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Dutch Metrology Institute

A calibrated physical flow standard for medical perfusion imaging

Flomeko, Lisbon, 26 June 2019

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EMPIR 15HLT05 PerfusImaging (July 2016 – June 2019)

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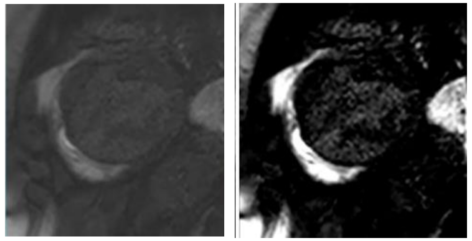
Background

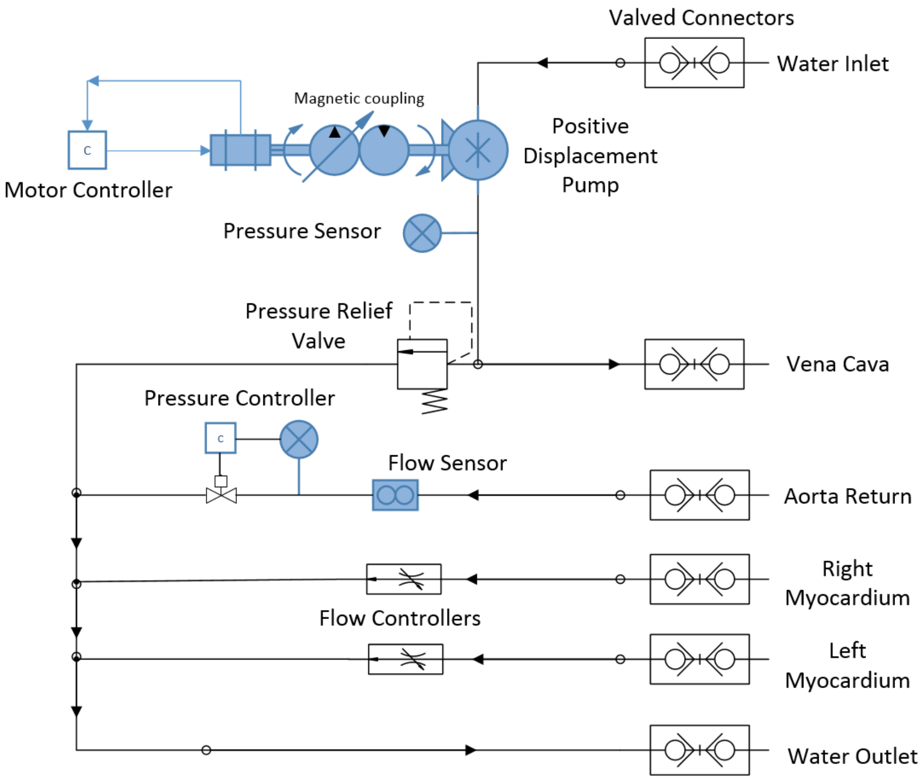
- Good blood flow through heart muscle is of vital importance for well being (otherwise heart attack)



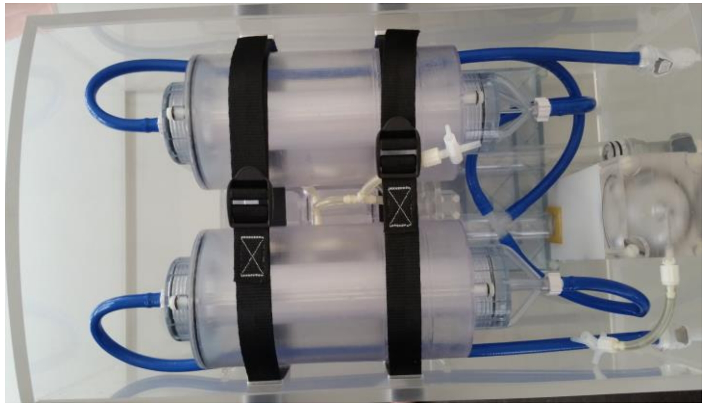
- Current practice: qualitative imaging of heart muscle with e.g. MRI, PET, CT.
- Image interpretation can be dependent on protocol, instrument, software, settings, operator (physician)

- In the EMPIR project 15HLT05 *Metrology for multi-modality imaging of impaired tissue perfusion*, a phantom has been developed that simulates the heart tissue and that can be used to assess the performance of imaging modalities like MRI, PET and CT
- PTB: coordinating work, phantom testing
- KCL: experimental work, various extensions of the phantom, data analysis
- ZMT: engineering and production of phantom
- TUD: measuring reference values of flow rates using UIV
- VSL: CFD simulations, some aspects of data analysis, possibility for traceable flow meter calibration

