Quantitative Dynamic Contrast-Enhanced MRI (DCE-MRI) of Tumor Angiogenesis

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June 20, 2011

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Outline

- What and why of DCE-MRI
- DCE-MRI classifications
- Quantitative DCE-MRI
  - Steps
  - Scientific issues

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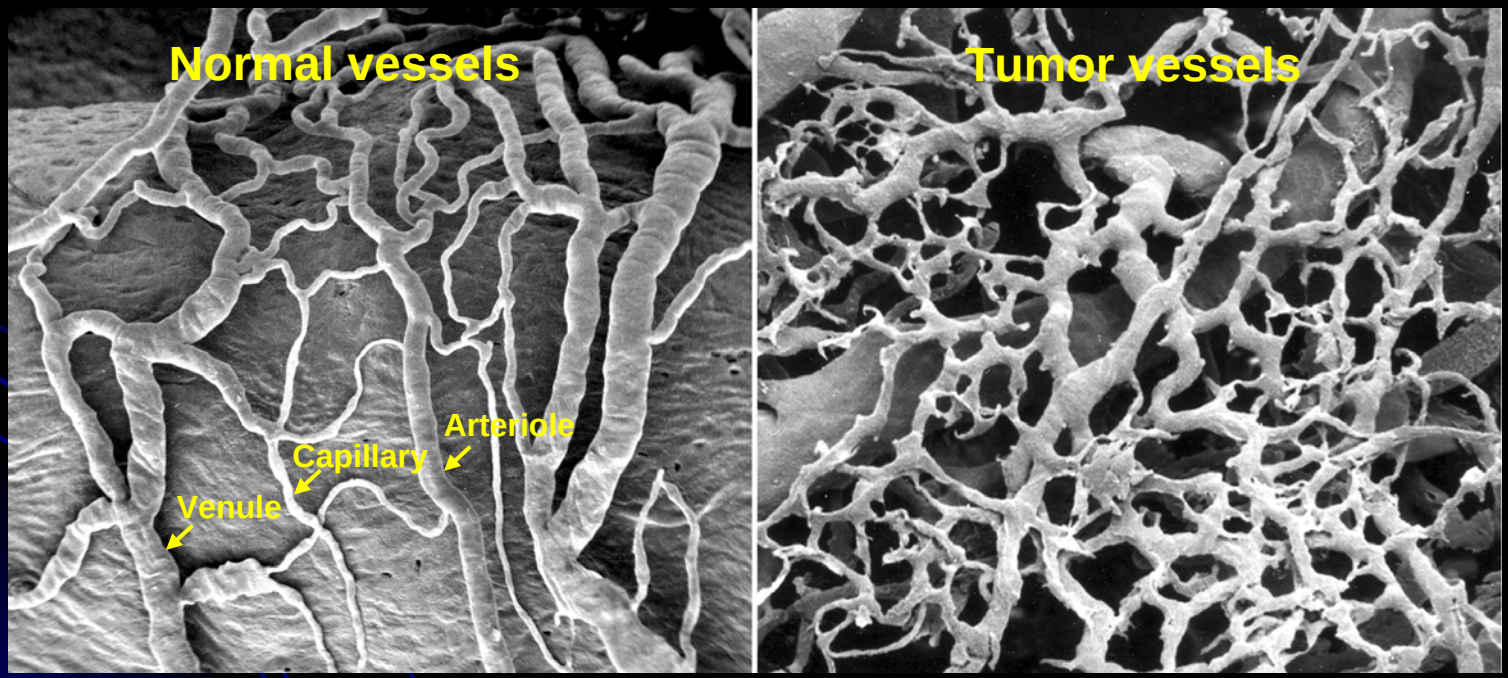
Tumor angiogenesis

- Tumor blood vessels differ from normal vasculature
  - Tortuous, dilated, AV shunts, rapidly proliferating endothelium
  - Leakier vessel walls, poor blood flow, decreased vessel stability



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Tumor angiogenesis

- Function and morphology of tumor vasculature determines tumor growth, metastatic potential, and therapeutic response
- New anti-cancer therapies selectively target tumor vasculature (e.g. prune immature vessels → reduced vascular permeability)
- Current need for specific quantitative biomarkers of tumor vascular function and morphology to guide selection of treatment strategy, understand biological effects, and monitor response

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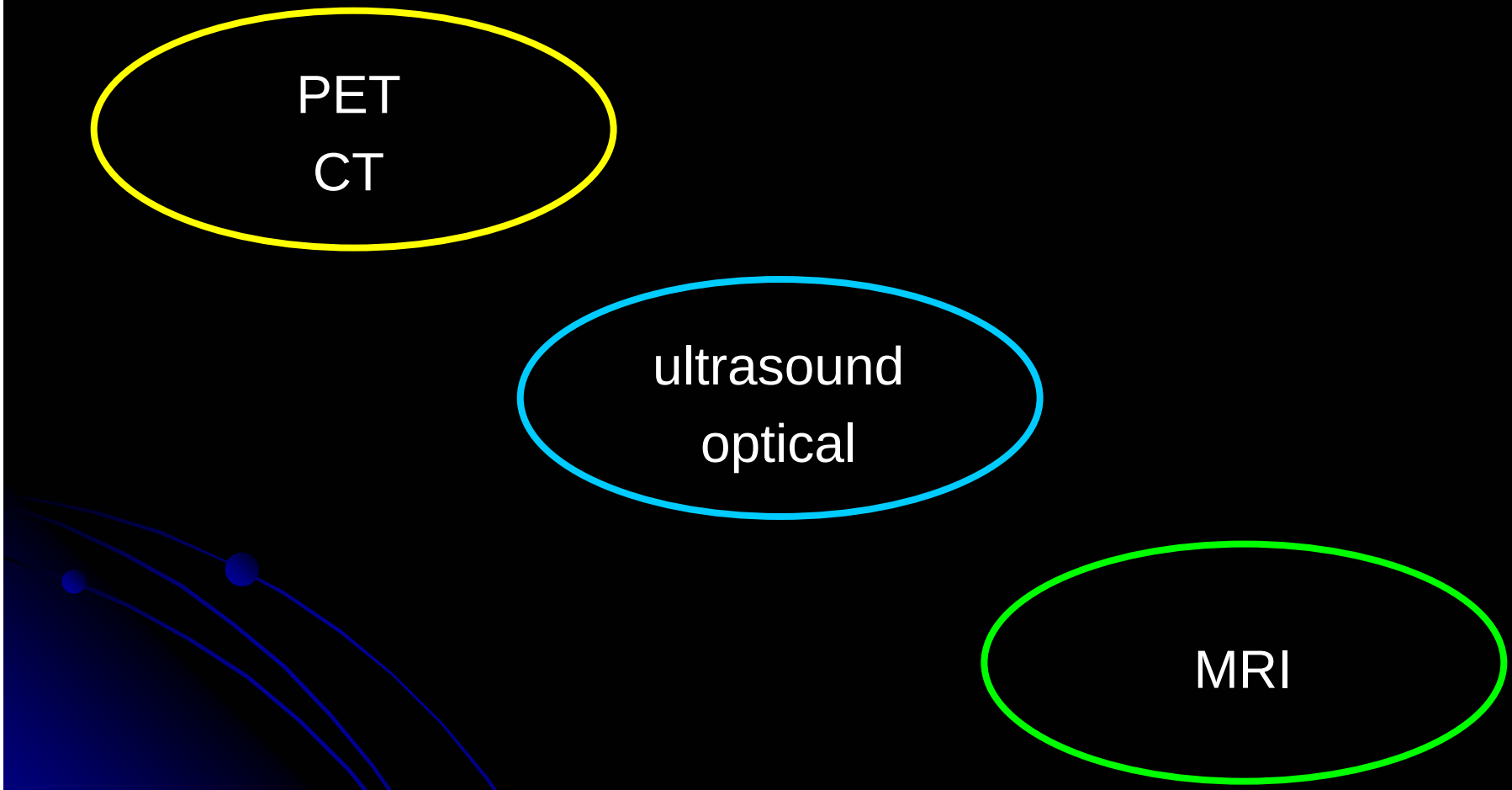
Imaging biomarkers of vascular function



