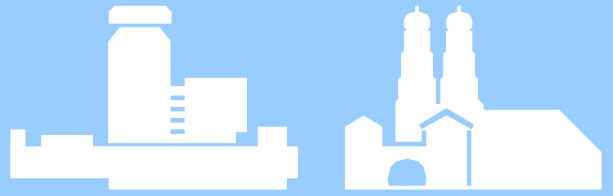


Tracer kinetics in the kidney with a two-compartment model

S. Sourbron

LMU Munich, Großhadern hospital

COST ACTION B21
Physiological Modelling of MR Image Formation
Renal MRI and Renal Modelling Working Groups Meeting

Bergen, 8 dec 2006

Contents

- Motivation
- Theory
- Study objectives and methods
- Results
  - 2 test-cases (ESMRMB 2006)
  - Volunteer data-base (ISMRM 2007)
- Future research

Motivation

Model-free analysis (perfusion)

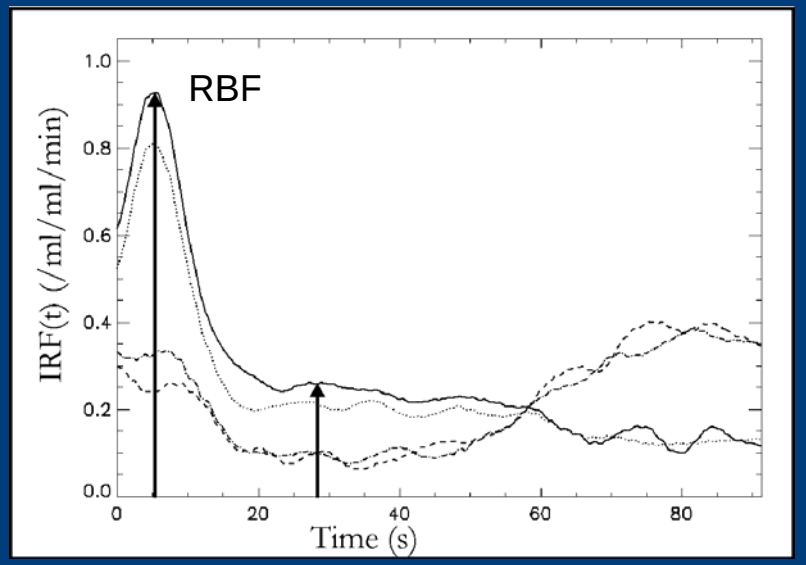
$$N(t) = C_{in}(t) * F\,R(t)$$

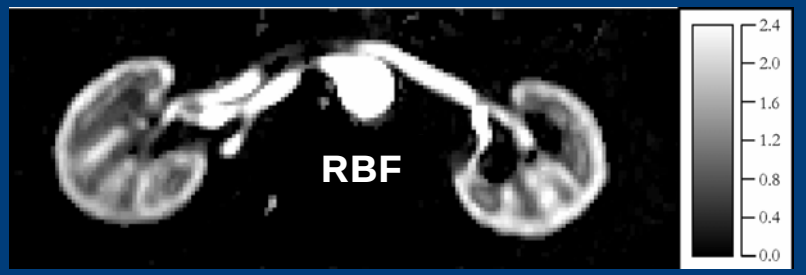
$$\downarrow$$

$$IRF(t) = F\,R(t)$$

$$\downarrow$$

$$F = \max(IRF)$$





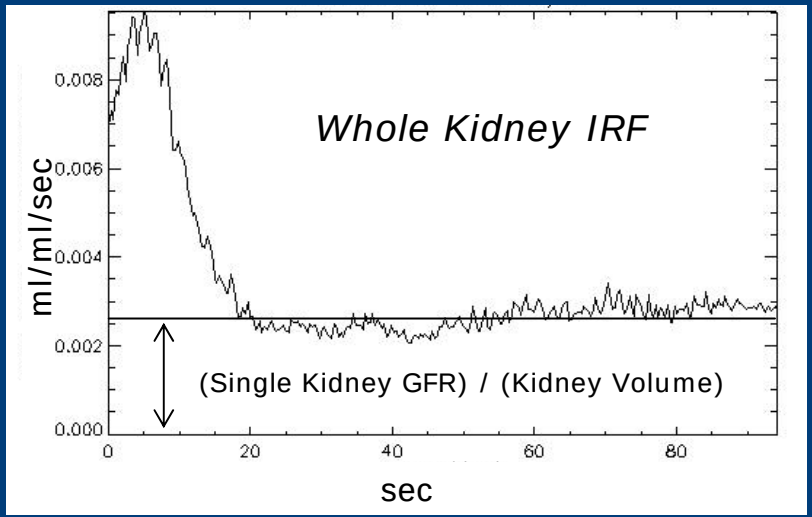
Sourbron (2005) PhD thesis, VU Brussel

Dujardin et al. (2005) *MRM* **54** 841

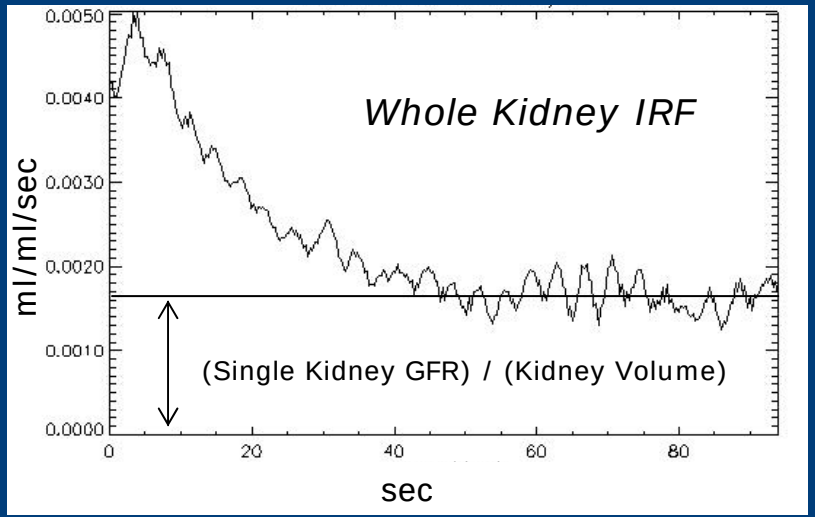
Motivation

Model-free analysis (filtration)

Male 53y (Healthy)
Serum creatinine 0.84 ml/100 ml
