Multimodal approach to assess tumour vasculature

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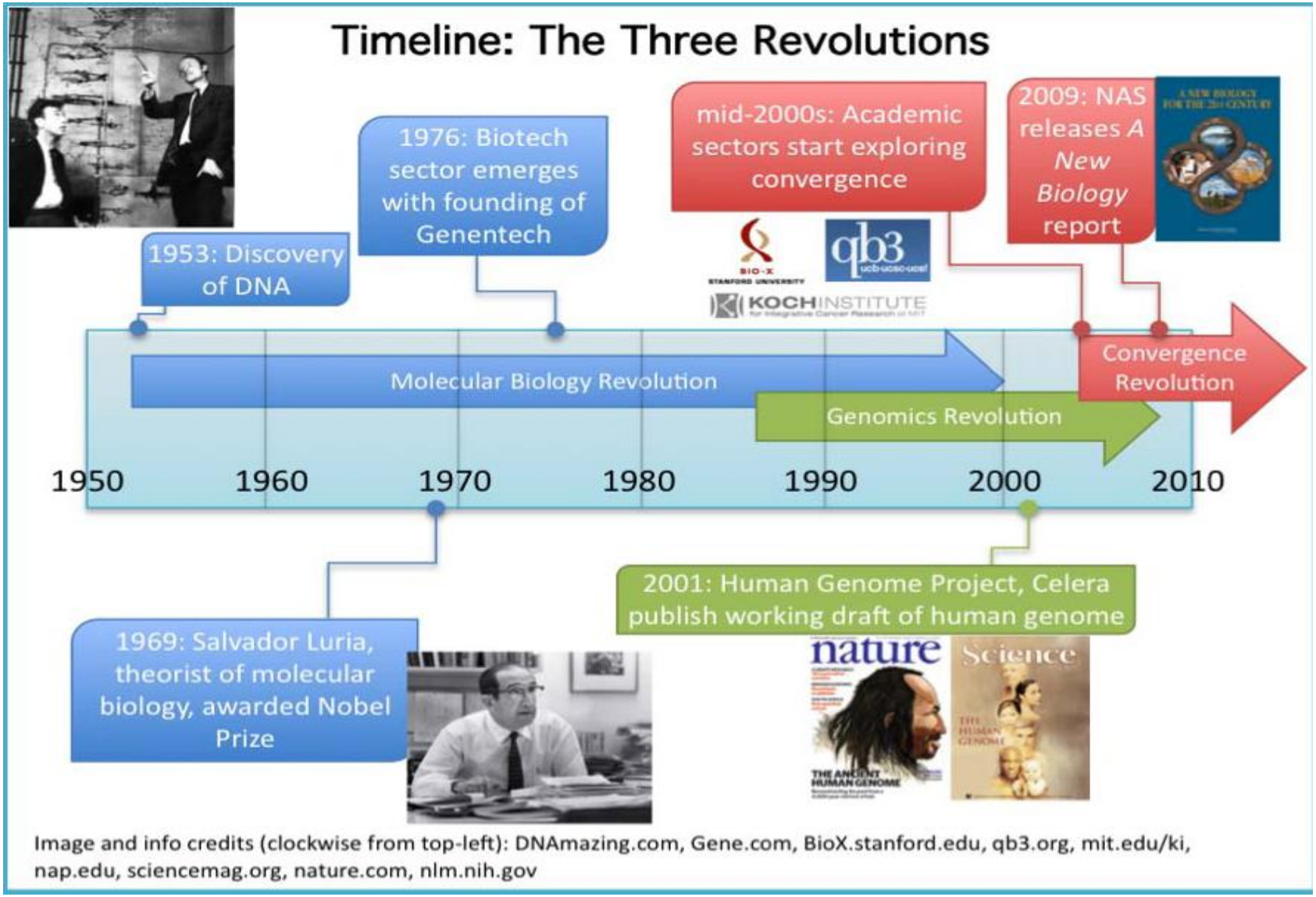
The 3 Revolutions of biomed



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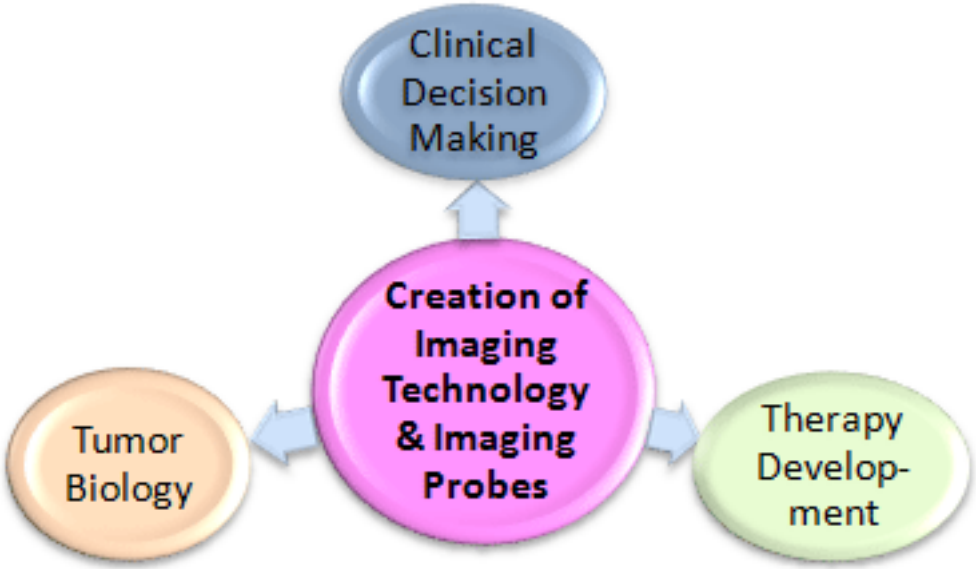
Imaging & the convergence of science

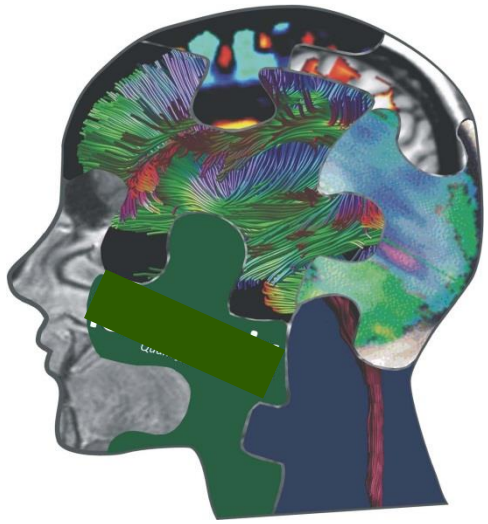


"Imaging allows the interrogation of an intact biologic system across the spectrum from sub-cellular to macroscopic and from discovery to clinical decision making."