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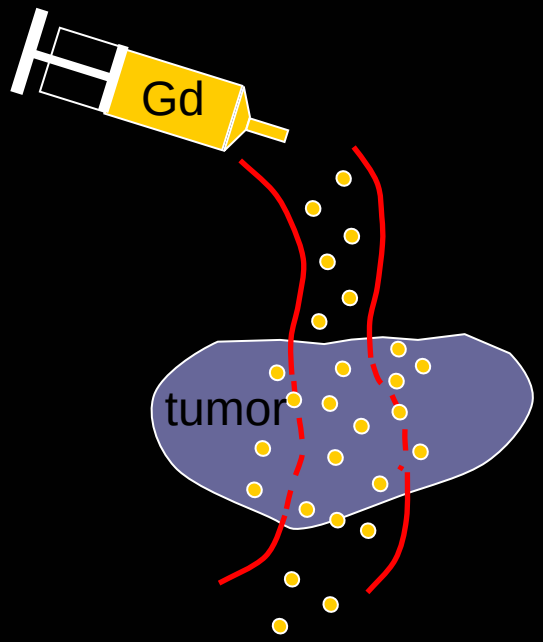
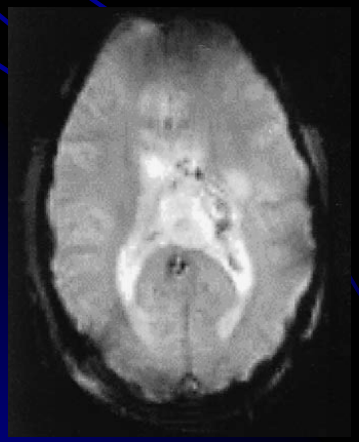
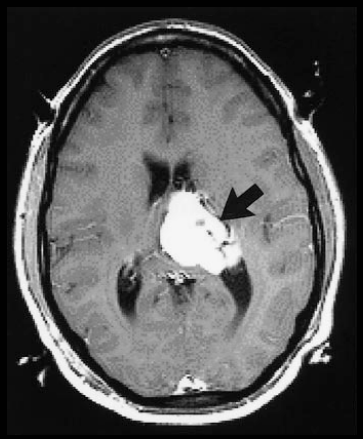
DCE-MRI – paradigm



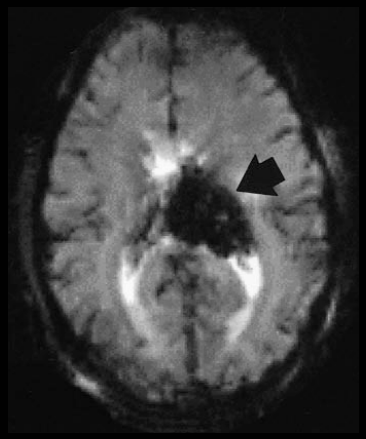
Pre-injection



T1 (DCE-MRI)



T2* (DSC-MRI)



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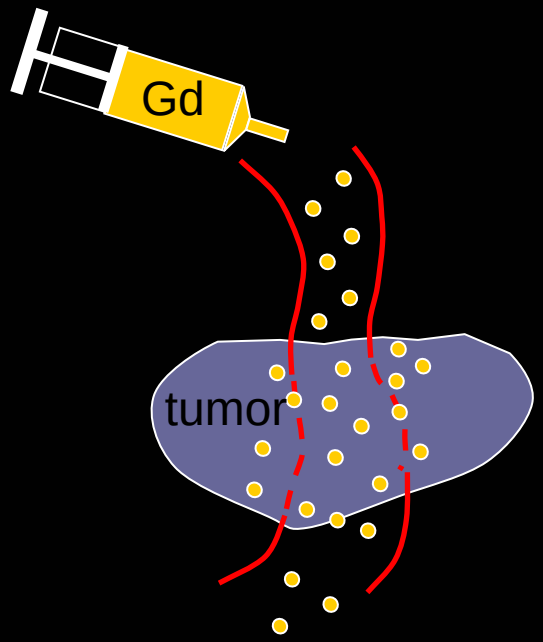
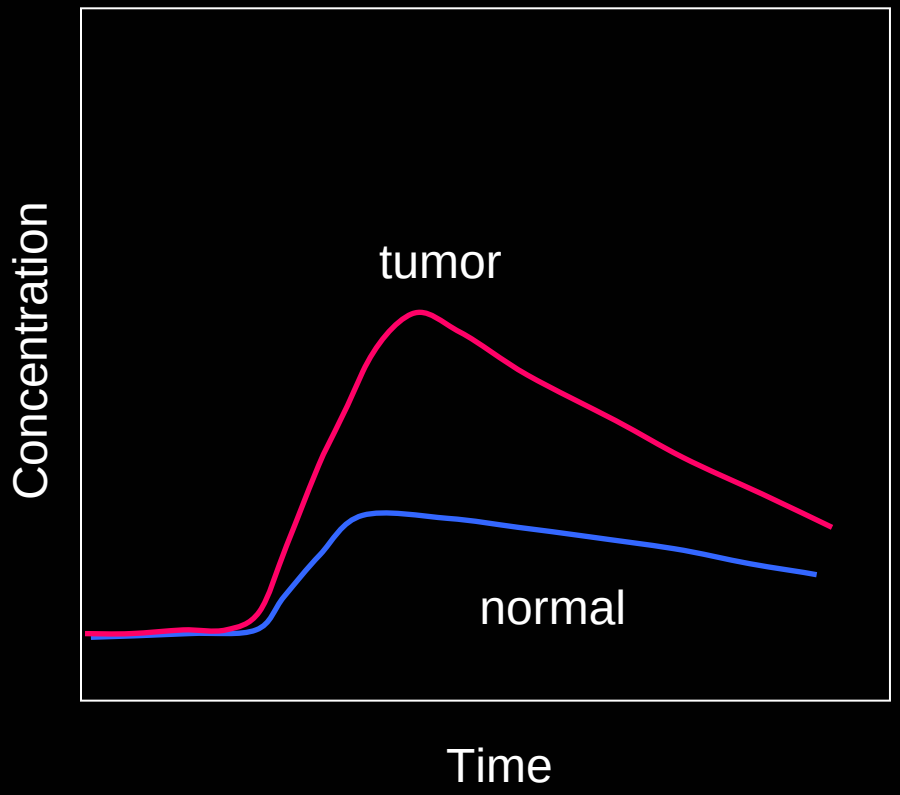
DCE-MRI – dynamic data





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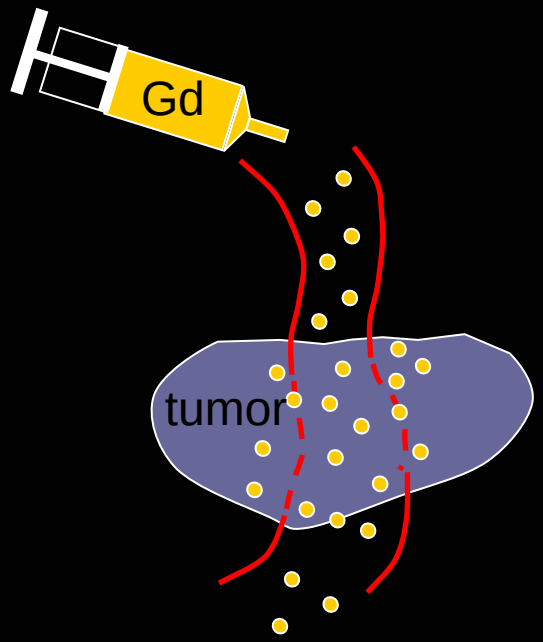
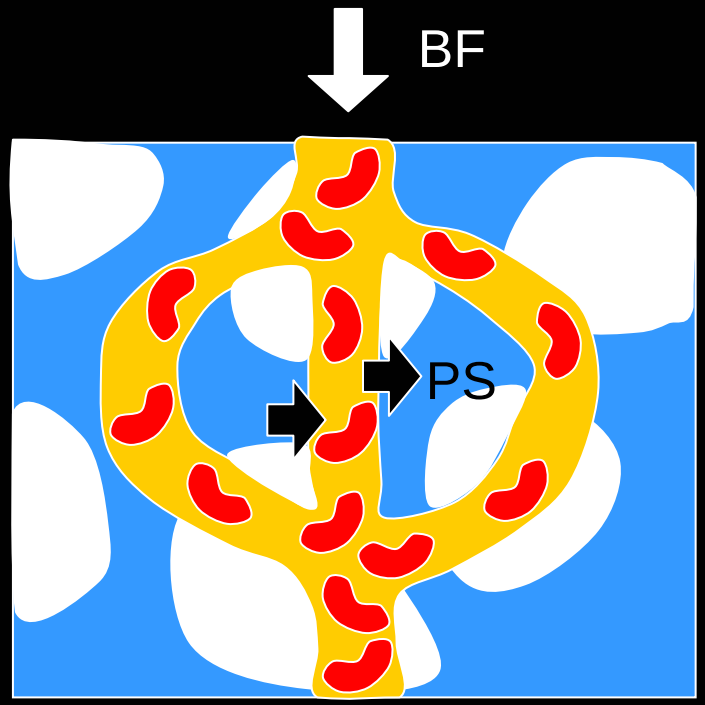
DCE-MRI – physiological parameters