Creatinine Clearance 57.6 ml/min
MRI-GFR 37.5 ml/min



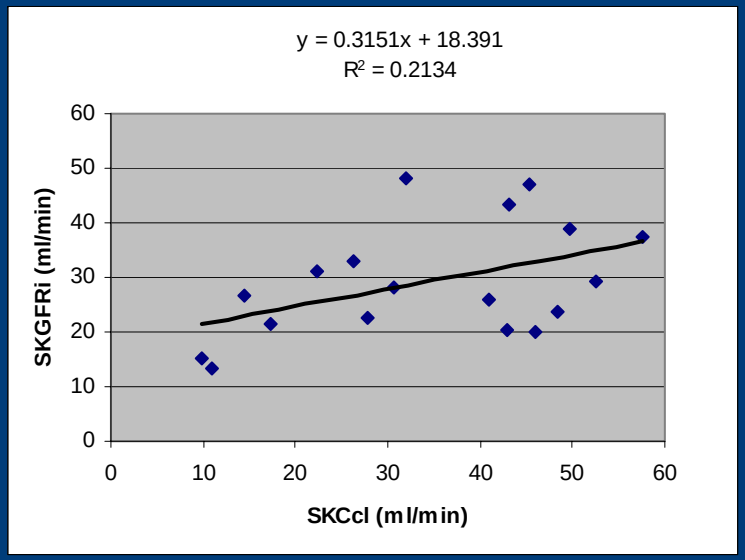
Male 54y (Under chemotherapy)
Serum creatinine 1.8 ml/100 ml
Creatinine Clearance 43 ml/min
MRI-GFR 22.7 ml/min



Dujardin et al. (2005) *ESMRMB* Basel

Motivation

Towards a modelling approach



Dujardin et al. (2005) *ESMRMB* Basel

Model-free filtration

- Weak correlation
- Justification?
- Subjective?

Modelling methods

- Clear interpretation
- User-independent
- Additional parameters

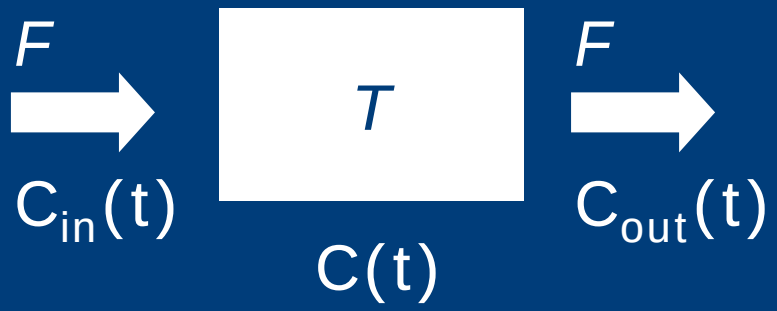
Motivation

Some Context

- 1-compartment model
  - ROI, rats (Baumann 2000)
- 2-compartment model
  - Patlak
    - ROI, humans (Hackstein 2003)
    - ROI, rats (Pedersen 2004)
    - Voxel, humans (Grenier 2006)
  - Tofts
    - ROI, humans (Buckley 2006)
  - Separable
    - ROI, rabbits (Annet 2004)
    - Voxel, ROI, humans (...)
- 3-compartment model
  - ROI, humans (Hackstein 2003)