-NCI

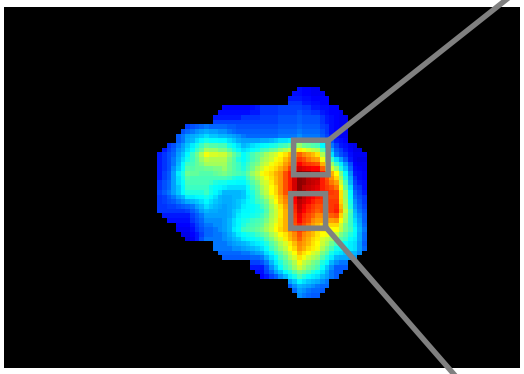
Imaging & the convergence of science

- Anatomical imaging
- Quantitative imaging

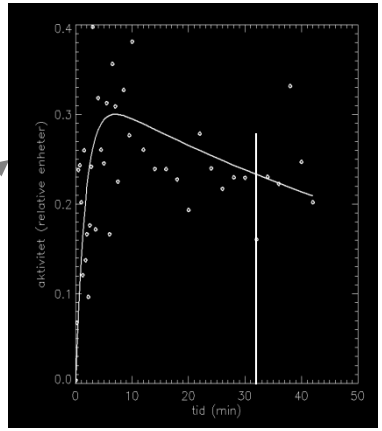


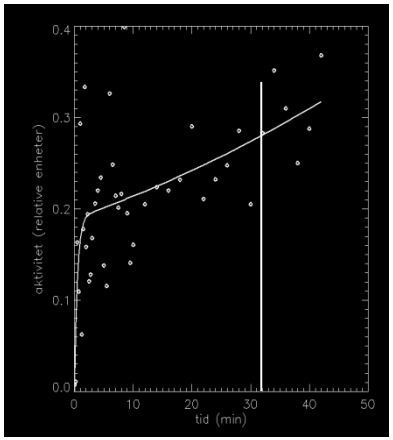
Quantitative imaging

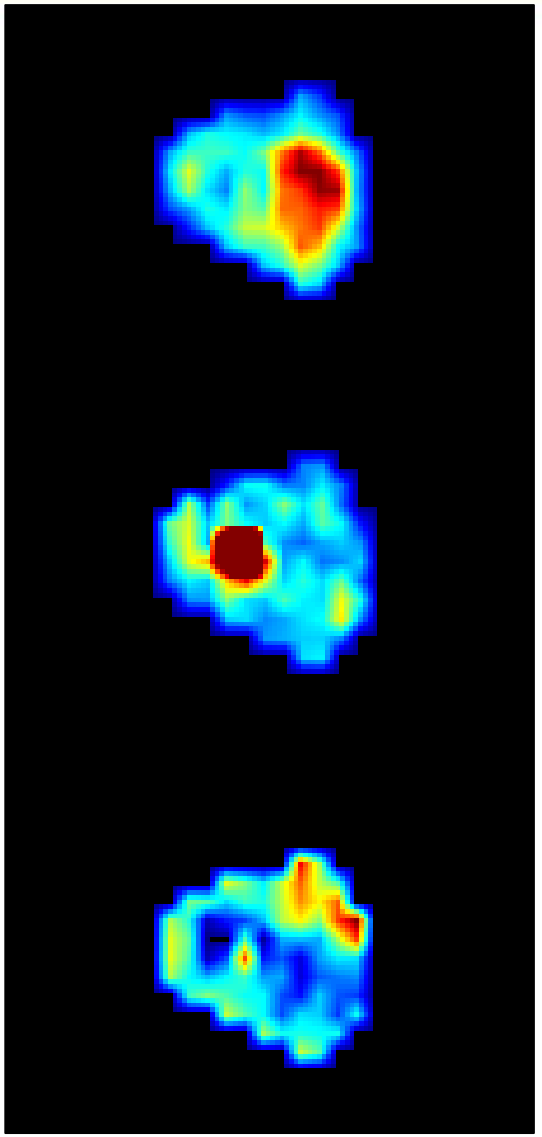
Quantittative PET imaging



32 min post injection of ^{18}F-FDG







A

kep

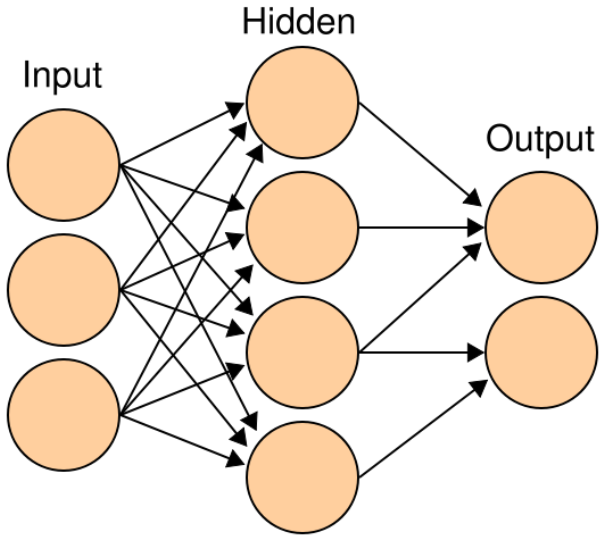
kel

Multi-parametric imaging

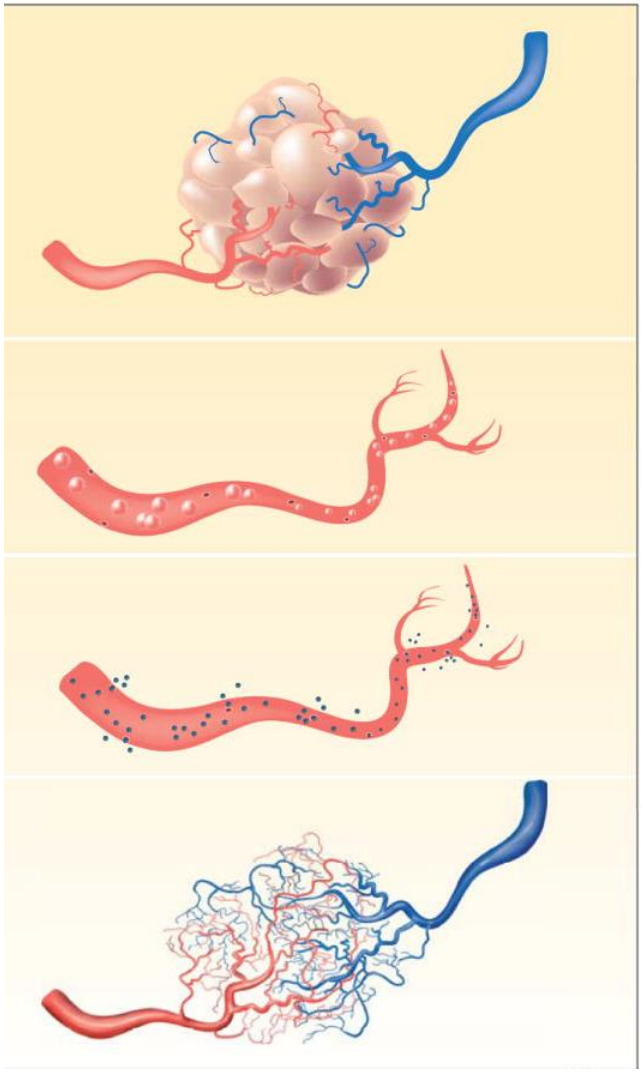
No single parameter will provide robust prediction about out-come/ response to therapy.