Phantom components



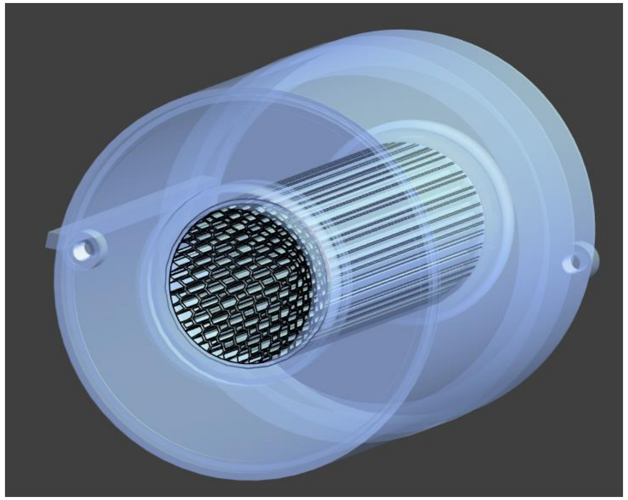
Simulated heart chambers and arteries

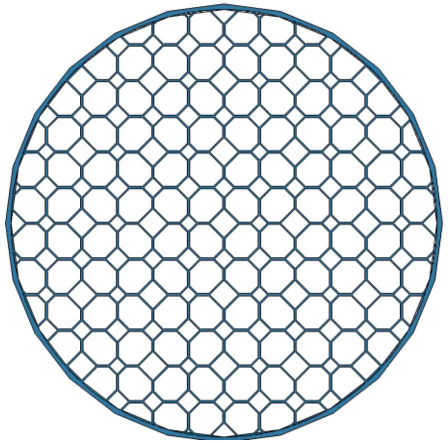


Myocardium

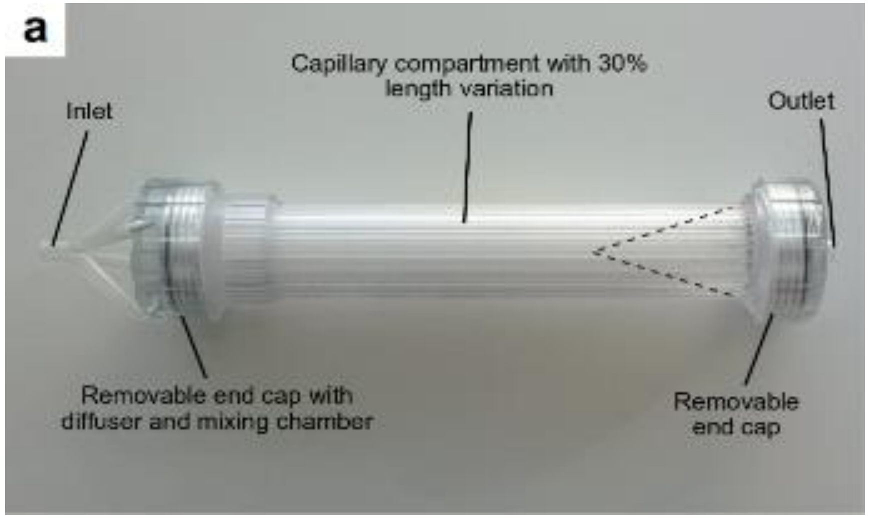
Control system

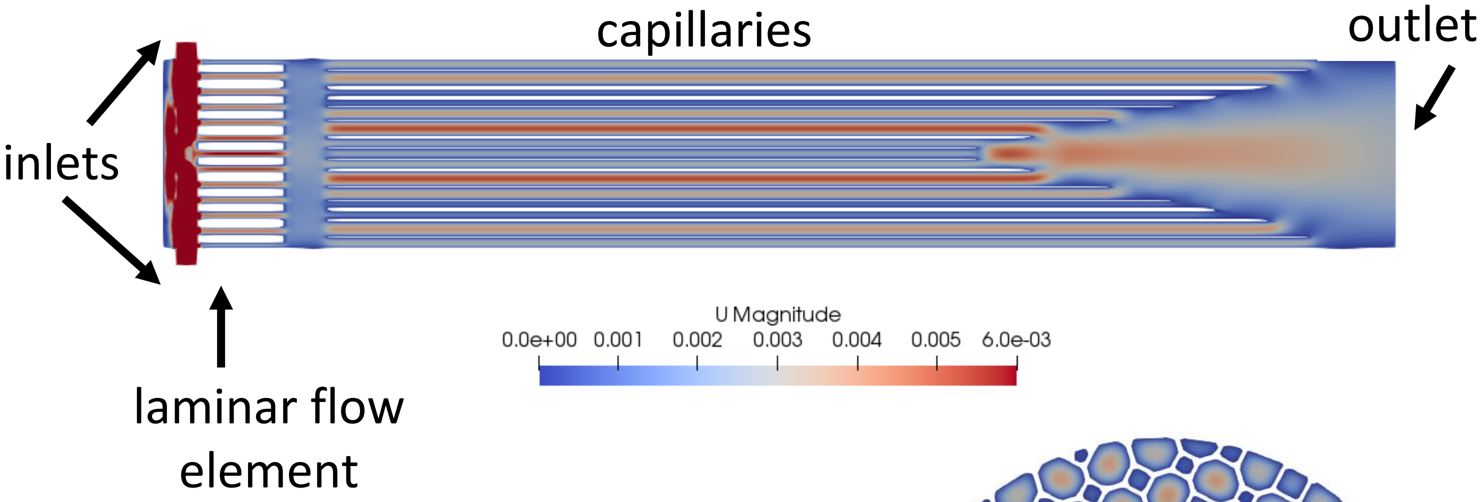
Detailed look at myocardium channel geometry