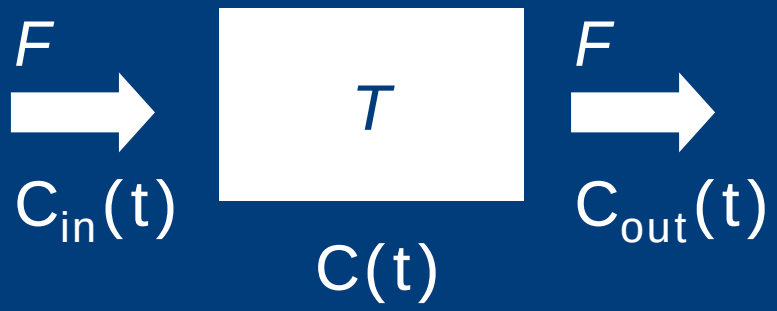
Theory

A single compartment



Theory

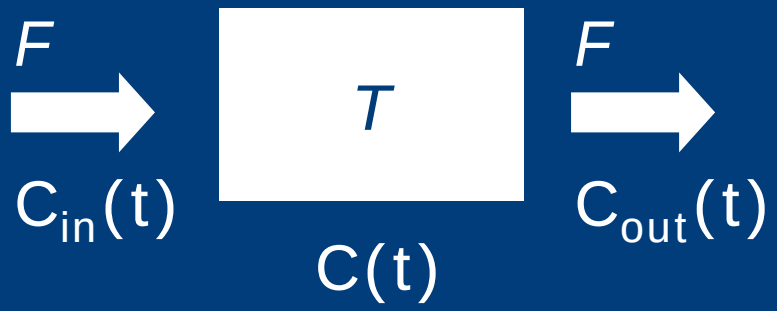
A single compartment



„A region of space where the contrast agent is well-mixed“

Theory

A single compartment



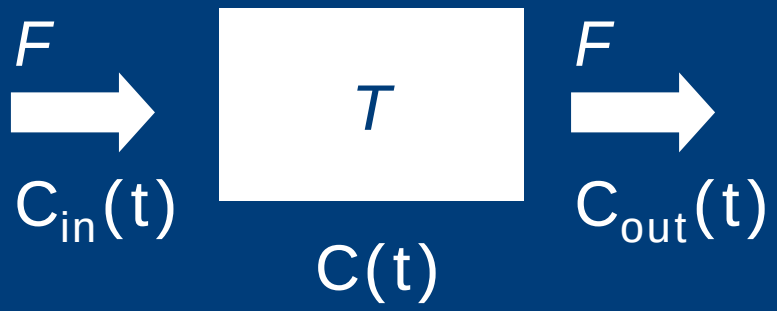
„A region of space where the contrast agent is well-mixed“

$$\Downarrow$$

$$C_{out}(t) = C(t)$$

Theory

A single compartment



„A region of space where the contrast agent is well-mixed“

$$\Downarrow$$

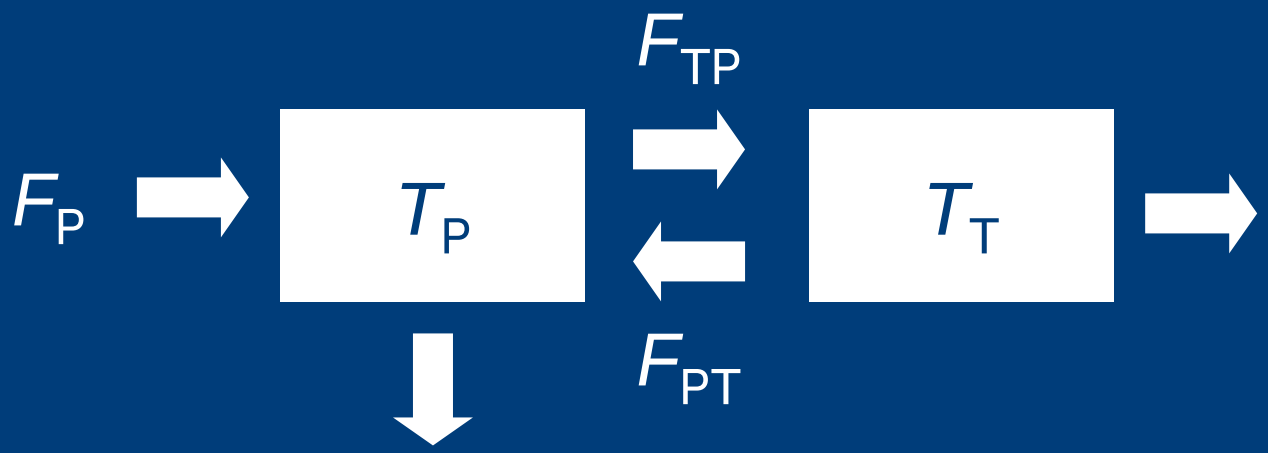
$$C_{out}(t) = C(t)$$

$$\Uparrow\Downarrow$$

$$N(t) = C_{in}(t) * F\, e^{-t / T}$$

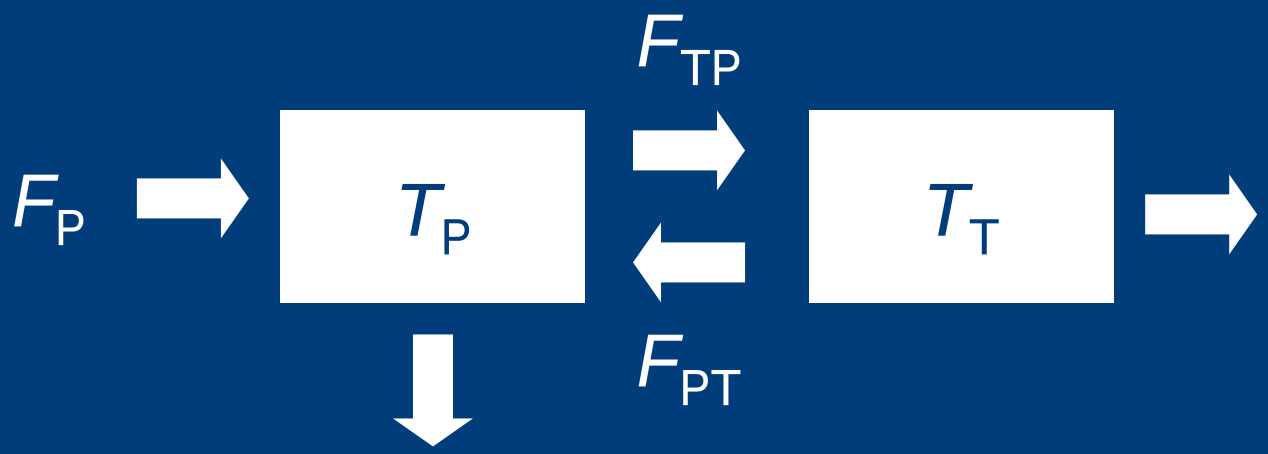
Theory

2-compartment model (single inlet)