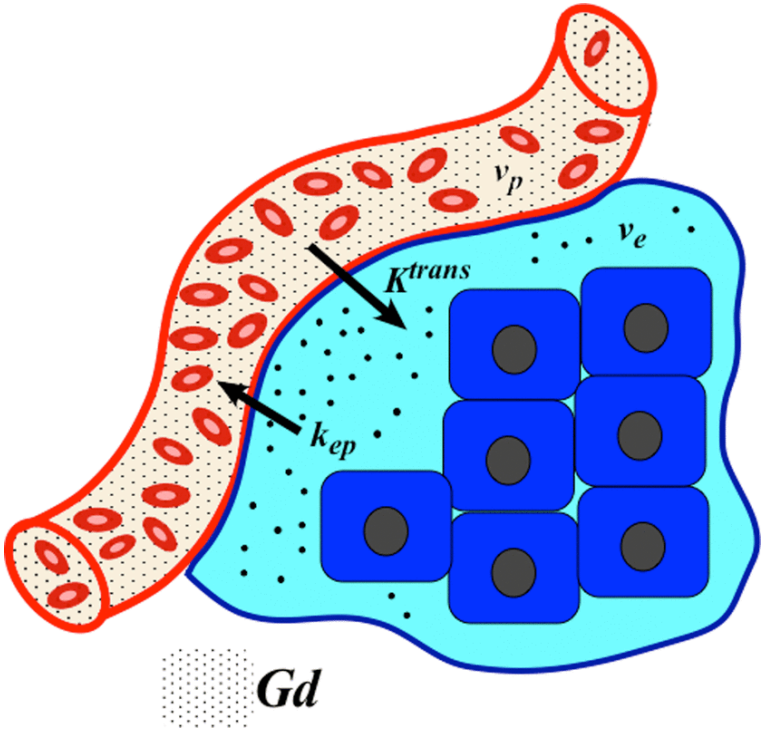
AI and systems biology approach

- Provide no insight into mechanisms
- Heuristic



Dynamic Contrast Enhanced (DCE) imaging



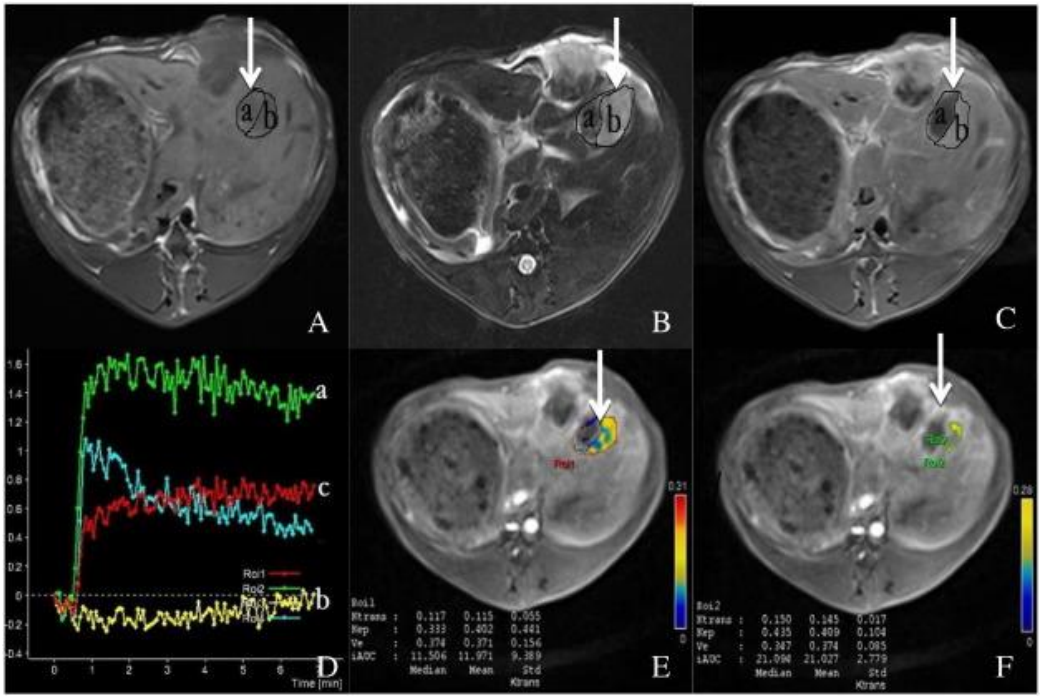


Fundamental parameters of DCR-MRI

Symbol	Parameter	Unit
K^{trans}	Volume transfer constant (or coefficient) between blood plasma and extravascular extracellular space (EES)	min^{-1}
v_e	Volume of EES per unit volume of tissue	None (%)
k_{ep}**	Rate constant between EES and blood plasma (backflux exchange rate)	min^{-1}

k_{ep}** = K^{trans}/v_e; DCE-MRI, dynamic contrast-enhanced magnetic resonance imaging.

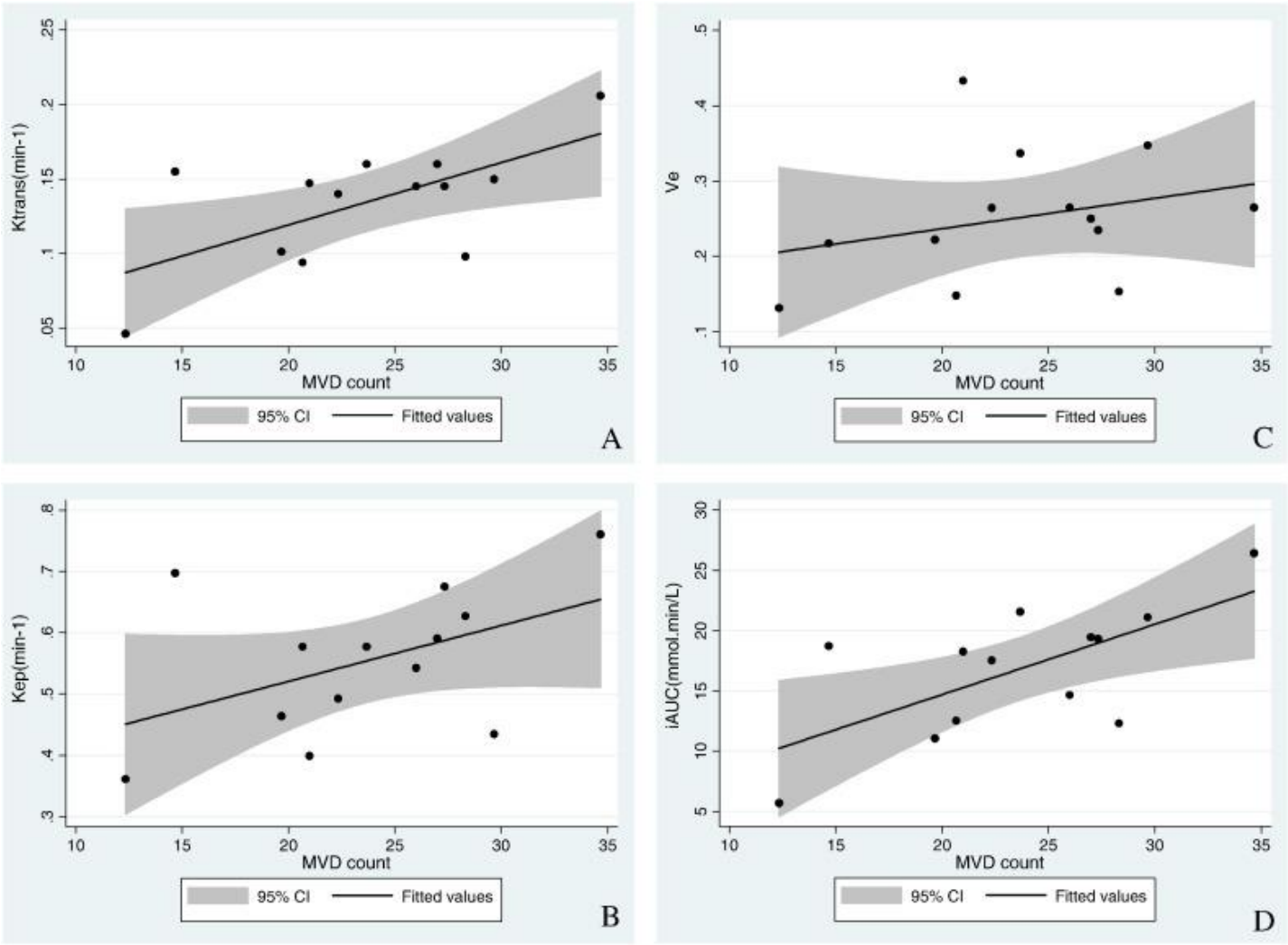
DCE-MRI & microvessel density



A-C: T1WI, T2WI and DCE-MRI of the VX2 liver tumor following therapy.
a – necrotic portion
b – viable tumor portion.