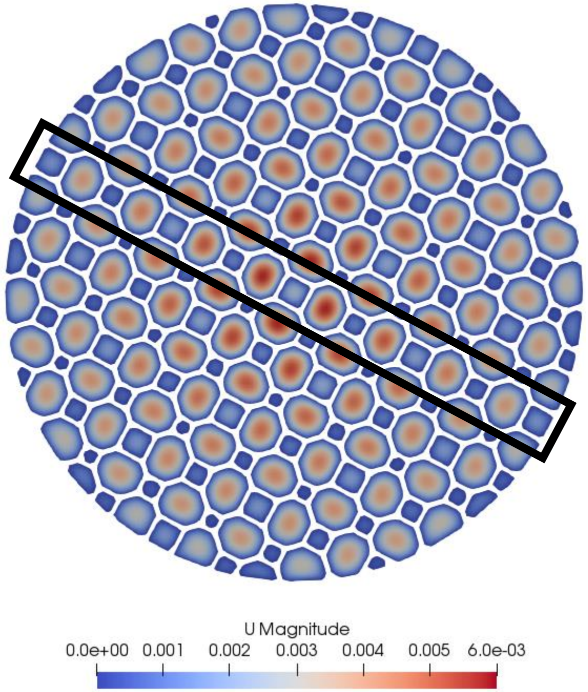


CFD simulation of flow through phantom myocardium



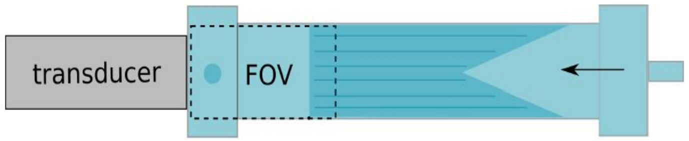


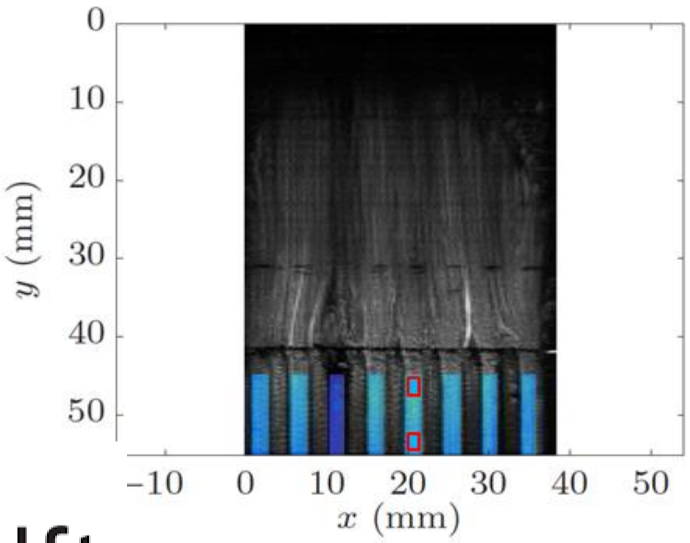
Channel nr.	1	2	3	4	5	6	7	8
Percentage	70%	78%	89%	100%	100%	89%	78%	70%