Theory

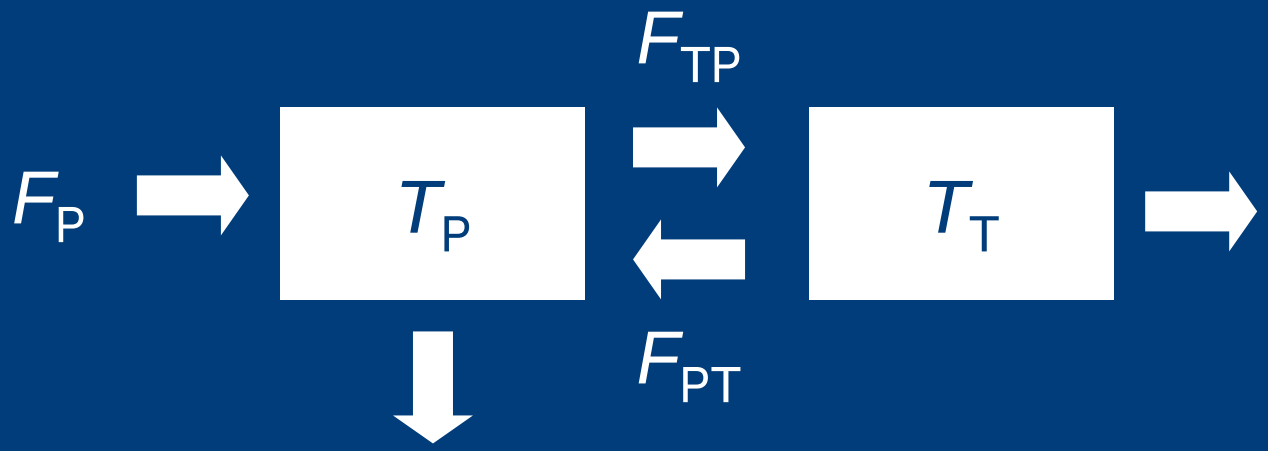
2-compartment model (single inlet)



$$N(t) = C_{in}(t) * (F_{-}e^{-t / T_{-}} + F_{+}e^{-t / T_{+}})$$

Theory

2-compartment model (single inlet)



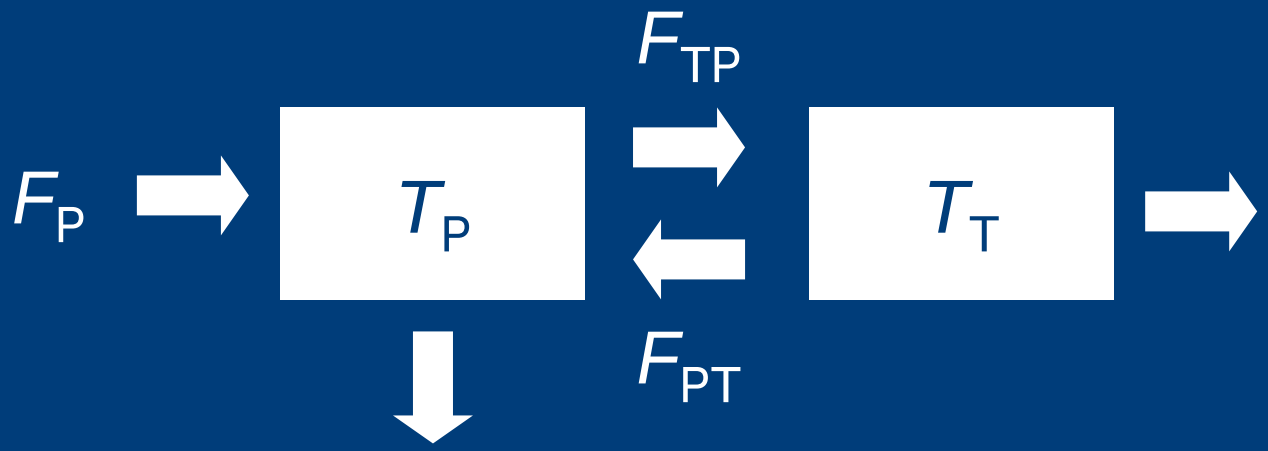
$$N(t) = C_{in}(t) * (F_- e^{-t / T_-} + F_+ e^{-t / T_+})$$

$\Downarrow$?