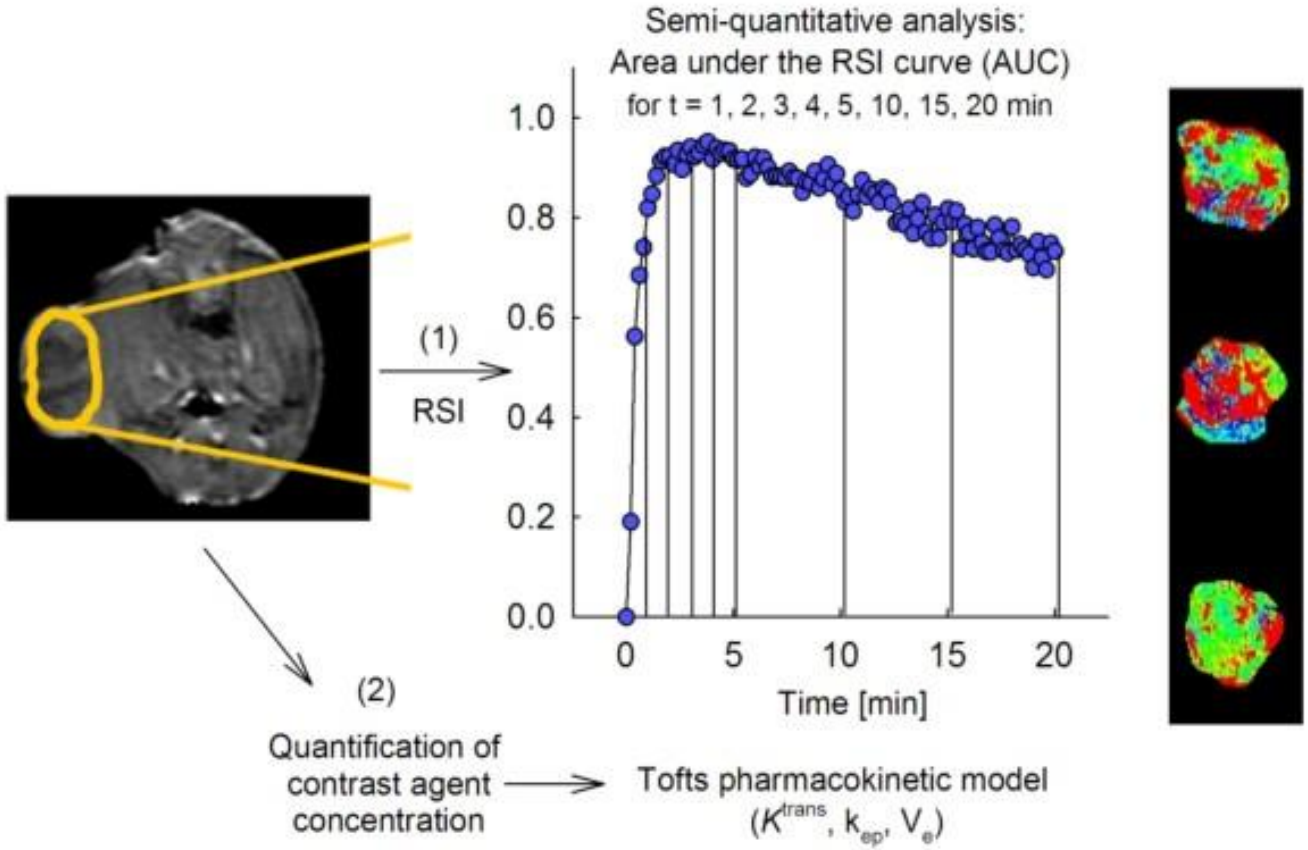
J. Chen et al. Magn. Res. Imaging. 34:2-177-82, 2016

DCE-MRI & microvessel density



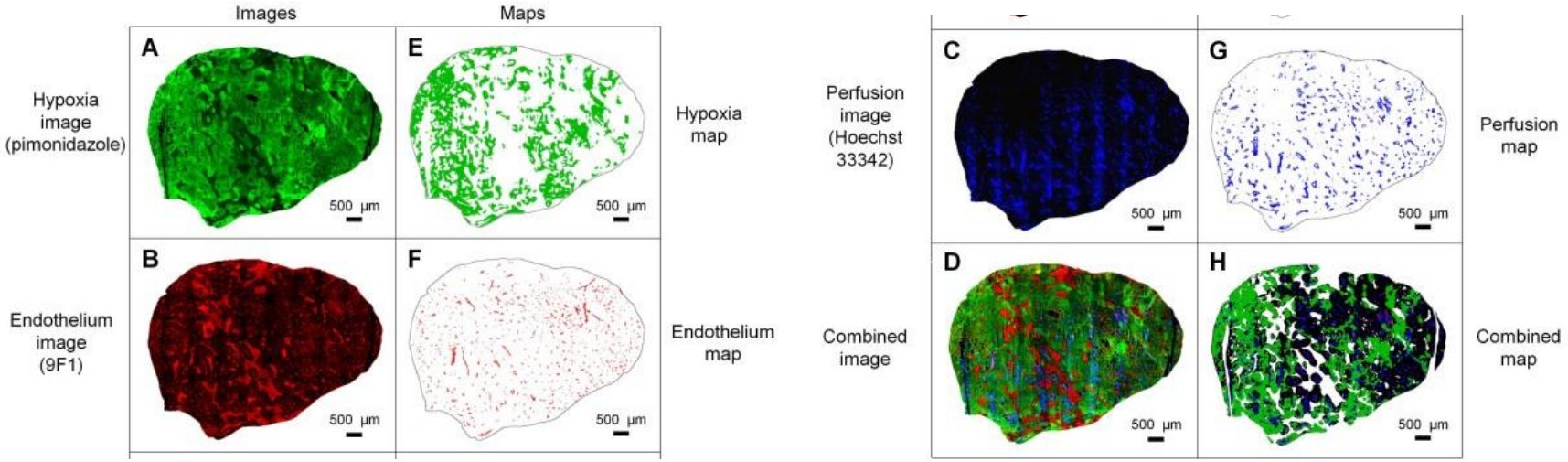
J. Chen et al. Magn. Res. Imaging. 34:2-177-82, 2016

DCE-MRI & tumor vasculature



K. Røe et al. Radiat Oncol.7:75, 2012

DCE-MRI & tumor vasculature



Parameter	VS	VD	VF	PF	DHV	NF	HF	AHS
K^{trans}	⊖	⊕	+	+	⊖	⊖	+	+
k_{ep}	⊖	⊕	⊕	⊕	⊖	⊖	−	⊕
V_e	−	+	+	+	−	−	+	+
Unfit fraction	⊕	⊖	⊖	⊖	⊕	⊕	−	−

K. Røe et al. Radiat Oncol.7:75, 2012

Multi-modality quantitative imagning

- Does a multi-modality approach provide more, independent parameters and better predictions of treatment response/out-come ?

……or…….

- Is the imaging modality of no importance and indifferent with respect to the DCE-derived tumour vasculature characteristics ?