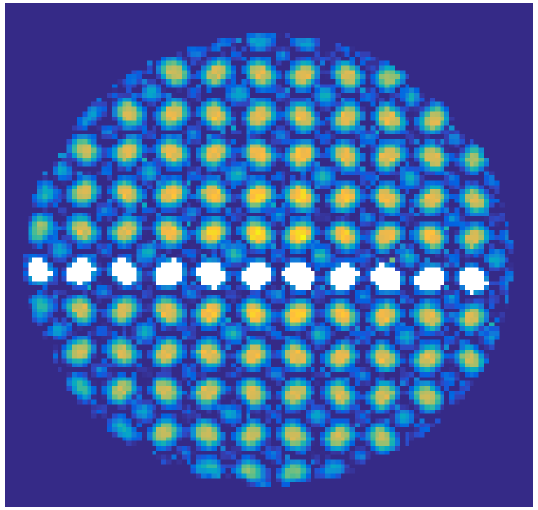
Reference flow measurement per channel

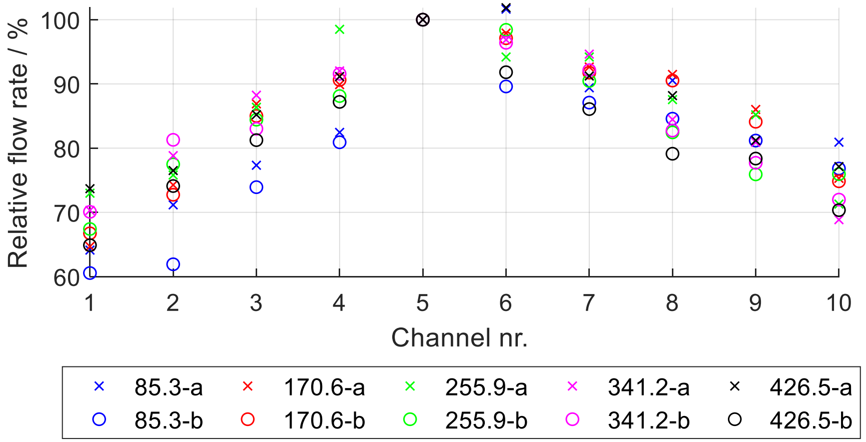
- UIV (ultrasound imaging velocimetry) at TUD
- 3D printed material turned out to be too thick for good UIV measurements
- Uncertainty > 10 %





- PC-MRI (Phase Contrast MRI) at KCL
- Uncertainty about 10 %
- Verification of linear decrease of flow rate with radius of in total 30 %, independent of flow rate (±8 %)

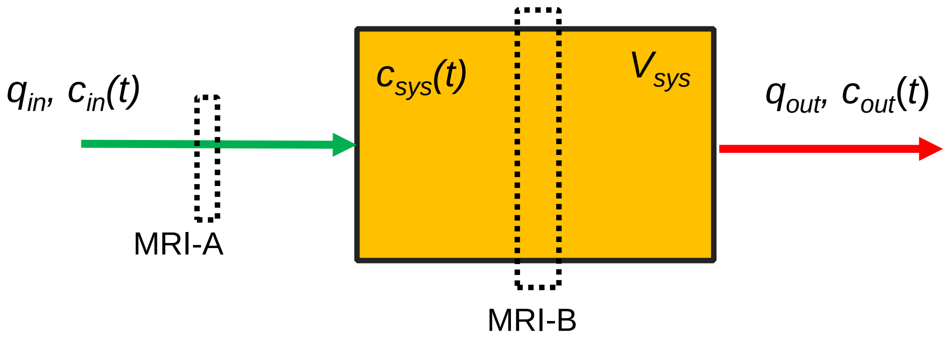




DCE-MRI

Dynamic Contrast Enhanced (DCE) MRI protocol:

- A bolus of contrast agent (CA) is injected in the phantom or patient.
- The dynamic signal is measured in a slice both at the aorta and at the myocardium.
- From the series of images the perfusion, i.e. flow rate normalized by tissue volume, is estimated.