Capillary blood flow (BF)

Capillary blood volume (BV)

Capillary permeability (PS)

Interstitial volume (EES)

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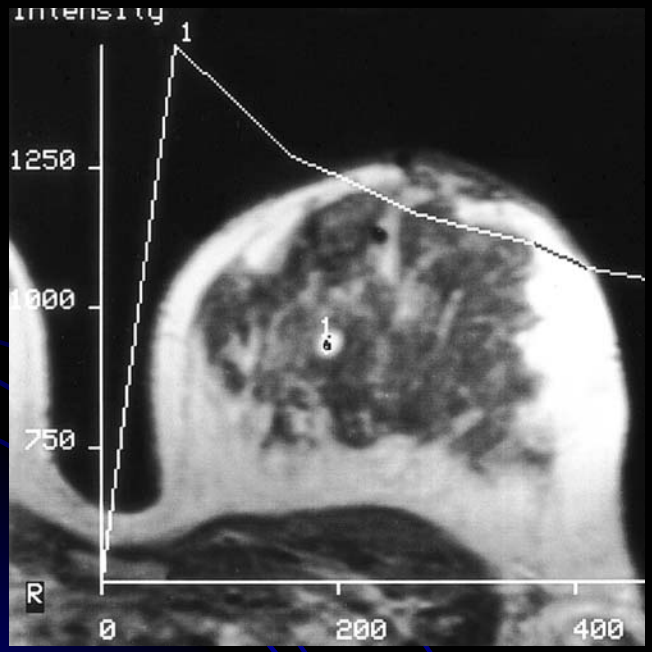
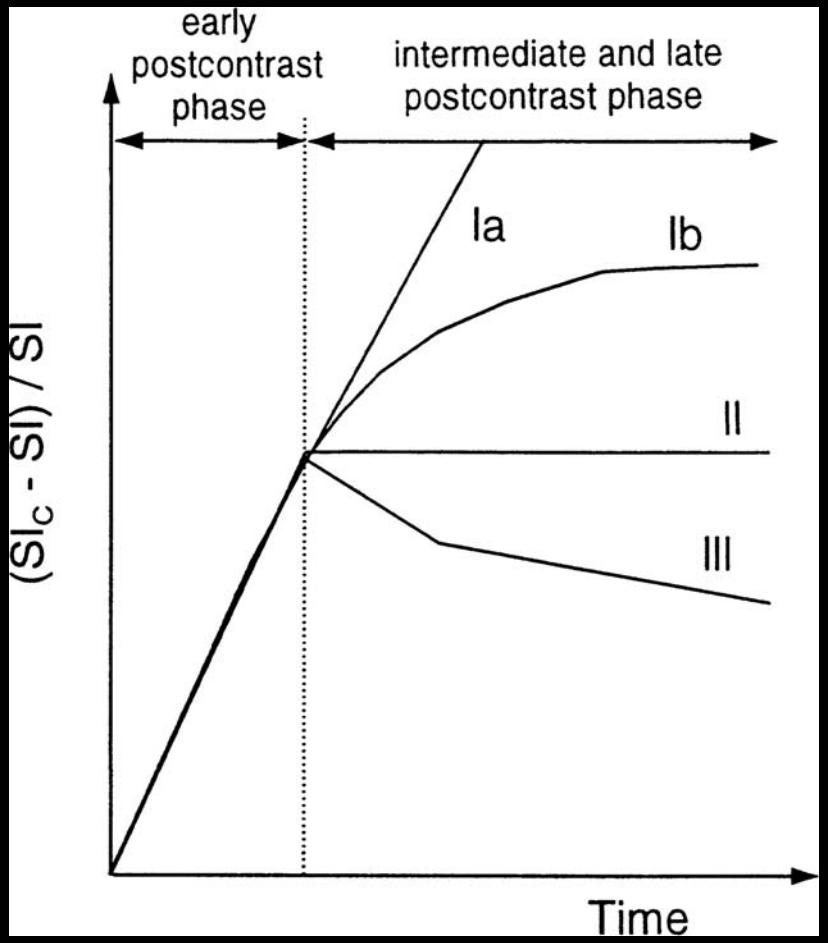
DCE-MRI analysis

- Visual – curve score





Kuhl CK et al. Radiology 211, 101-110, 1999.

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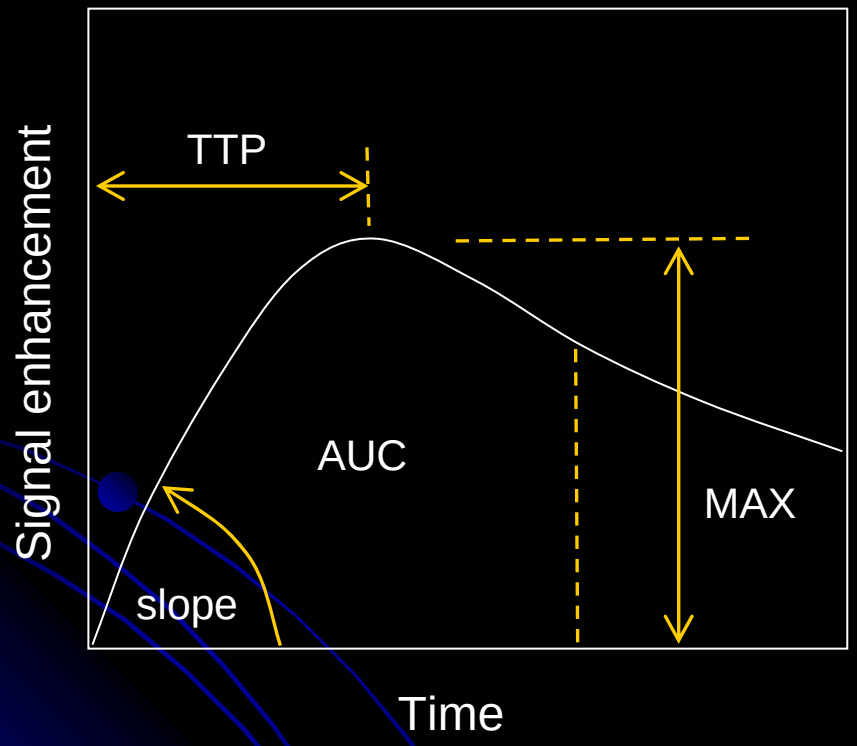
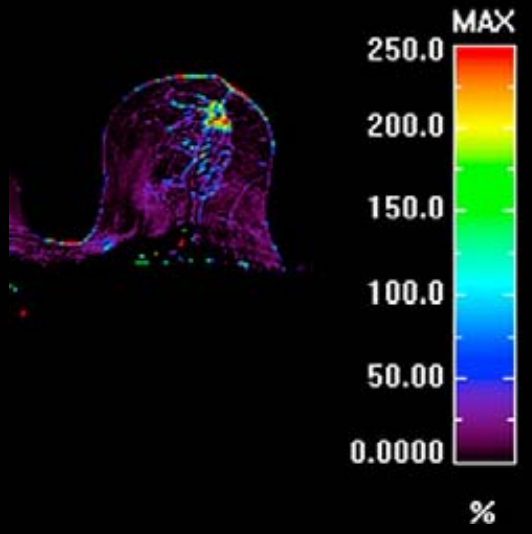
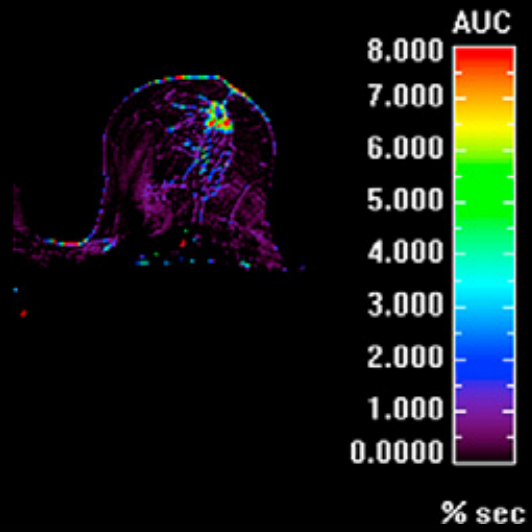
DCE-MRI analysis