Multi-modality quantitative imagning

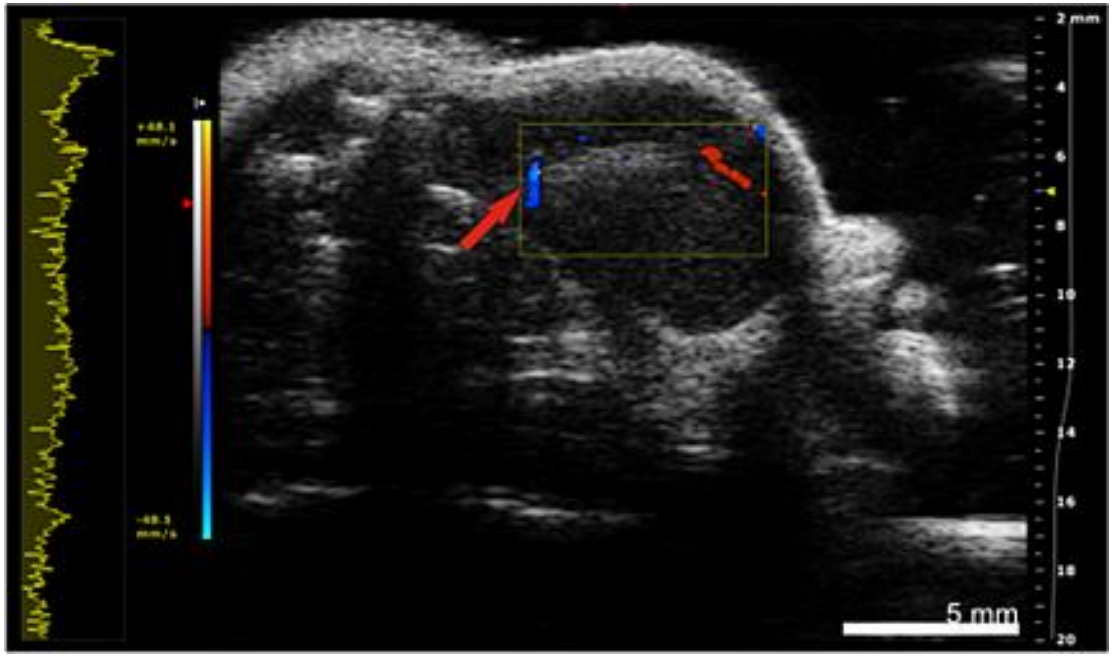
- DCE-US & DCE-MRI
- Prostate tumour xenografts
- Pre-treatment and 24 h post-treatment DCE-imaging
- Treatment: 7.5 Gy single fraction irradiation
- Tumour vasculature assessed by Brix analysis of DCE-images

$$\mathrm{RSI}\,(t) = \frac{\mathrm{SI}\,(t) - \mathrm{SI}(0)}{\mathrm{SI}(0)}$$

$$\mathrm{RSI}\,(t) = \frac{A \cdot k_{ep}}{k_{el} - k_{ep}} \cdot \left(e^{-k_{ep}t} - e^{-k_{el}t}\right).$$

N. Arteaga-Marrero et al. Contrast Media & Mol. Imaging, 10 (6): 428-437, 2015

Power Doppler



Power Doppler imaging of a prostate tumour xenograft visualizes a feeding vessel (left part of the tumour shown in blue and marked with a red arrow)

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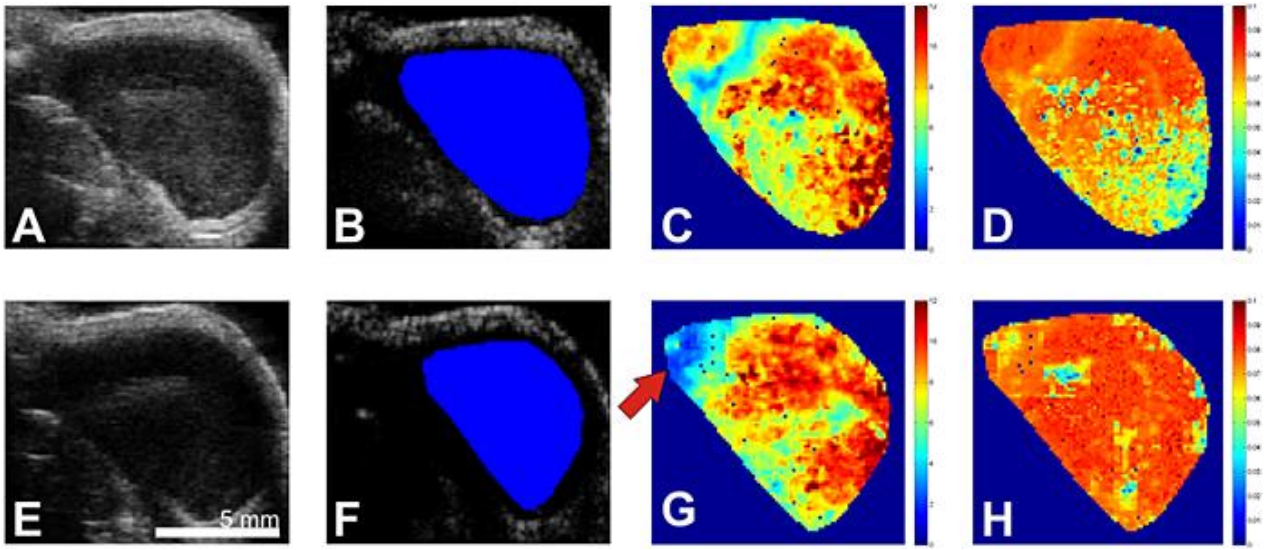
DCE-US analysis

Day 0

Day 2



B-mode images (A, E), tumour delineation (B, F), and the parametric maps associated to the microvascular parameters k_{ep} (C, G) and k_{el} (D, H)

Red arrow shows the blood vessel detected.

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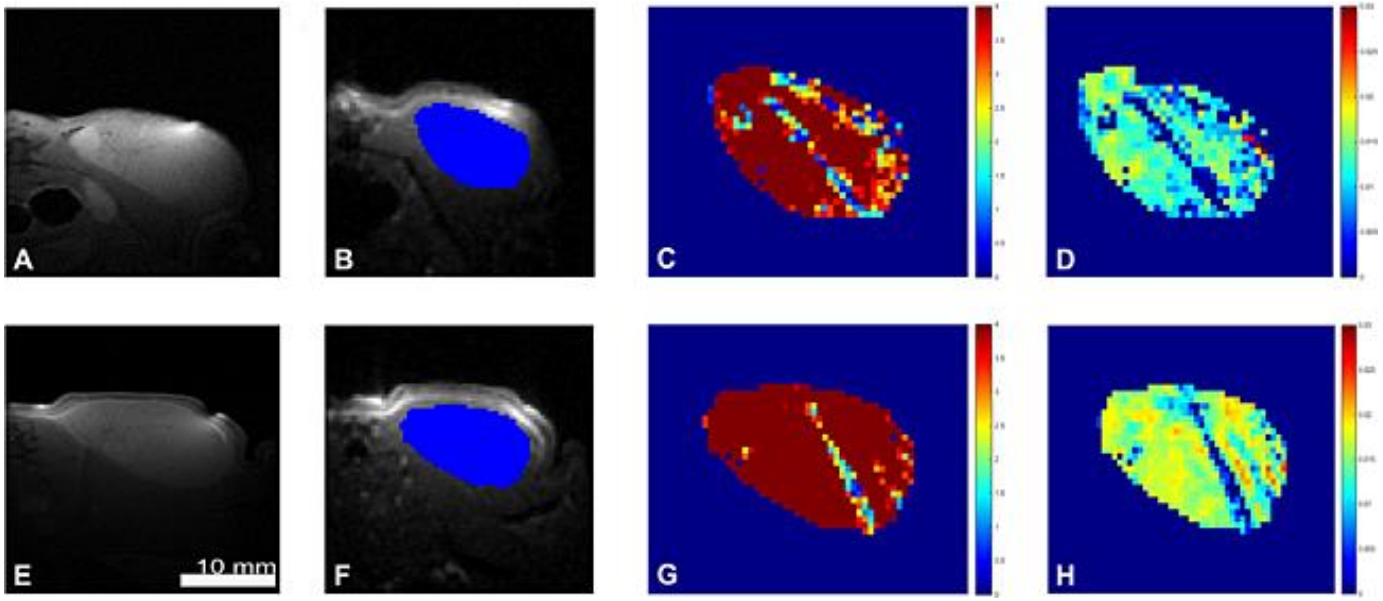
DCE-MRI analysis

Day 0

Day 2



T1-weighted images (A,E), dynamic T1-weighted images with illustration of tumour delineation (B, F), and parametric maps associated to the microvascular parameters k_{ep} (C, G) and k_{el} (D, H).