F_P , F_{TP} , F_{PT} , T_P , T_T

Theory

2-compartment model (single inlet)



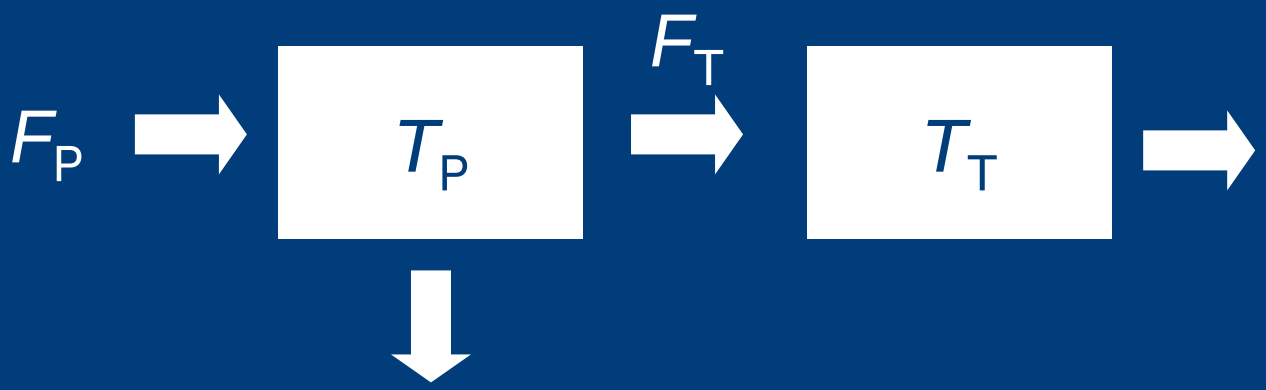
$$N(t) = C_{in}(t) * (F_- e^{-t / T_-} + F_+ e^{-t / T_+})$$

4 parameter fit → 5 parameter model !

$$F_P , F_{TP} , F_{PT} , T_P , T_T$$

Theory

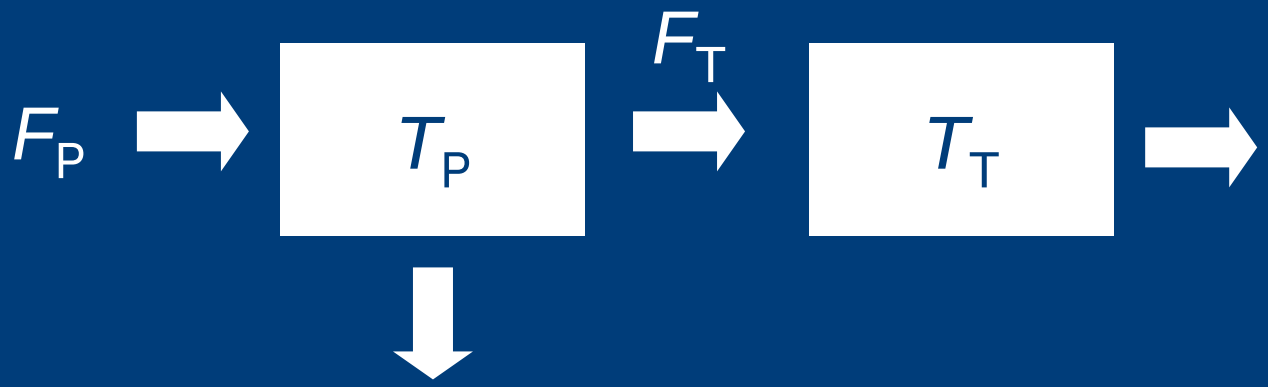
Separable 2-compartment model (single inlet)



Annet et al. (2004) with different terminology

Theory

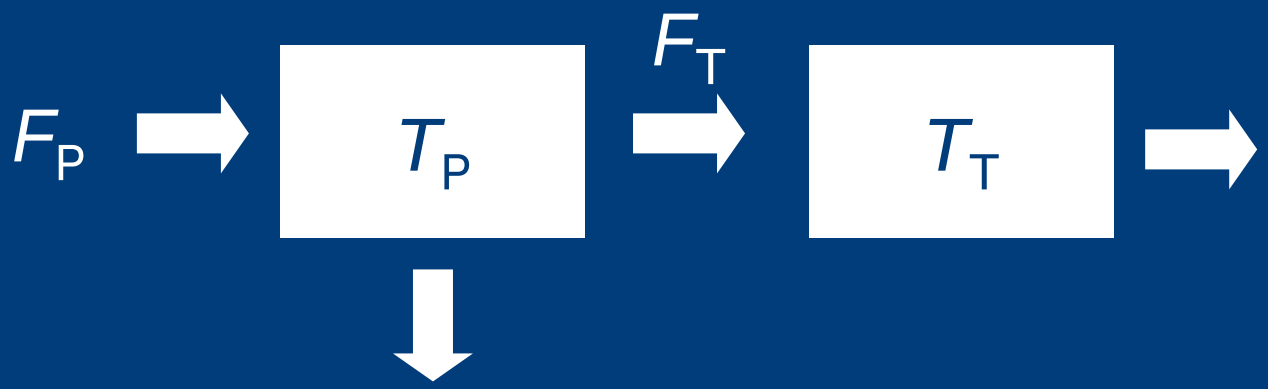
Separable 2-compartment model (single inlet)