- Parametric – descriptive







Schlossbauer T et al. Acad Radiol 17, 441-449, 2010.

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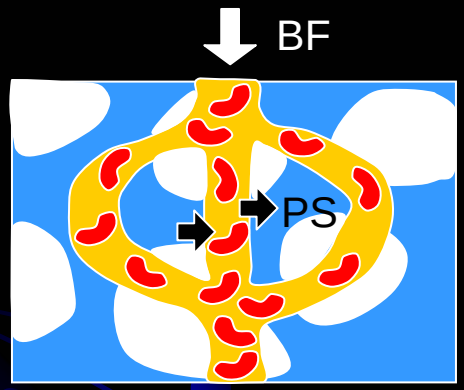
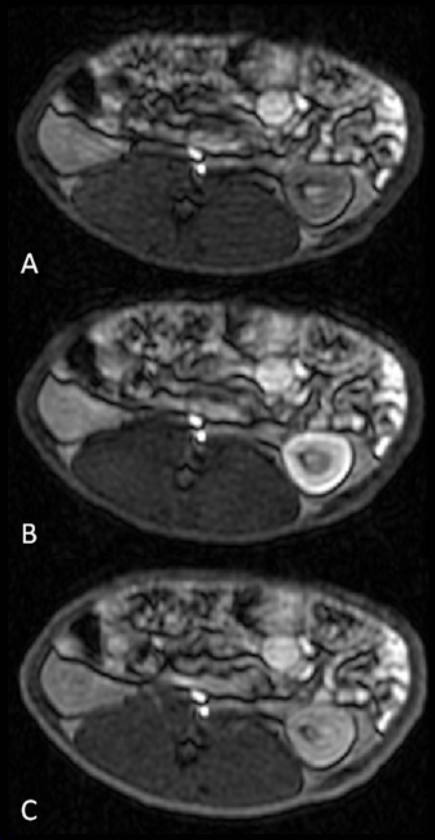
DCE-MRI analysis

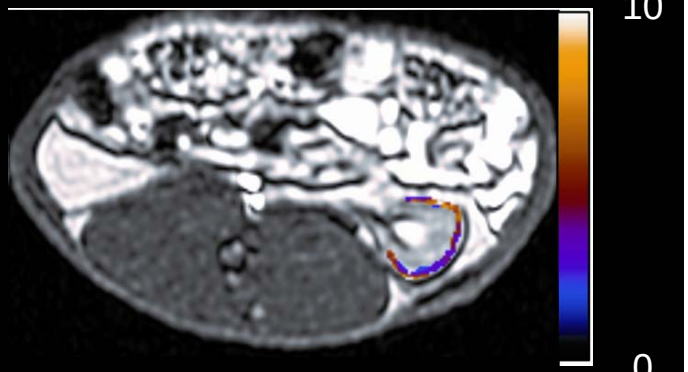
- Parametric – quantitative



Dynamic series



Plasma flow
(ml/min/g)



Winter JD, St. Lawrence KS, Cheng HL. J Magn Reson Imaging (in press)

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Quantitative DCE-MRI analysis

Pre-processing Signal to concentration Parameter estimation

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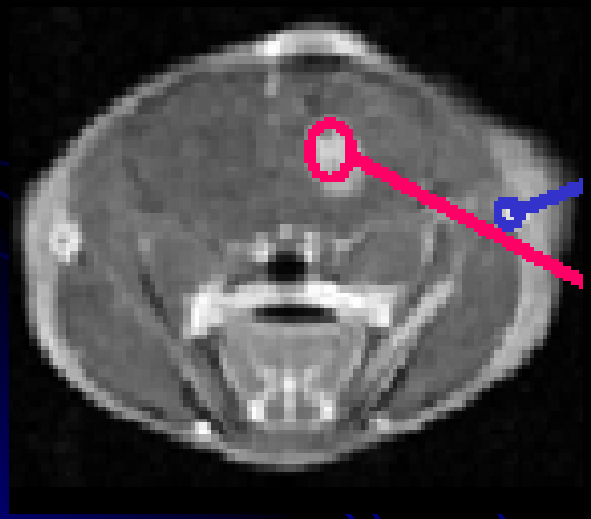
Quantitative DCE-MRI analysis

Pre-processing Signal to concentration Parameter estimation

- Motion correction
- Segmentation



AIF (essential for quantitative analysis)

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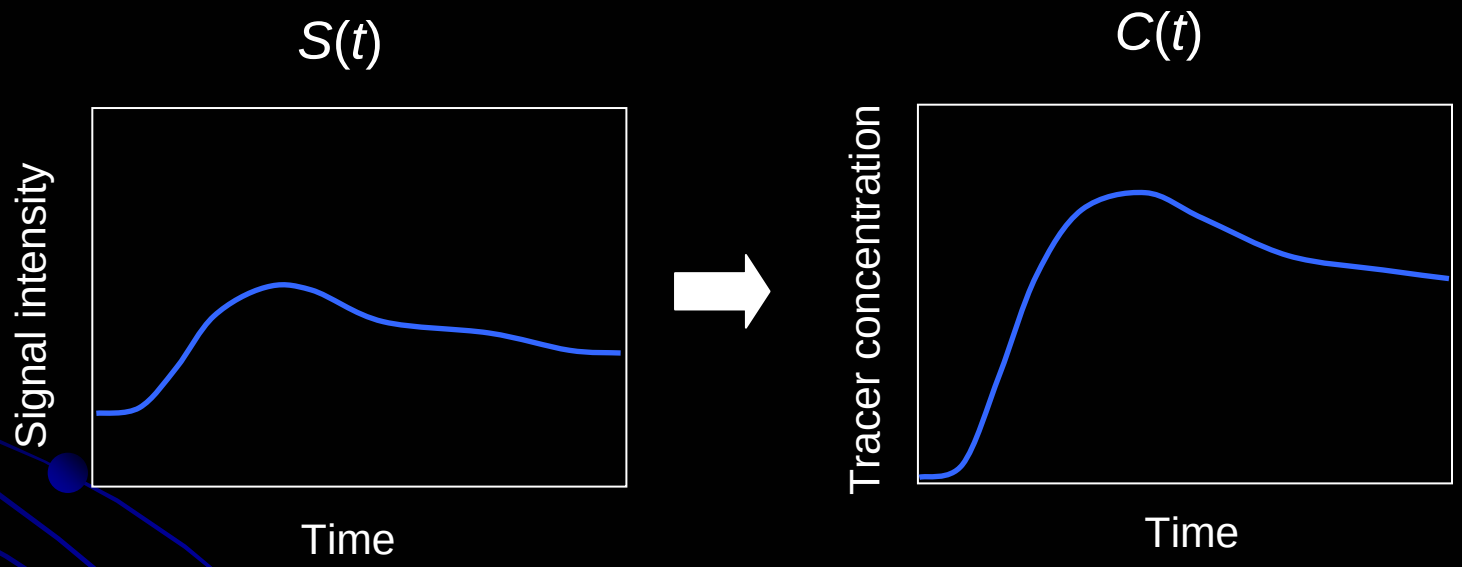
Quantitative DCE-MRI analysis