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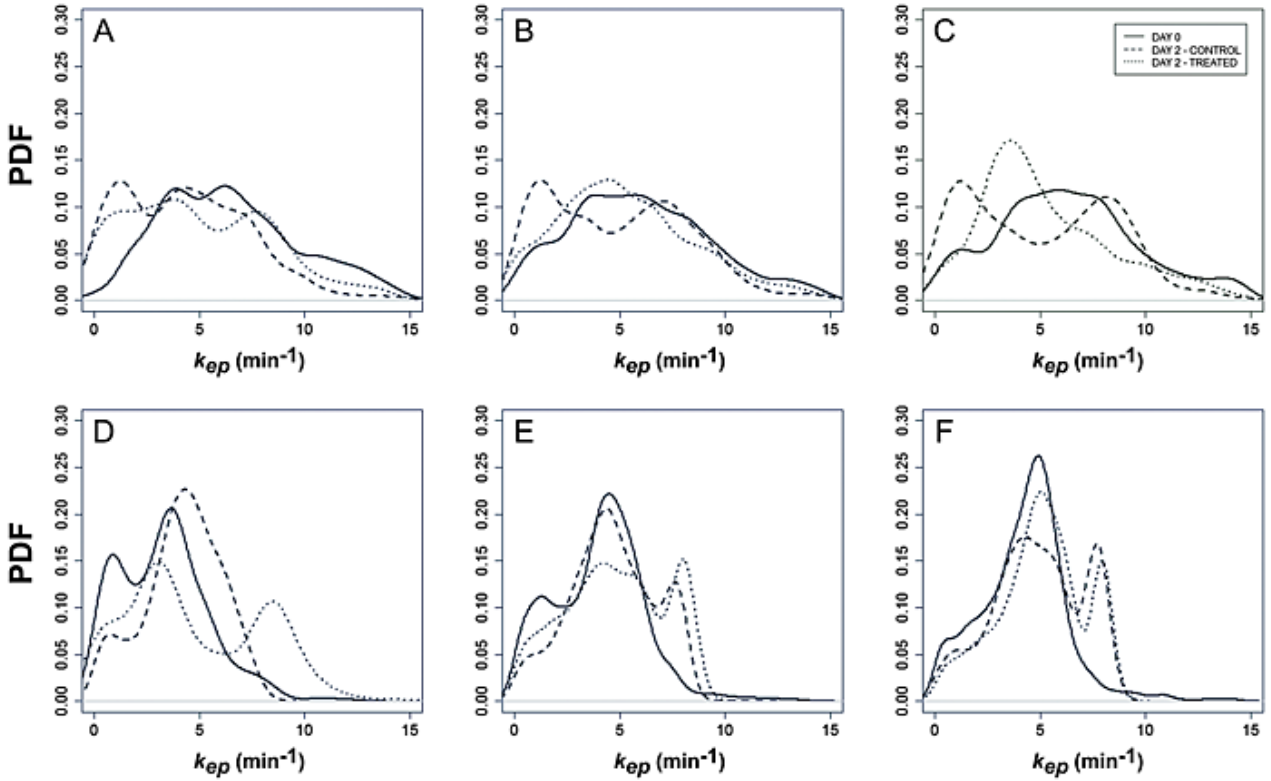
Probability density analysis



PDF of k_{ep} derived from DCE-US (A) low-, (B) intermediate-, and (C) high-enhancement regions and from DCE-MRI (D) low, (E) intermediate and (F) high enhancement regions.

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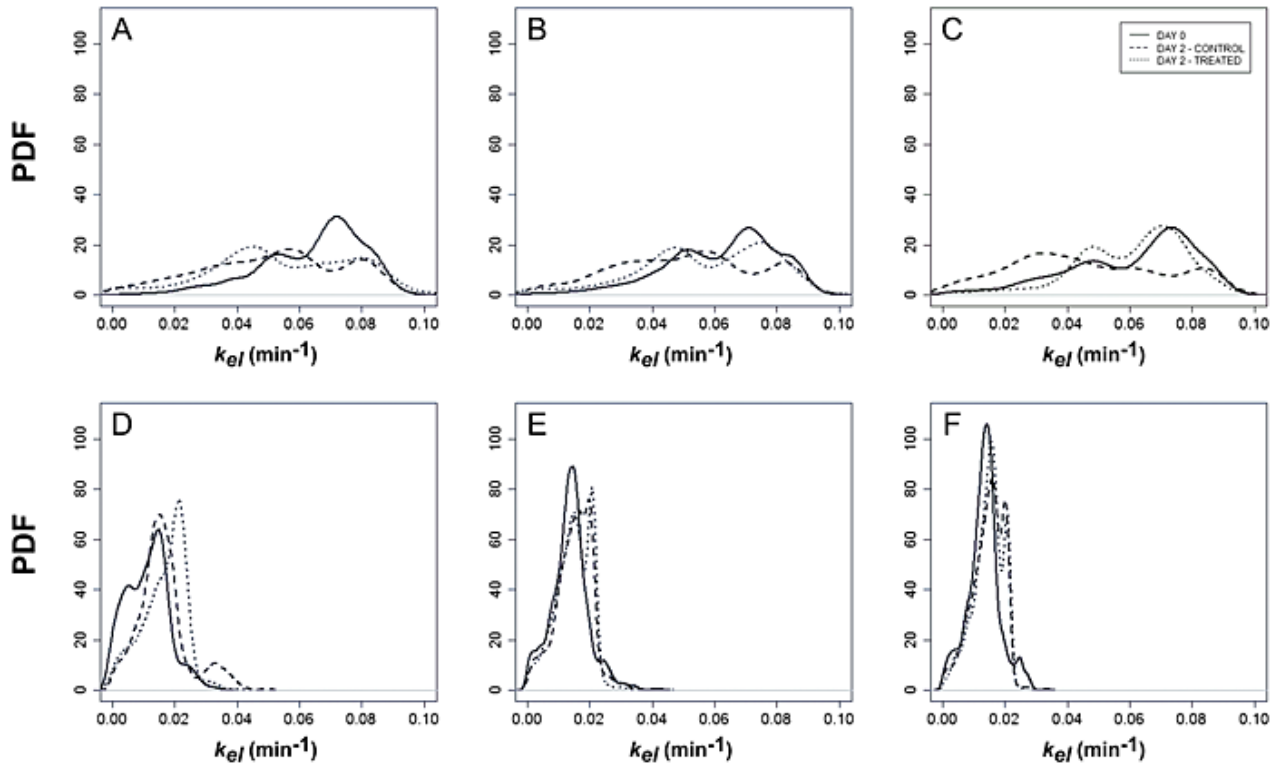
Probability density analysis



PDF of k_{el} derived from DCE-US (A) low-, (B) intermediate-, and (C) high-enhancement regions and from DCE-MRI (D) low, (E) intermediate and (F) high enhancement regions.