$$N(t) = C_{in}(t) * F_P R_P(t) + C_{in}(t) * H_P(t) * F_T R_T(t)$$

Theory

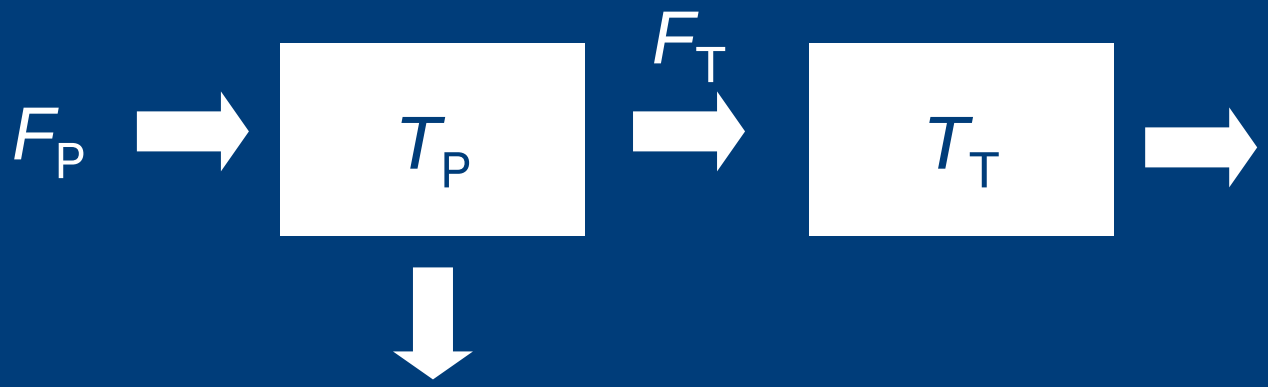
Separable 2-compartment model (single inlet)



$$N(t) = C_{in}(t) * F_P \, e^{-t / T_P}$$
$$+ C_{in}(t) * T_P^{-1} e^{-t / T_P} * F_T \, e^{-t / T_T}$$

Theory

Separable 2-compartment model (single inlet)



$$N(t) = C_{in}(t) * F_P \, e^{-t / T_P}$$
$$+ C_{in}(t) * T_P^{-1} e^{-t / T_P} * F_T \, e^{-t / T_T}$$

$$\Downarrow$$

$$F_P , F_T , T_P , T_T \qquad (\Rightarrow V_X = F_X T_X)$$

Theory

Common approximations

$$N(t) = C_{in}(t) * F_P \, e^{-t / T_P} + C_{in}(t) * T_P^{-1} e^{-t / T_P} * F_T \, e^{-t / T_T}$$

$\Downarrow$ $T_P \rightarrow 0$, $V_P = const$ („Tofts“ approximation)

$$N(t) = C_{in}(t) \, V_P + C_{in}(t) * F_T \, e^{-t / T_T}$$

Theory

Common approximations

$$N(t) = C_{in}(t) * F_P \, e^{-t / T_P} + C_{in}(t) * T_P^{-1} e^{-t / T_P} * F_T \, e^{-t / T_T}$$

$\Downarrow$ $T_P \rightarrow 0$, $V_P = const$ („Tofts“ approximation)

$$N(t) = C_{in}(t) \, V_P + C_{in}(t) * F_T \, e^{-t / T_T}$$

$\Downarrow$ $T_T \rightarrow \infty$, $F_T = const$ („Patlak“ approximation)

$$N(t) = C_{in}(t) \, V_P + C_{in}(t) * F_T$$

Study objectives

Why approximate?

Or: Optimize and evaluate the separable 2-compartment model for the quantification of filtration and perfusion in humans on ROI- and voxel level

Methods

Measurement protocol

- MRI protocol
  - 1.5 T (Siemens Avanto)
  - 2D SR-TURBO-FLASH (TR 254ms, TE 1.04ms, FA 12°, Matrix 192x154)
  - 1 sec , 4 slices (1 axial, 3 coronal)
- 15 Volunteers
  - 7ml Gd-BOPTA (0.5 mM) at 4ml/sec (Multihance, Bracco-Altana)
  - Breath-hold for 60s + PACE triggering
- 1 Patient
  - Left renal artery stenosis
  - 7ml Gadobutrol (1.0 mM) at 4ml/sec (Gadovist, Schering)
  - Free-breathing + triggering on post-processing

Methods
Post-processing

- Signal → Signal Enhancement
- Manual ROI selection
  - Aorta, Whole Kidney, Cortex
  - Manual motion correction!
- Tracer kinetic analysis

(1) Deconvolution

(2) Patlak 2-compartment model
  - Linear fit (40-110 sec after contrast arrival)

(3) Tofts + open 2-compartment models
  - Non-linear fit (all dynamics)
  - Fixed initial values (= literature values)

First Results

2 test-cases, no motion correction

First Results

Curve fits (volunteer)