Pre-processing Signal to concentration Parameter estimation



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Quantitative DCE-MRI analysis

Pre-processing | Signal to concentration | Parameter estimation

Step 1: $S(t) \rightarrow R_1(t)$

$$S(t) = \underbrace{\Omega \cdot M_0 \cdot c \cdot \exp(-T_E R_2^*)}_{\text{constant}} \cdot \underbrace{f\,(R_1(t);\, T_R\,, \ldots)}_{\text{T1 effects from contrast agent}}$$

$$S(t) = S' \cdot f\,(R_1(t))$$

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Quantitative DCE-MRI analysis

Pre-processing Signal to concentration Parameter estimation

Step 1: $S(t) \rightarrow R_1(t)$

Need a measurement of pre-injection R_{1o}

$$R_1(t) = f^{-1}\{ f(R_{1o}) \cdot S(t)/S_o \}$$ (non-linear)

$$R_1(t) = R_{1o} \cdot S(t)/S_o$$ (linear)

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Quantitative DCE-MRI analysis

Pre-processing | Signal to concentration | Parameter estimation

Step 2: $R_1(t) \rightarrow C(t)$

$$R_1(t) = R_{1o} + r_1 C(t)$$ (fast water exchange assumption)

$$C(t) = (R_1(t) - R_{1o}) / r_1$$

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Quantitative DCE-MRI analysis

Pre-processing | Signal to concentration | Parameter estimation

Tissue concentration measured

$$C(t) = \mathrm{IRF}(t) \otimes C_A(t)$$

AIF measured

Impulse response function unknown

Deconvolution

$$F = \max \{ \mathrm{IRF}(t) \}$$

$$V = \int \mathrm{IRF}(t)\, dt$$

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Quantitative DCE-MRI analysis

Pre-processing Signal to concentration Parameter estimation

- Deconvolution
  - Model-free, constrained, model-based

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Quantitative DCE-MRI analysis

Pre-processing Signal to concentration Parameter estimation

- Deconvolution
  - Model-free, constrained, model-based

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Quantitative DCE-MRI analysis

Pre-processing Signal to concentration Parameter estimation

- Model-based deconvolution

$$\mathrm{IRF}(t) = v_p\,\delta(t) + K^{trans}\exp(-K^{trans}\,t / v_e) \qquad \text{(modified Tofts model)}$$

$$\mathrm{IRF}(t) = \begin{cases} F_p\,, & t < T_c \\ EF_p \exp(-EF_p(t-T_c) / v_e)\,, & t > T_c \end{cases} \qquad \text{(AATH model)}$$

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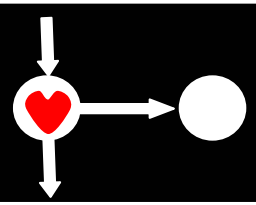
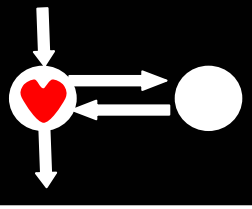
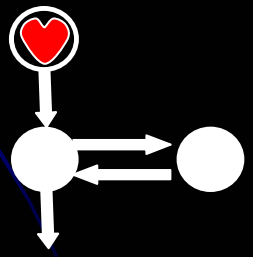
Quantitative DCE-MRI analysis

Pre-processing Signal to concentration Parameter estimation

- Model-based deconvolution

# parameters	Two-compartment models	Parameters estimated
2	 *Patlak*	$K^{trans} = EF_p$ v_p
3	 *modified Tofts*	$K^{trans} = EF_p$ v_p v_e
4	 *AATH*	E F_p v_p v_e

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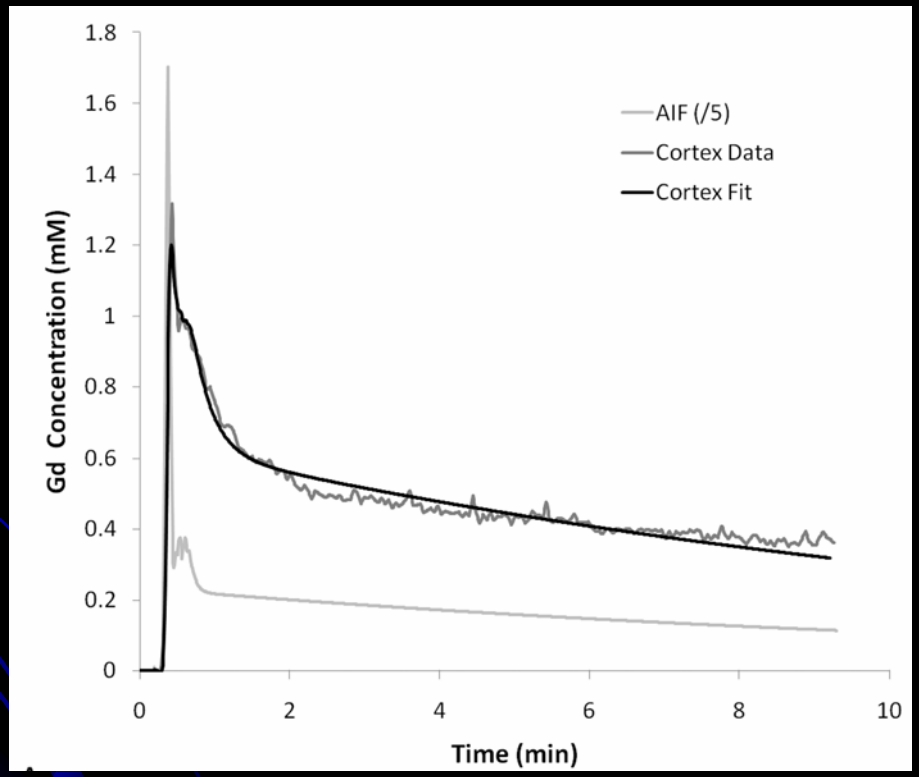
Quantitative DCE-MRI analysis

Pre-processing Signal to concentration Parameter estimation

- Model-based deconvolution



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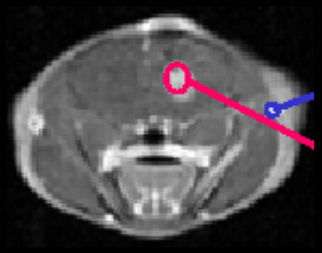
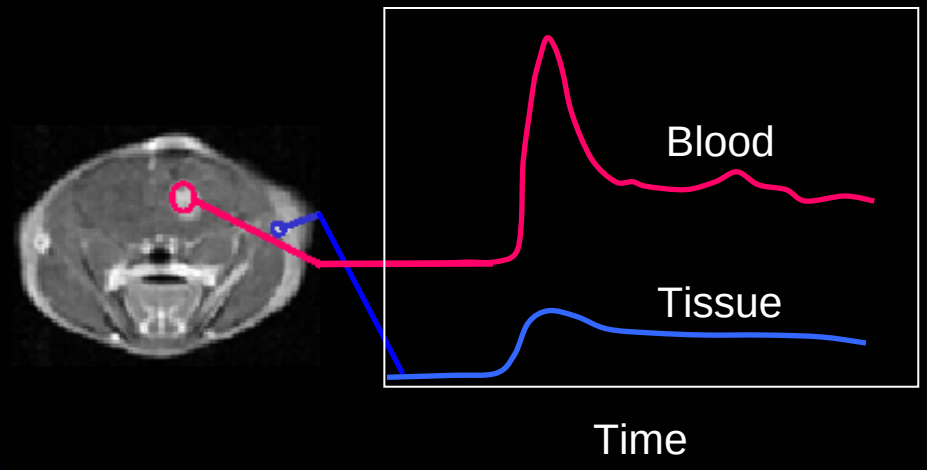
DCE-MRI – an illustrative walk-through

