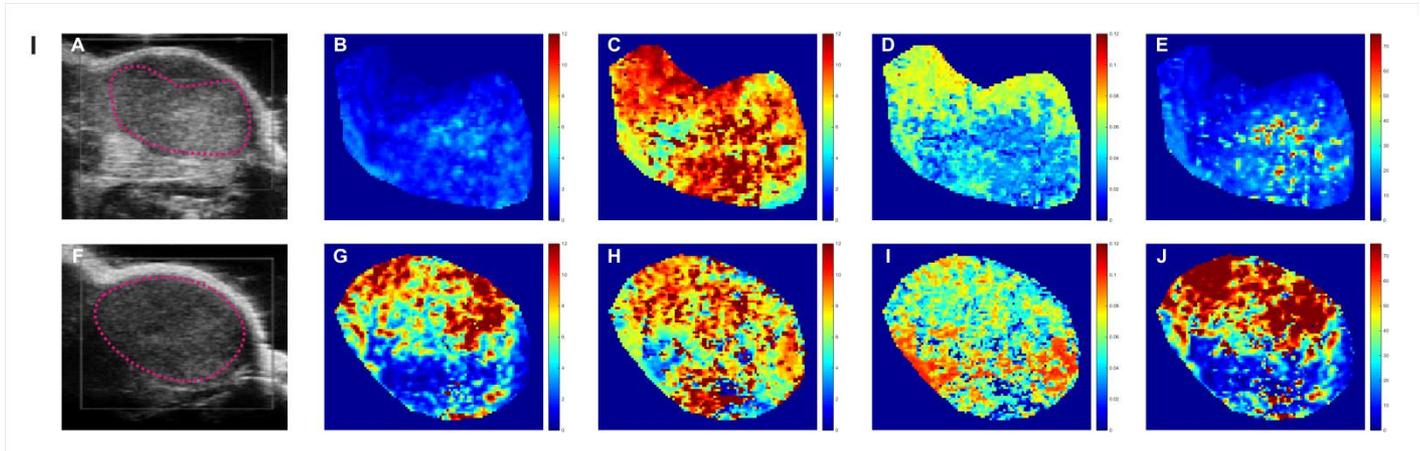
^{18}F -Fluorocholeline (^{18}F -FCH)

- ^{18}F -FCH – Cell division marker
- Elevate choline kinase activity in prostate tumours
- 30 min between tracer injection and PET/CT acquisition
- Post-treatment
No changes observed