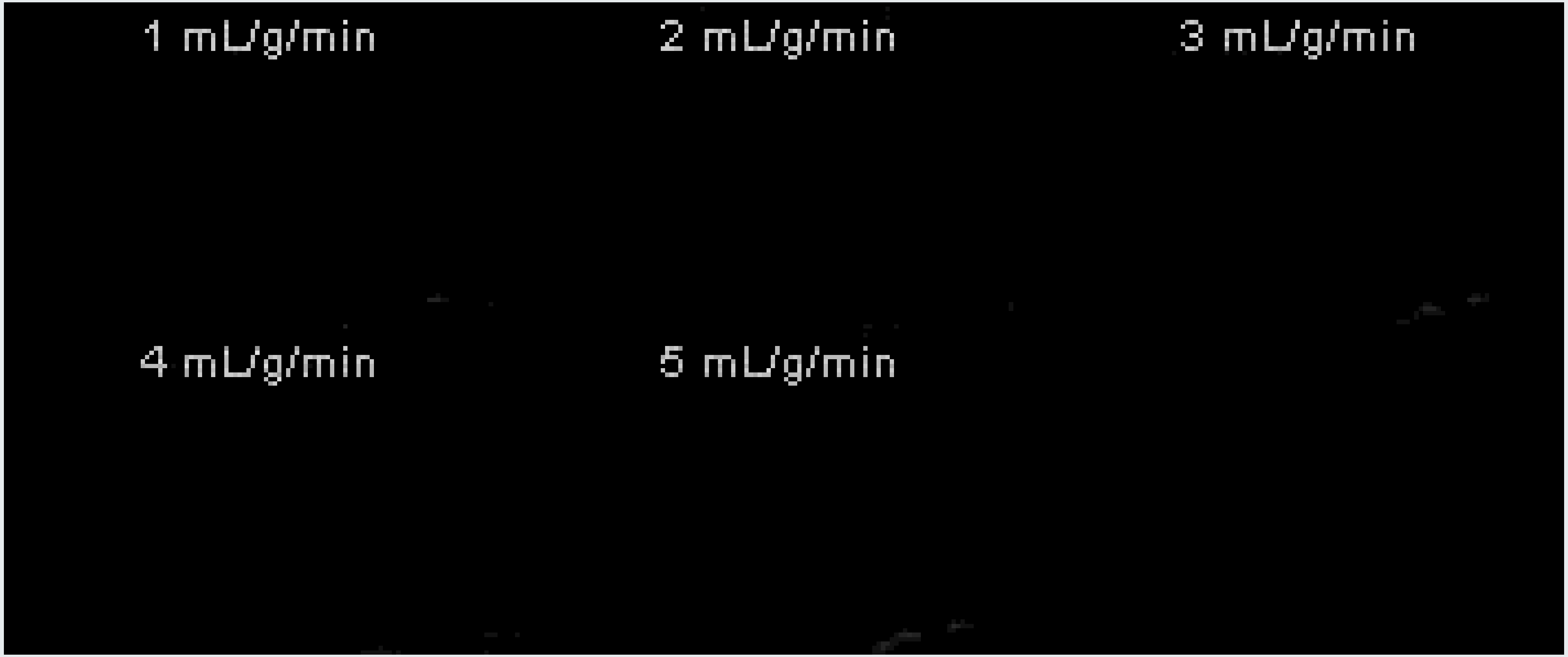


- Standard theory:
  - Signal intensity proportional to CA concentration
  - Mass conservation of CA in system
  - MRI-A: measures inlet concentration AIF or $c_{in}(t)$
  - MRI-B: measures average system concentration $C(t)$ or c_{sys}(t)
  - Single perfusion value $f_{sys} = \frac{q_{in}}{V_{sys}} = R_f(0) = \max(R_f(t))$

$$V_{sys} c_{sys}(t) = \int_0^t q_{in} c_{in}(s) ds - \int_0^t q_{out} c_{out}(s) ds$$

$$c_{sys}(t) = \frac{q_{in}}{V_{sys}} \int_0^t c_{in}(t-s) R(s) ds = \int_0^t c_{in}(t-s) R_f(s) ds$$