Inject contrast agent (CA)



DCE-MRI – an illustrative walk-through

Inject contrast agent (CA) → **Acquire data**



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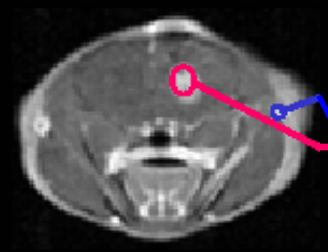
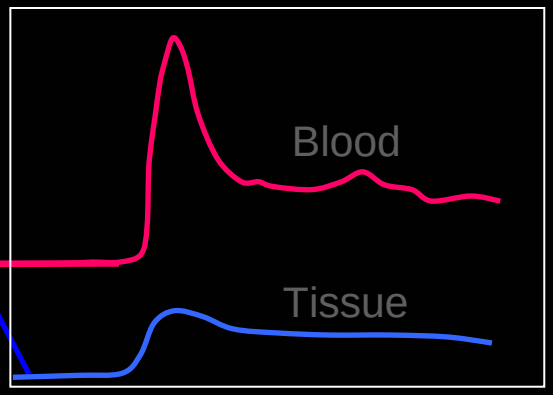
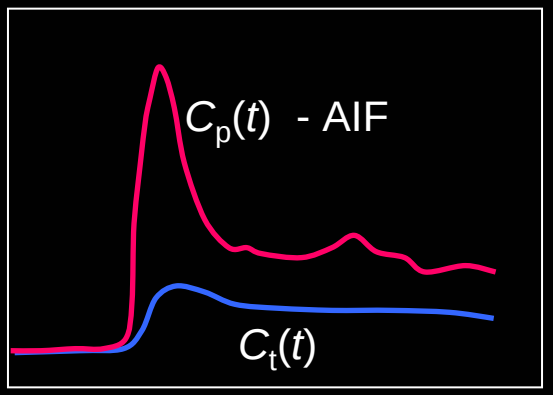
DCE-MRI – an illustrative walk-through

Inject contrast agent (CA) → **Acquire data**





Baseline T1 →



Cheng HL, Wright GA. Magn Reson Med 55, 566-74, 2006.

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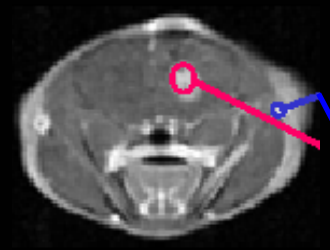
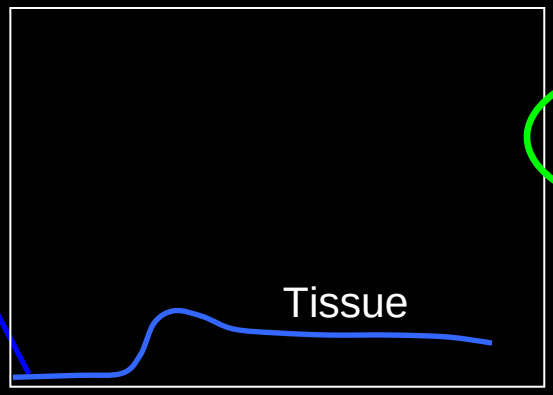
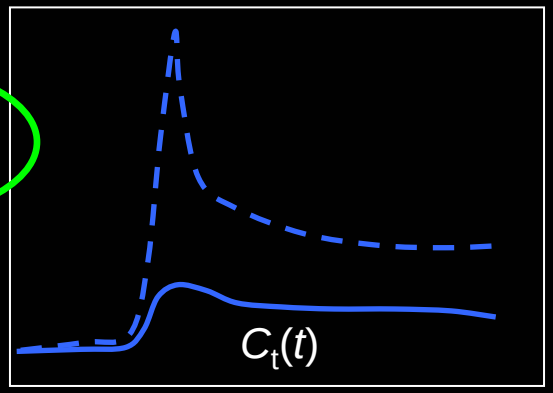
DCE-MRI – an illustrative walk-through

Inject contrast agent (CA) → **Acquire data**





Baseline T1



Cheng HL. J Magn Reson Imaging 25, 1073-1078, 2007.
Tofts PS et al. Magn Reson Med 33, 564-568, 1995.
Di Giovanni P et al. Phys Med Biol 55, 121-132, 2010.

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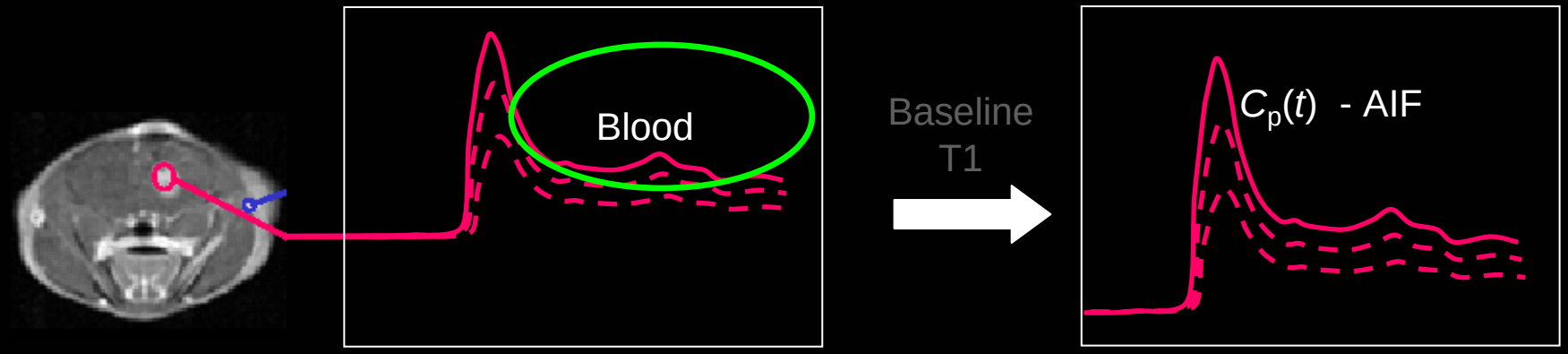
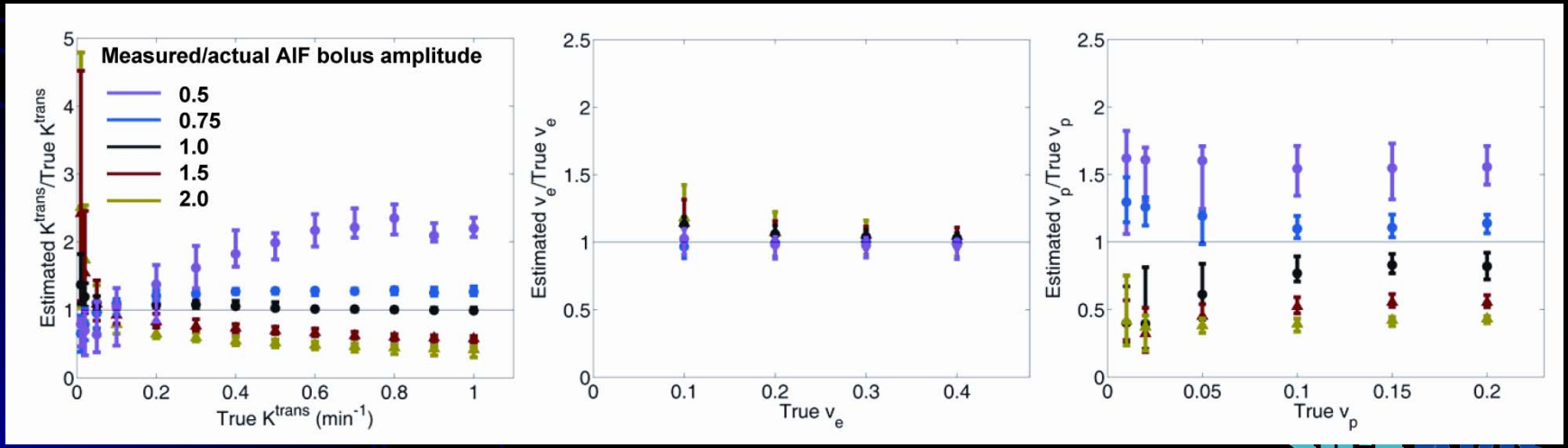
DCE-MRI – an illustrative walk-through