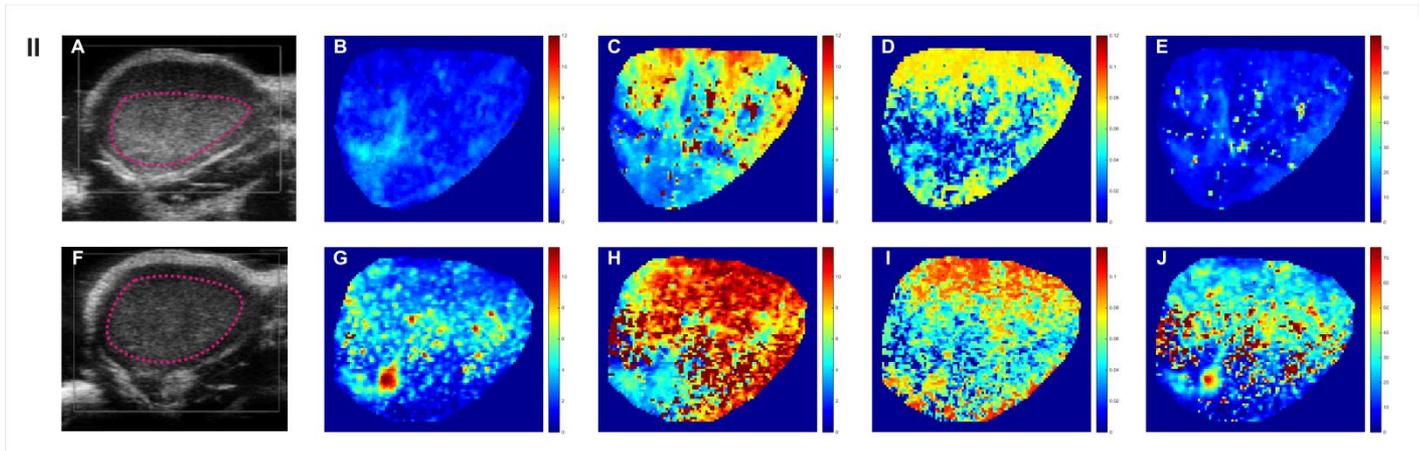


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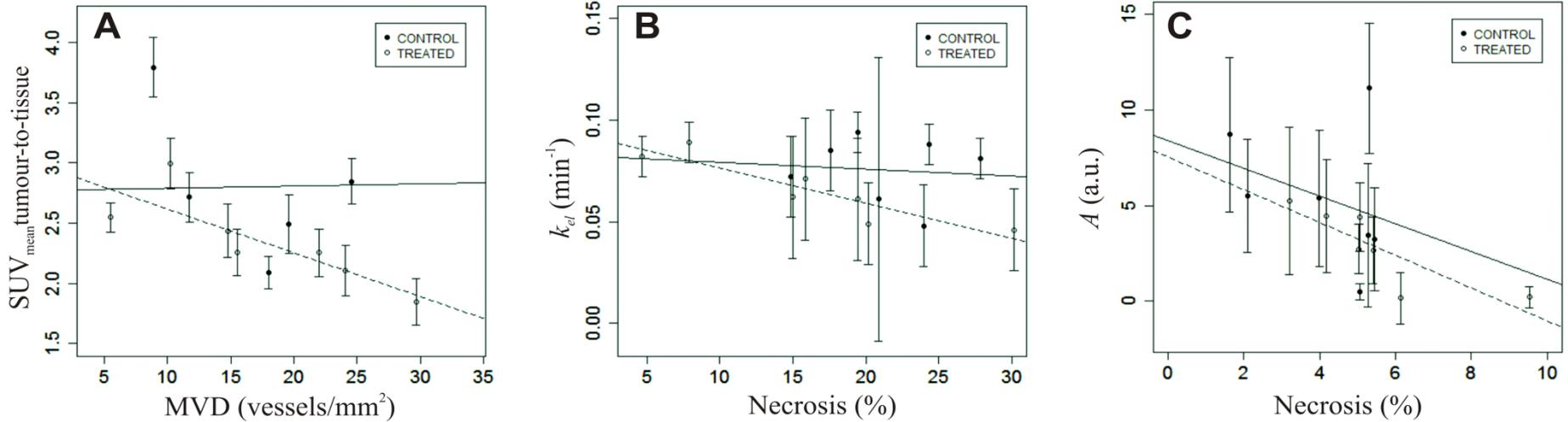
→ ^{18}F -FMISO
 Longitudinal changes detected for k_{el} in the treated mice



→ ^{18}F -FCH
 ↓ A (kurtosis) ($p < 0.05$) for the control group



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→ For ¹⁸F-FMISO

- SUV_{tumour-to-muscle} correlated to MVD for the treated group ($r\tau = -0.9, p < 0.05$)
- k_{el} correlated to MVD for the control group ($r\tau = -0.9, p < 0.05$)
- k_{el} correlated to necrosis for the treated group ($r\tau = -0.8, p < 0.05$)
- A correlated to necrosis for the treated group ($r\tau = -0.8, p < 0.05$)

→ For ¹⁸F-FCH

- No correlation found

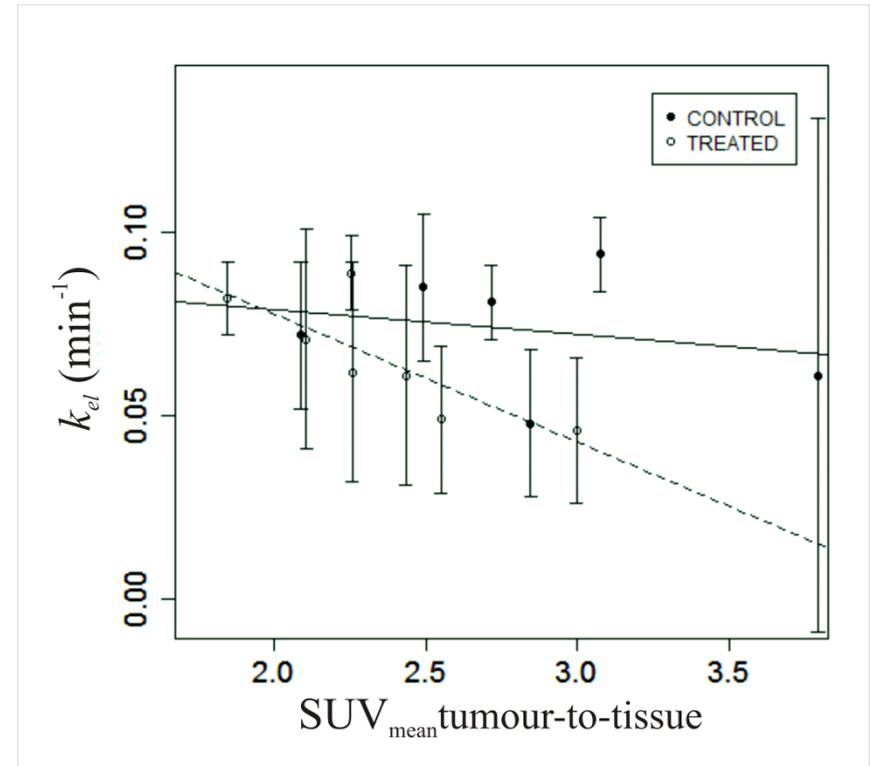
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Results – Correlation between PET/CT & DCE-US

^{18}F -FMISO

→ k_{el} correlated to $\text{SUV}_{\text{tumour-to-muscle}}$ for the treated group ($r_{\tau} = -0.8, p < 0.05$)



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Conclusion

- Longitudinal changes detected for ^{18}F -FMISO PET/CT
 - Lower SUV_{mean} & SUV_{max} indicating decrease in hypoxia in irradiated tumours
 - Significant correlations between techniques and to histology
- The eliminating rate constant of the contrast agent from the plasma k_{el} derived from DCE-US seems reliable in the assessment of both microvasculature and necrosis
- The multimodal approach ^{18}F -FMISO PET/CT and DCE-US has valuable diagnostic potential for early non-invasive evaluation of radiotherapy



THANK YOU!!