Perfusion MRI at KCL – Dyanimic Contrast Enhanced MRI scans



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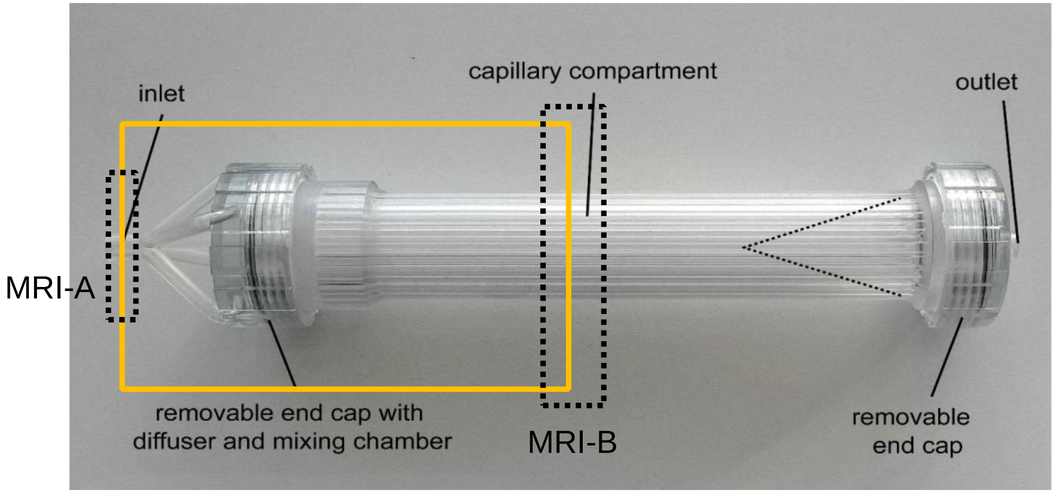
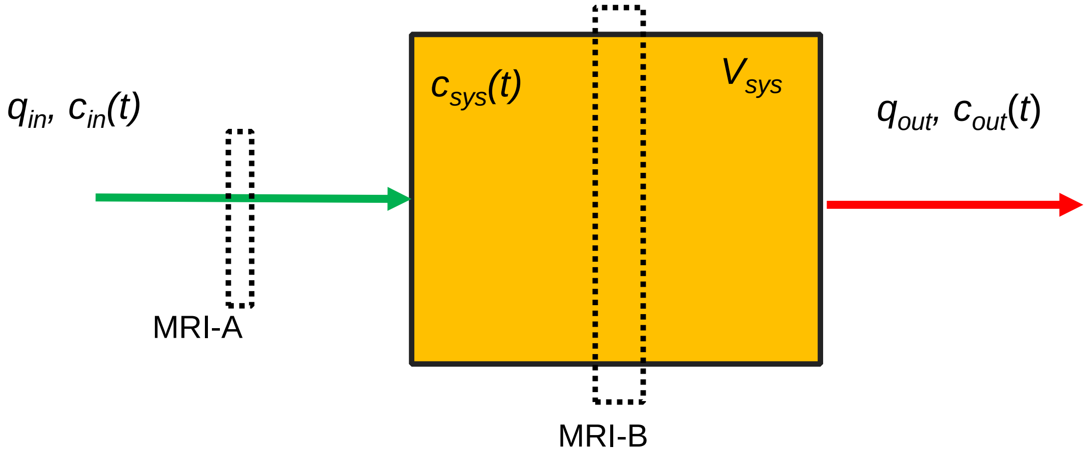
Questioning the standard model...

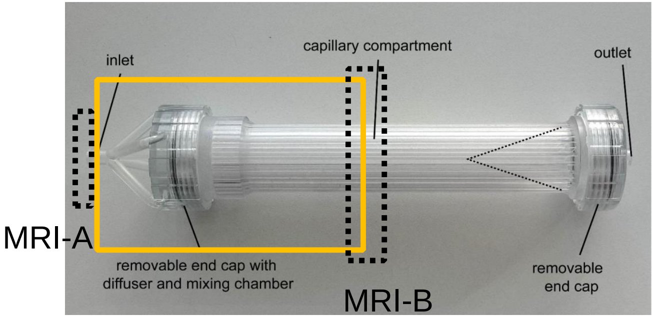
- Is the standard data analysis approach valid for the phantom?
- Is it reasonable to expect a 30 % variation in perfusion rate over the cross section?
- To what corresponds a voxel-wise or segment-wise perfusion value in the mathematical model?
- What is the definition of a voxel-wise or segment-wise perfusion value?