Inject contrast agent (CA) → **Acquire data**



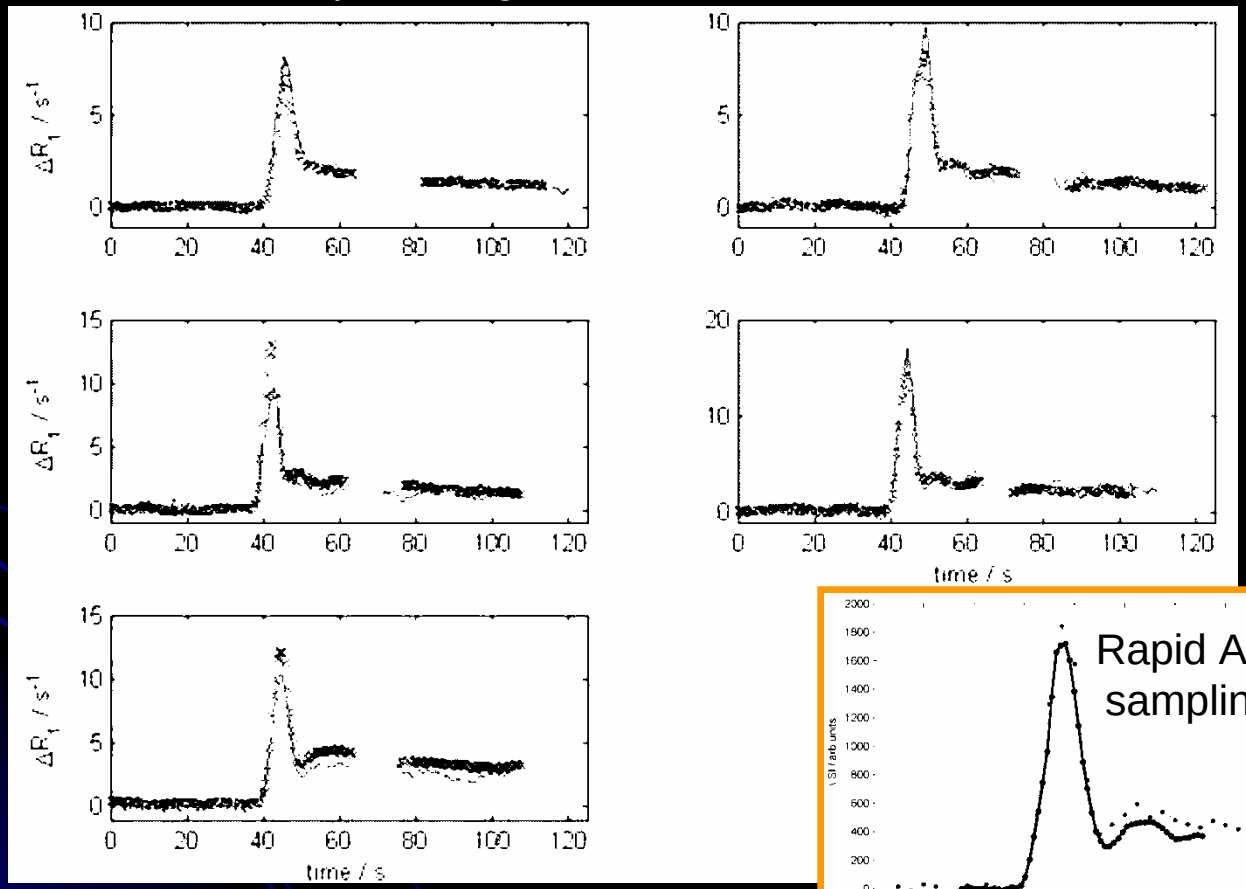


Cheng HL. J Magn Reson Imaging 28, 736-43, 2008.

DCE-MRI – an illustrative walk-through

- Measuring the AIF – dual bolus injection

Prebolus AIF for predicting full bolus AIF



Kershaw LE, Cheng HL. Magn Reson Imaging 29, 160-166, 2011.

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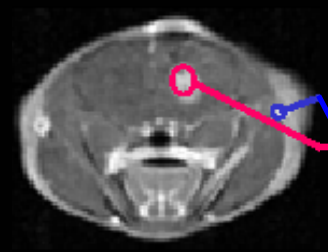
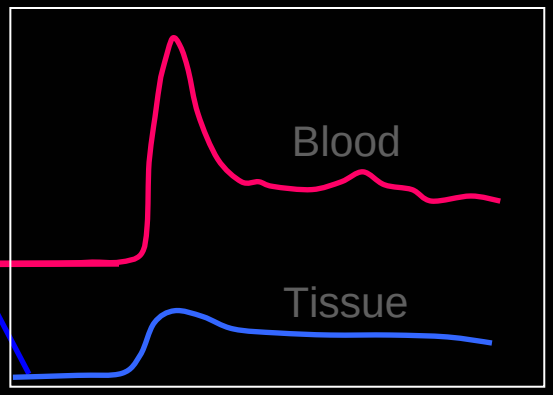
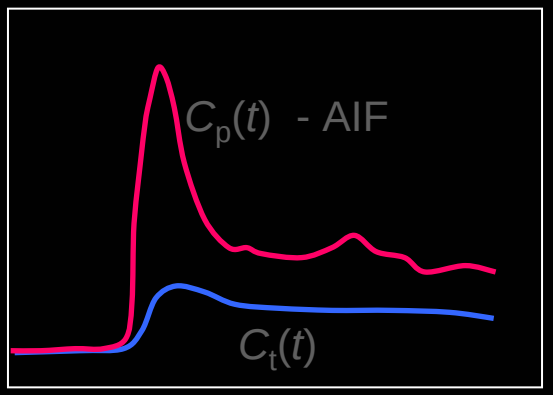
DCE-MRI – an illustrative walk-through