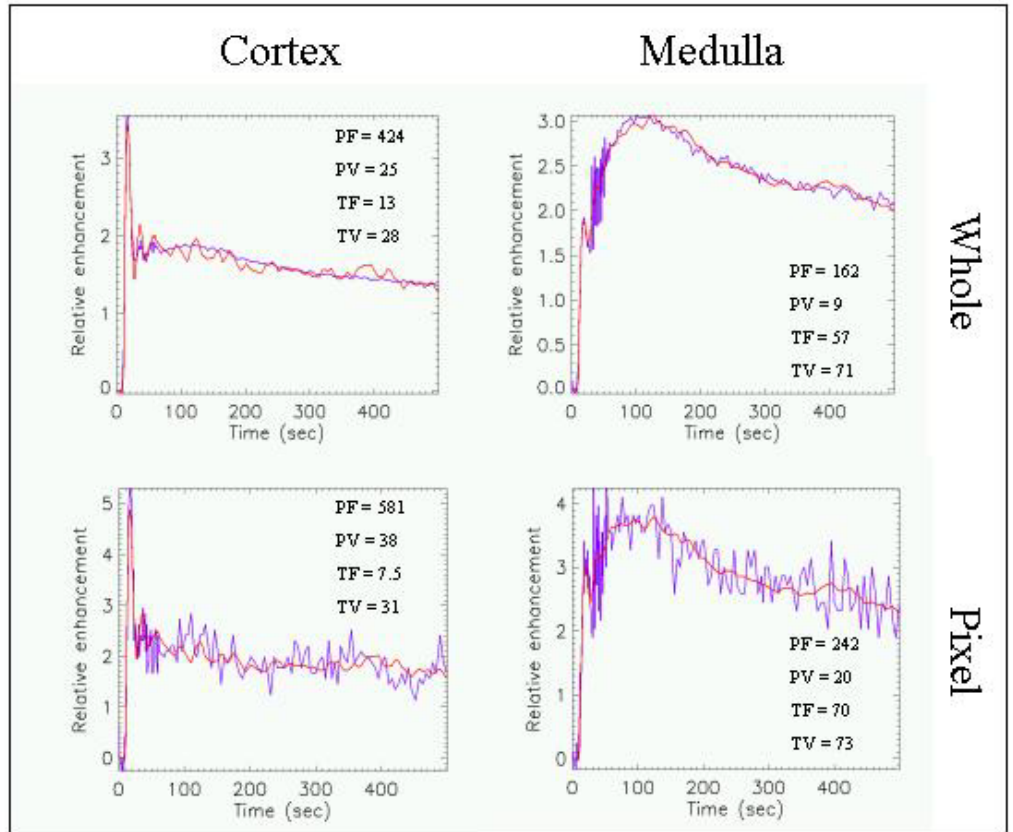
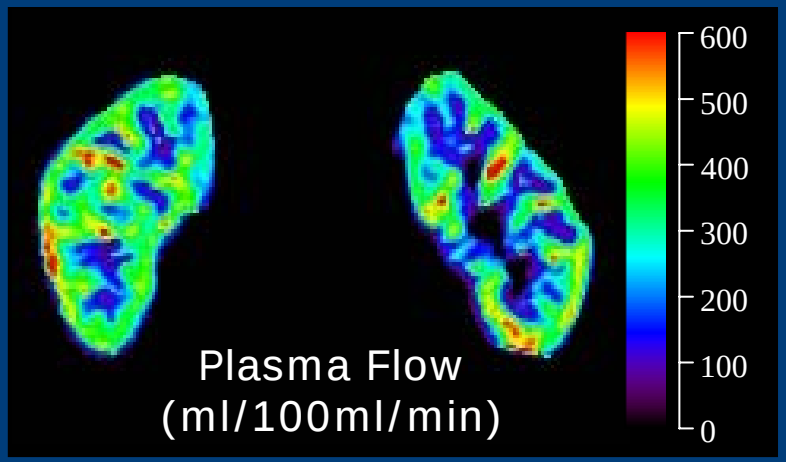
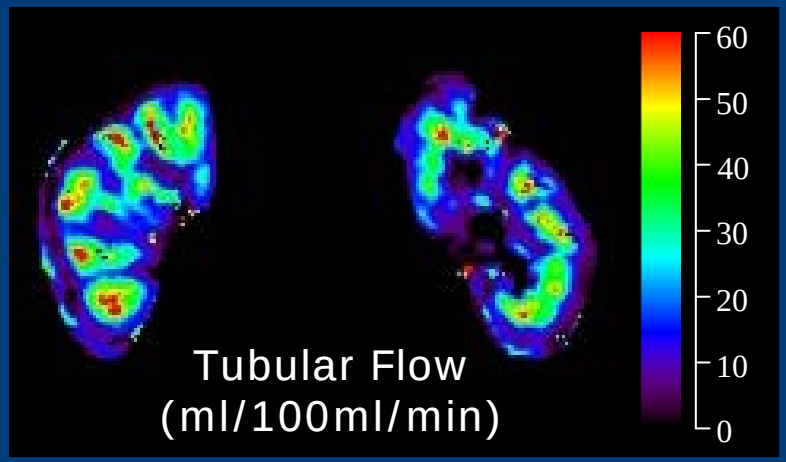


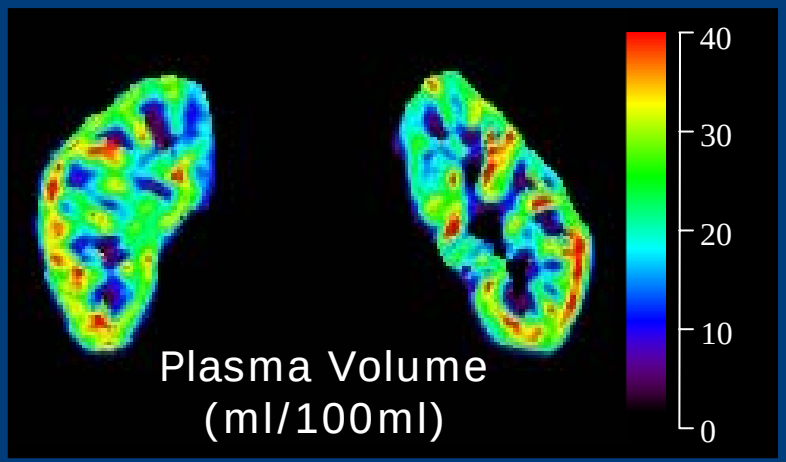
Figure 1. A plot of the data (blue) and the fit provided by the model (red) for the cortex (left column) and the medulla (right column). The top row gives the result for the whole-ROI curves, the bottom row for an individual pixel inside the ROI. Values for the fitted model parameters are presented next to the curves. Flow values (PF and TF) are given in ml/100ml/min, volumes (PV and TV) in ml/100ml.