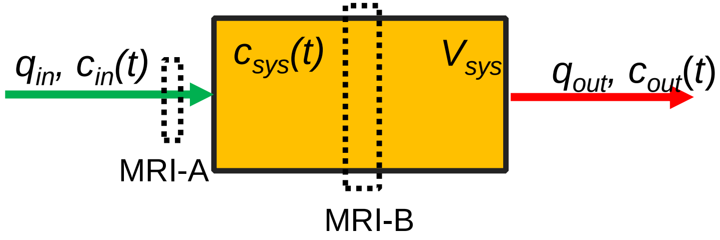


$$c_{sys}(t) = \int_0^t c_{in}(t-s) R_f(s) ds$$

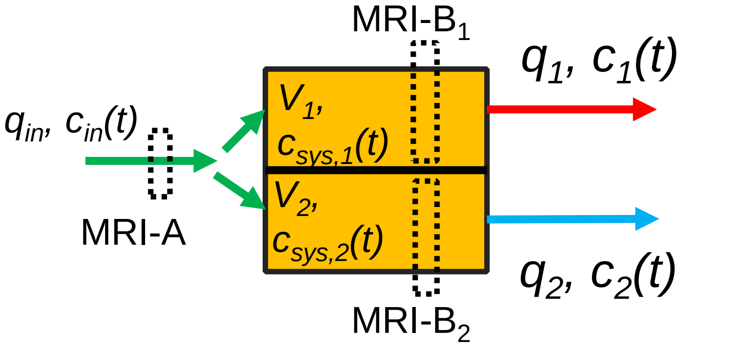
Model worries



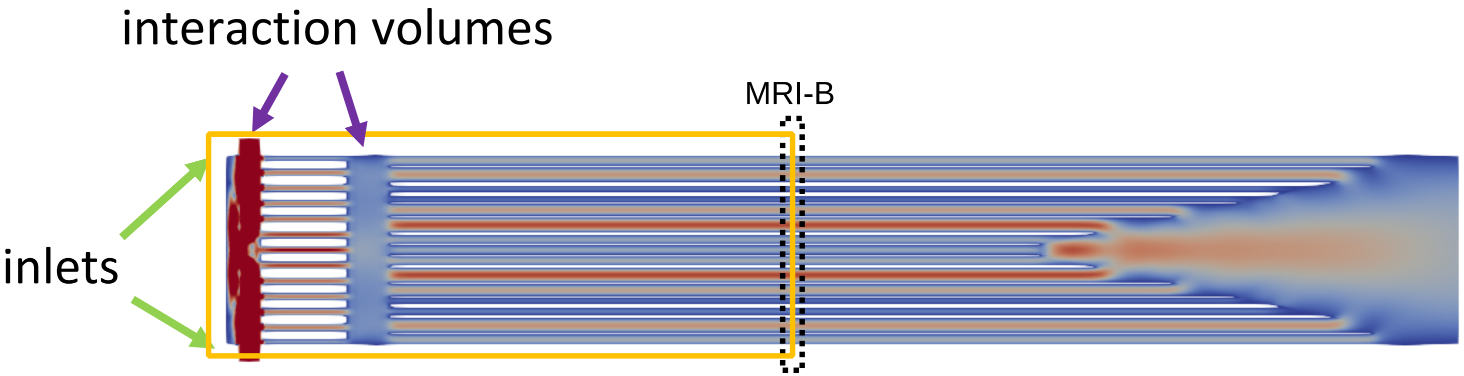
- At least for the phantom it is rather the **outflow concentration** $c_{out}(t)$ than the average system concentration $c_{sys}(t)$ which is measured (and $c_{sys}(t) \neq c_{out}(t)$)

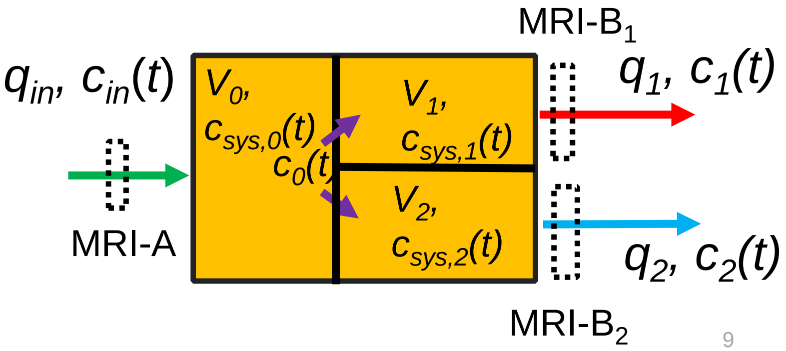


- The model does not explcitly take into account voxel-wise or channel-wise or **segment-wise perfusion**, there is just one perfusion value

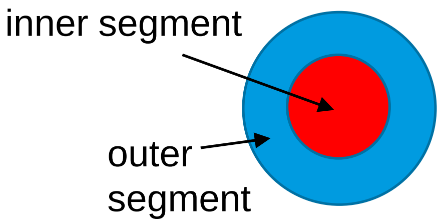


- **Juxtaposition** of multiple standard approache models doesn't take into account fluid dynamics of large pre-chamber
- **Explicit modeling of pre-chamber and segments** (voxels, channels), and of measuring the outflow concentration $c_{out}(t)$ may be more realistic

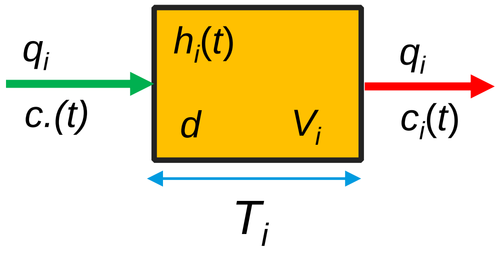




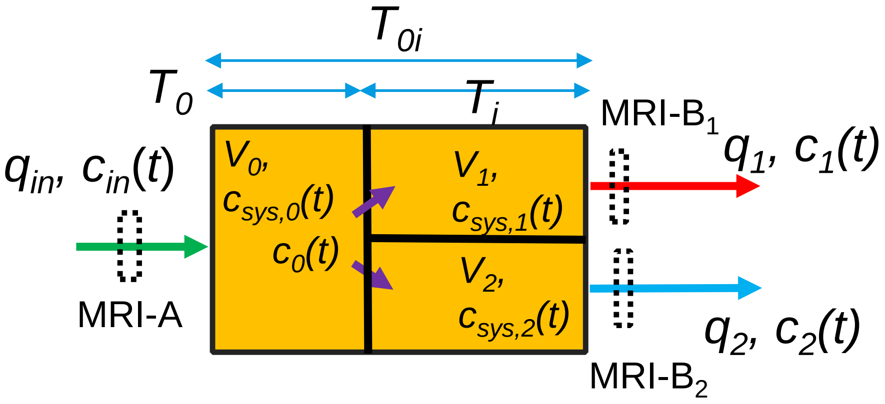
Alternative:
outflow concentation & multiple compartments