Inject contrast agent (CA) → **Acquire data** → **Analyse data**





Baseline T1



Pharmacokinetic model

Plasma volume v_p

EES volume v_e

Transfer constant K^{trans}

permeability

flow

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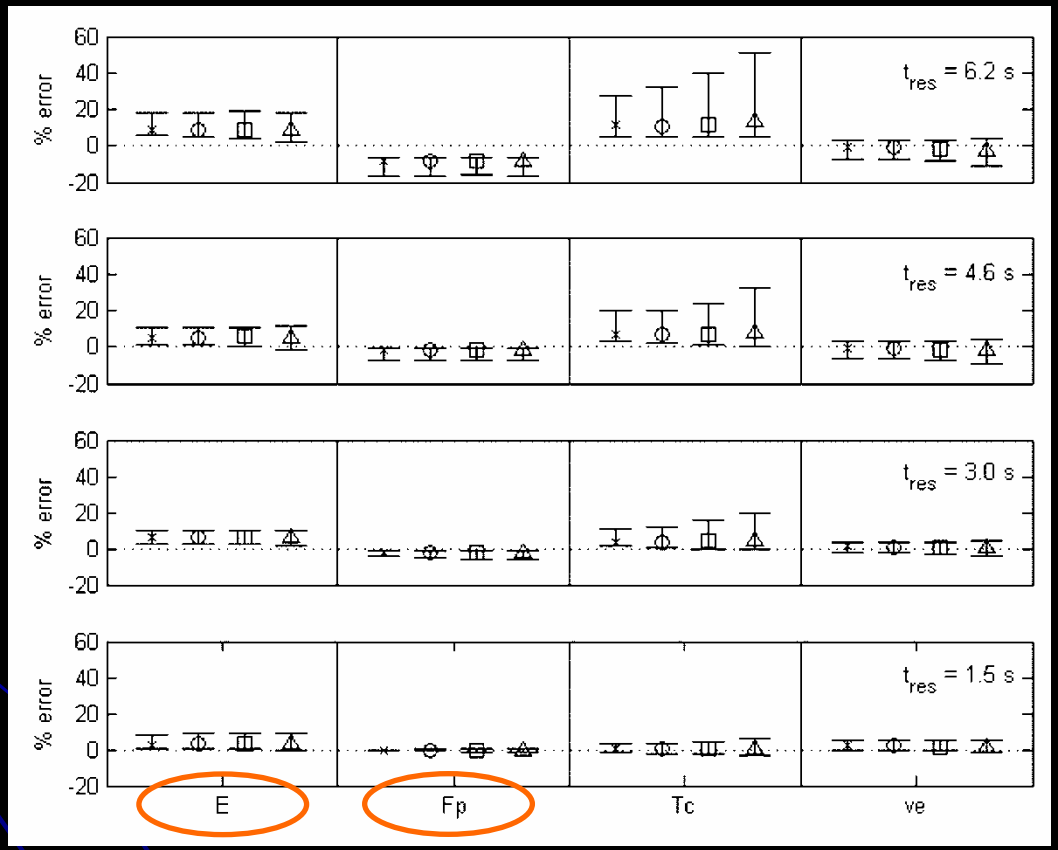
DCE-MRI – an illustrative walk-through

- Requirements for more specific pharmacokinetic models



Kershaw LE, Cheng HL. Magn Reson Med 64, 1772-80, 2010.

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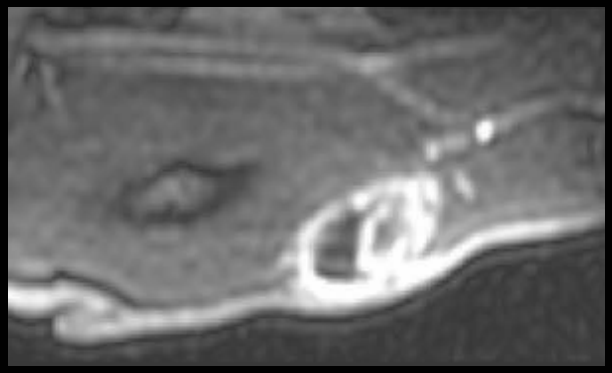
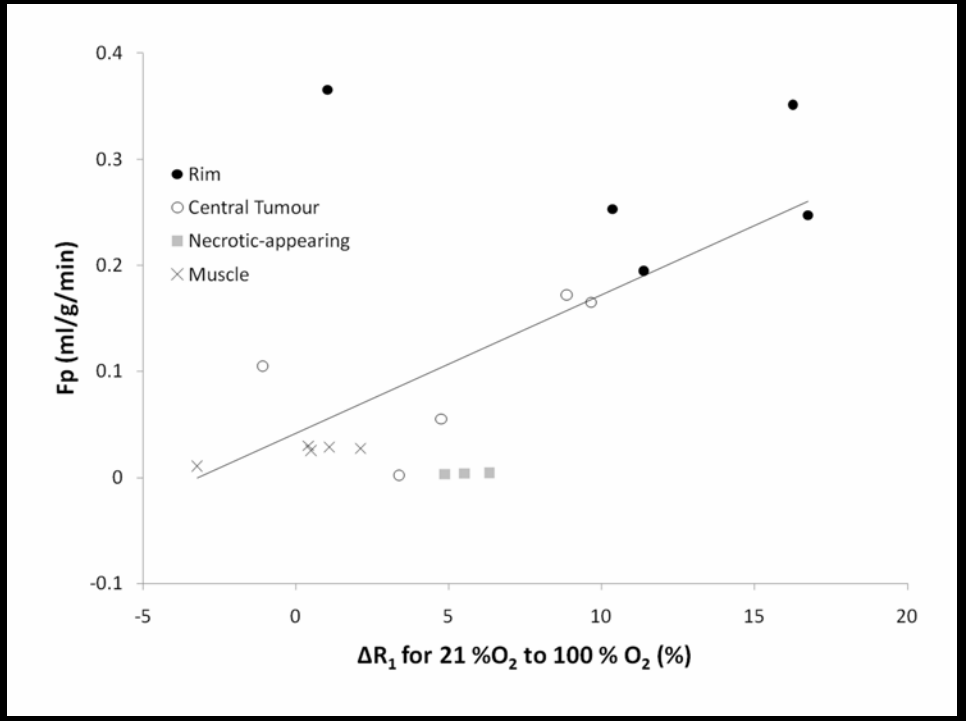
DCE-MRI in practice

- VX2 rabbit tumor model



23 days post-implantation



Winter JD, Akens MK, Cheng HL. Phys Med Biol 56, 1225-1242, 2011.

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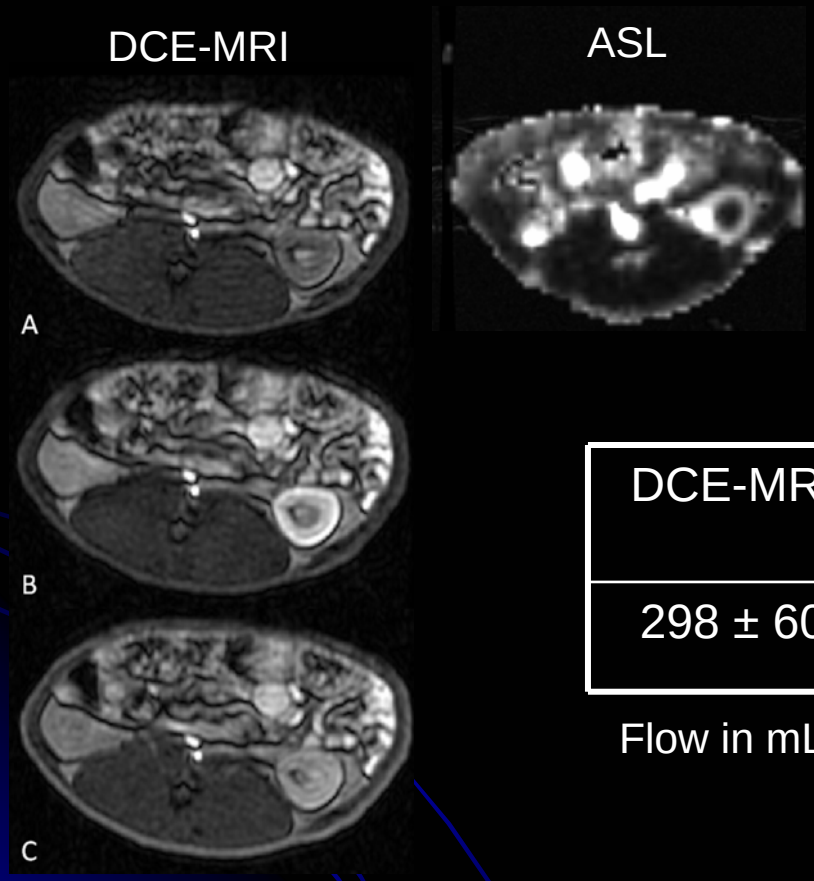
DCE-MRI in practice

- Blood flow in normal rabbit kidney cortex



DCE-MRI	ASL MRI	Microspheres
298 ± 60	328 ± 59	325 ± 123

Flow in mL/100g/min

Winter JD, St. Lawrence KS, Cheng HL. J Magn Reson Imaging (in press)

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Summary

- DCE-MRI can play a critical role in non-invasive measurement of vascular function for disease assessment and treatment planning and monitoring
- Unsolved scientific problems
  - Optimal DCE-MRI measurement and analysis approaches for improved sensitivity and specificity remain an area of research
- Unmet clinical needs
  - International consensus on standardized DCE-MRI methods
  - Automated post-processing methods
- Translate into clinical workup

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Thank you!

Hai-Ling.Cheng@sickkids.ca

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