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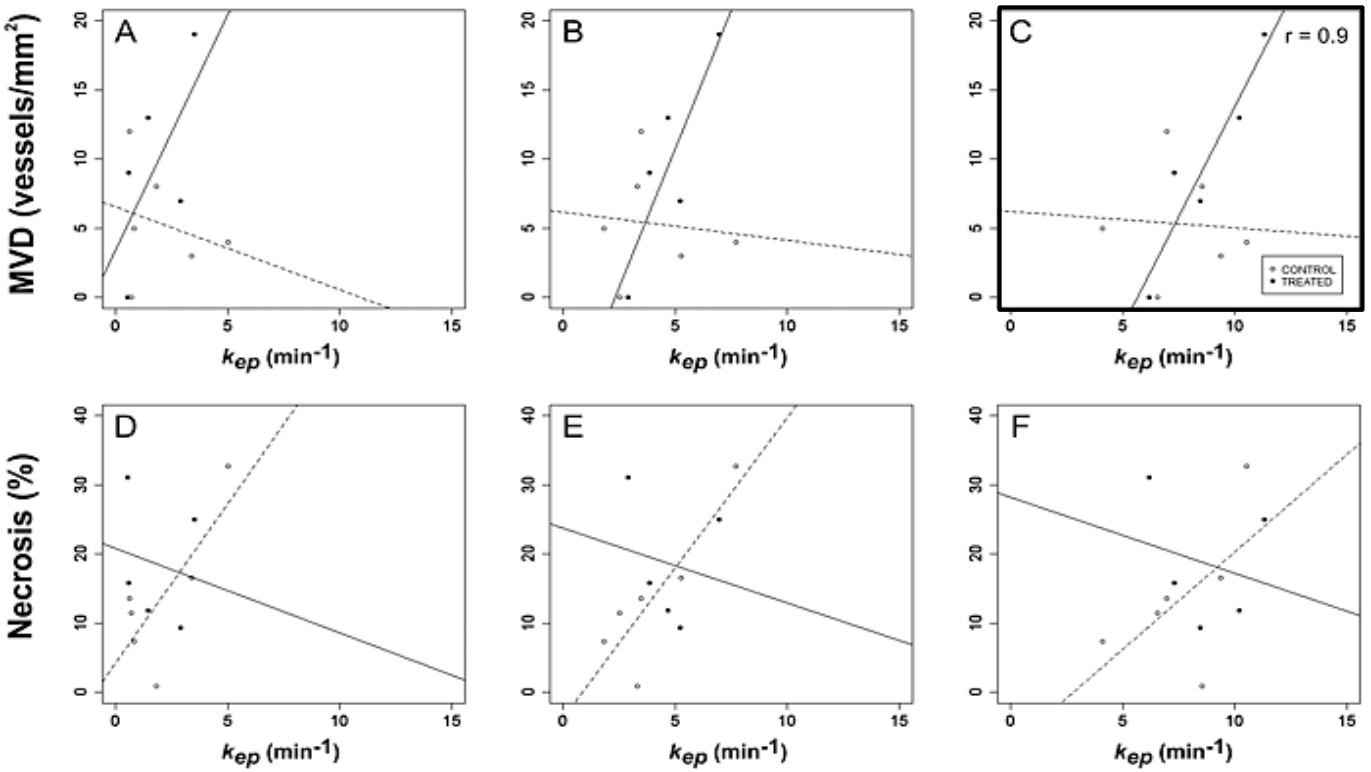
Vasculature and image parameters



MVD and k_{ep} from DCE-US (A) low-, (B) intermediate-, and (C) high-enhanced regions for the treated and the control group. Necrosis and k_{ep} from DCE-US(D) low, (E) intermediate and (F) high enhancement.

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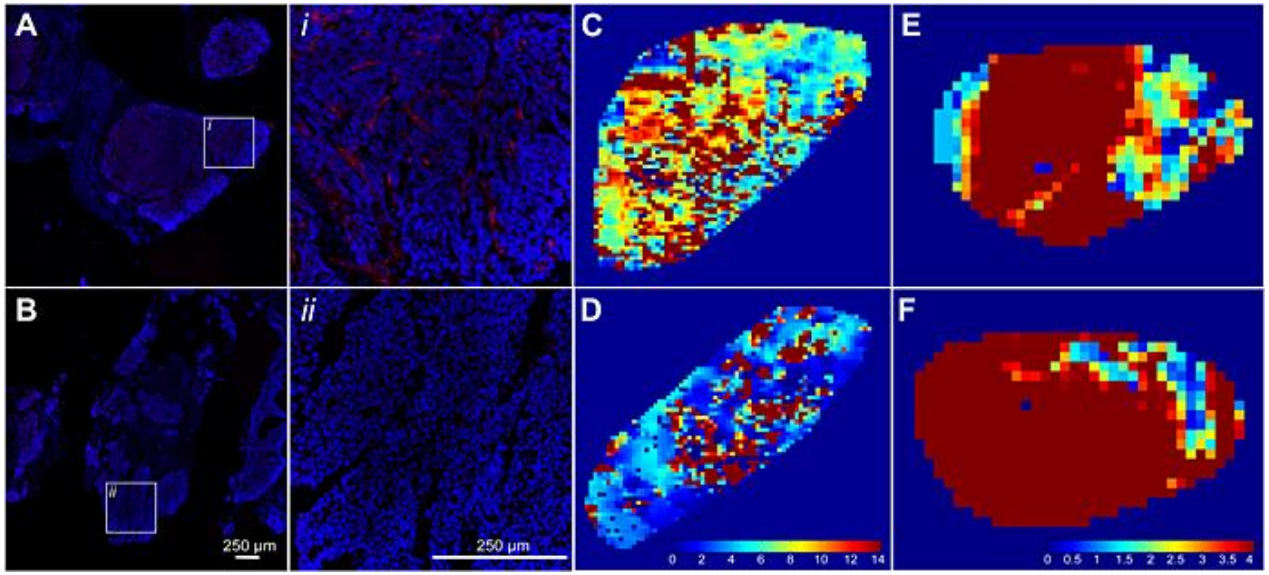
Vasculature and image parameters



High MVD (A) and low MVD (B). Blood vessels by CD31(red) and nuclei were counterstained with DAPI (blue). The areas *i* and *ii* are enlarged from the outlined regions of the images. k_{ep} DCE-US association to MVD (C, D), but not from DCE-MRI (E, F).

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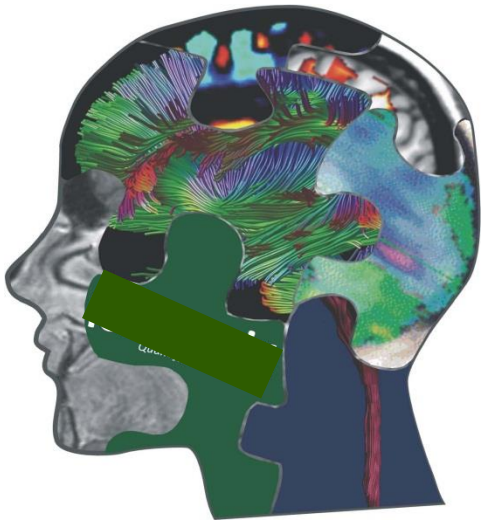
Summary of findings:

- k_{ep} and k_{el} based on both DCE-MRI and DCR-US changed following therapy
- k_{ep} and k_{el} values from DCE-US were significantly higher than those from DCE-MRI
- k_{ep} from DCE-US was correlated to MVD in high-enhancement areas for the treated
- microvascular parameters from DCE-US seem to provide reliable biomarkers during radiotherapy as validated by histology
- DCE-US could be a stand-alone or a complementary technique