- Each compartment i has:
  - Volume V_i
  - Flow rate q_i
  - Inlet concentration from predecessor
  - Outlet concentration $c_i(t)$
  - Impulse response function $h_i(t)$
  - Mean transit time T_i
  - Tissue delay factor d
  - Perfusion $f_i = \frac{q_i}{V_i} = \frac{d}{T_i}$



$$c_i(t) = h_i(t) * c_.(t)$$



$$c_i = h_{0i} * c_{in} \qquad h_{0i} = (h_i * h_0)$$

$$T_{0i} = \int_0^\infty t\, h_{0i}(t)\, dt \qquad T_{0i} = T_0 + T_i$$

$$f_{0i} = \frac{d}{T_{0i}} \qquad f_i = \frac{d}{T_i} = \frac{q_i}{V_i}$$

- Of interest may be ratio $r = \frac{f_1}{f_2}$ (or $r' = \frac{f_{01}}{f_{02}}$)

$$T_{01} = \frac{d\, V_0}{q_{\text{in}}} + \frac{d\, V_1}{q_1}$$

$$T_{02} = \frac{d\, V_0}{q_{in}} + \frac{d\, V_2}{q_2}$$

$$q_{\text{in}} = q_1 + q_2$$

- Additional assumptions:
  - Existence of a constant tissue delay factor d, such that $T = d\, V/q$
  - Known compartment volumes V_0, V_1 and V_2 (or volume fractions)

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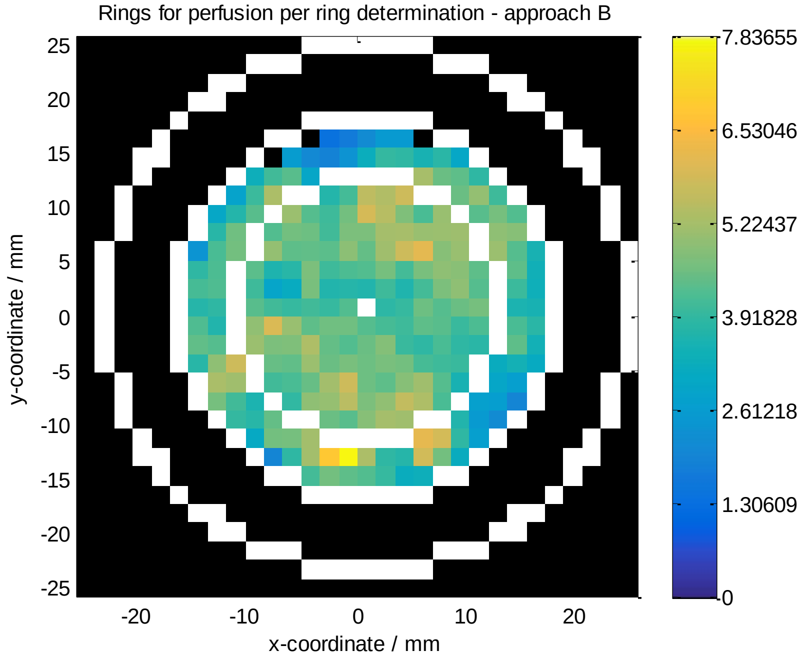
Application to phantom data

- Good reconstruction of global perfusion rate value (1 to 5 mL/min/g)
- Estimate of ratio of local perfusion rate through two segments not any better than following standard approach ☹
- Many voxels towards edge needed to be discarded
- Various effects of differences in the data analysis approaches mixed in this analysis
- Other non-ideal phenomena (e.g. non-ideal mixing) have their influence as well



q_0^{ref} / (mL/min)	r^A	r^B
55	0.89	0.79
110	0.79	0.82
165	0.85	0.87
220	0.91	0.92
275	0.82	0.85

$r^{ref} = 0.87 \pm 0.05$

Outlook

- Project partners are finishing a comparison with the phantom using different modalities (MRI, CT, PET)
- Separation of various effects involving the different data analysis methods using simulated data
  - Be there (again) @LNEC for MATHMET conference 20 - 22 November 2019!
- Application to patient data of alternative method (but turns out to be too time consuming for this project)

- **Final meeting & public engagement event** @ KCL London on Thursday 29 August 2019

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