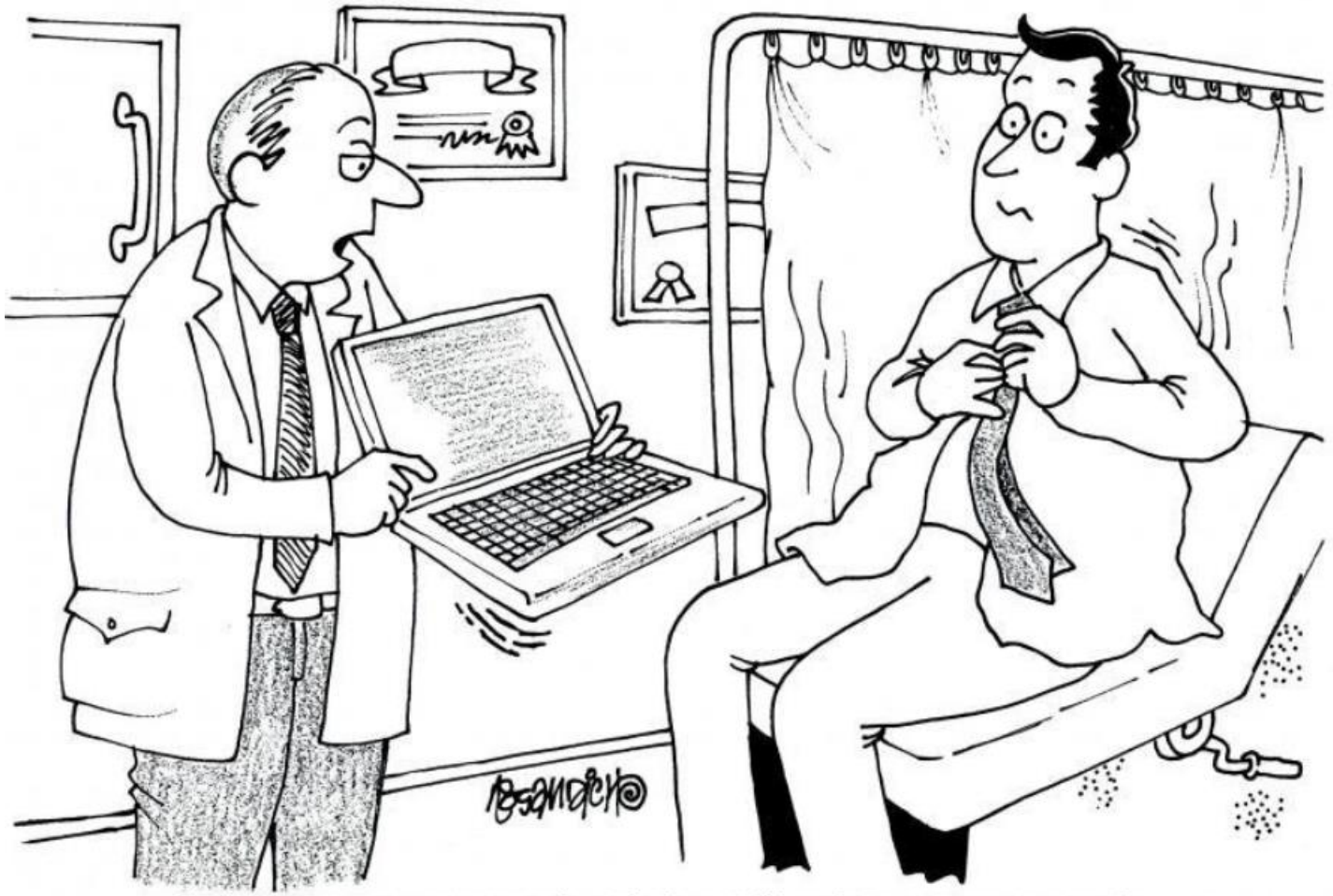
Quantification

Validation

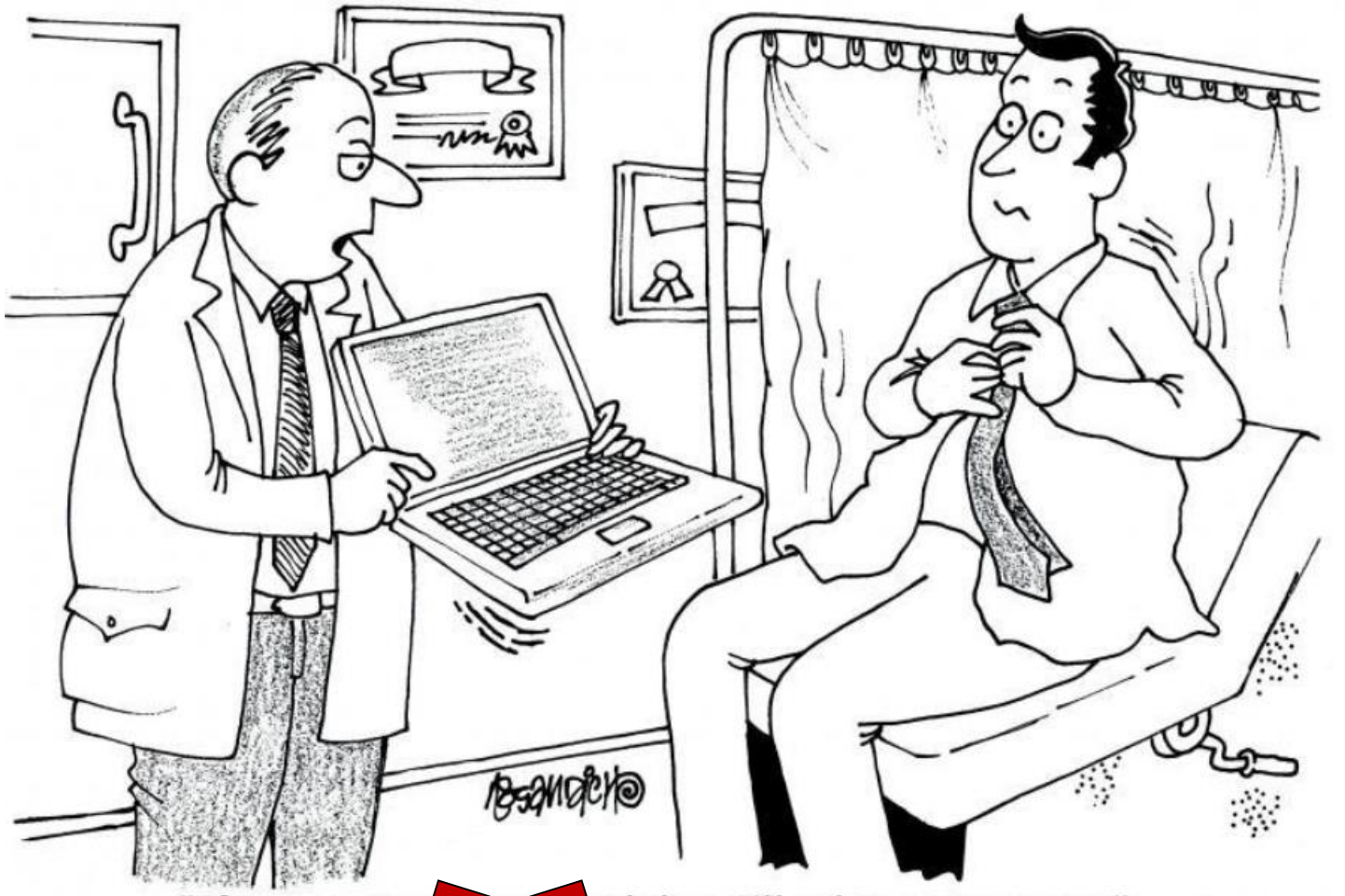


Visualization

Computer-assisted decision-making



"If you want a second opinion, I'll ask my computer."



"If you want a s[illegible] opinion, I'll ask my computer."