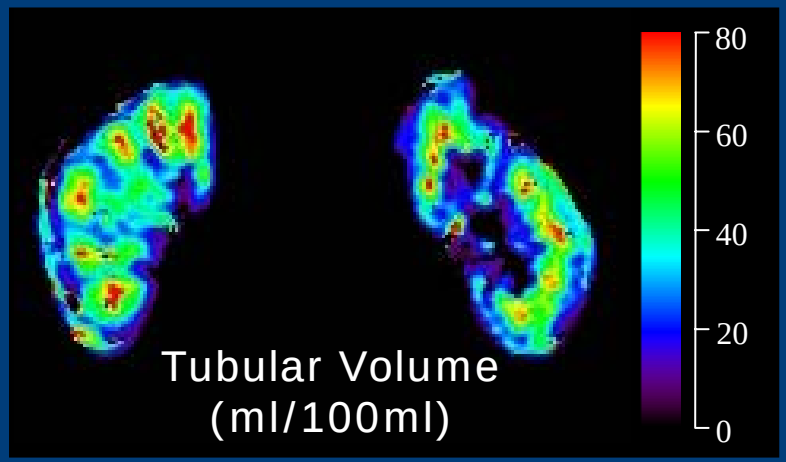
First Results

Pixel data (volunteer)





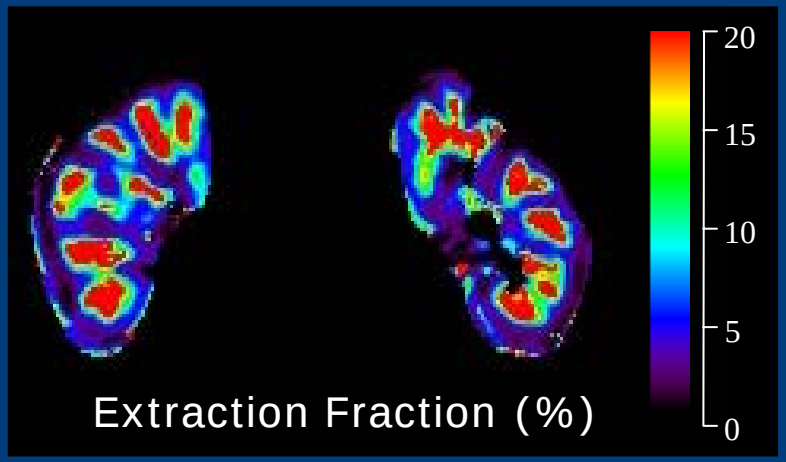


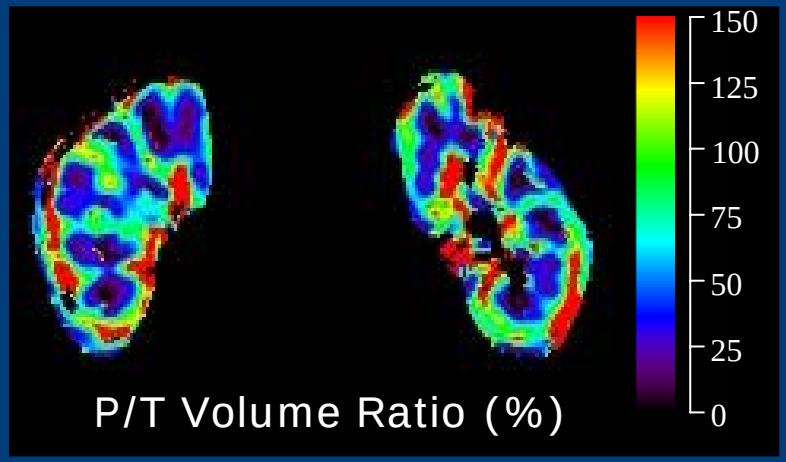


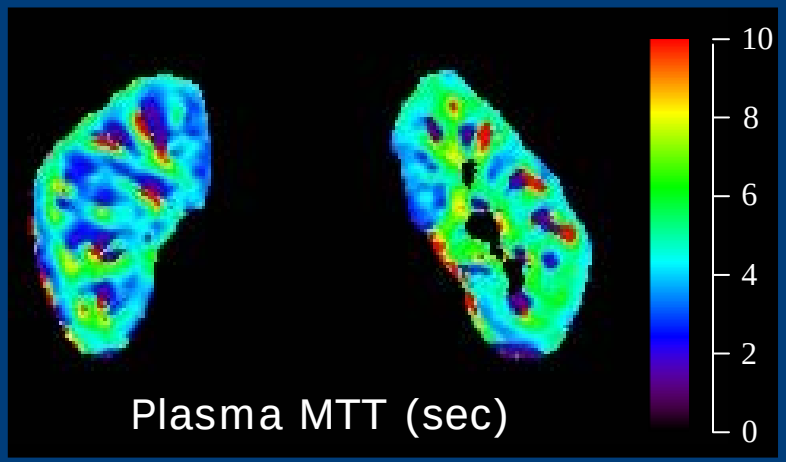
Note: interpretation invalid in the medulla

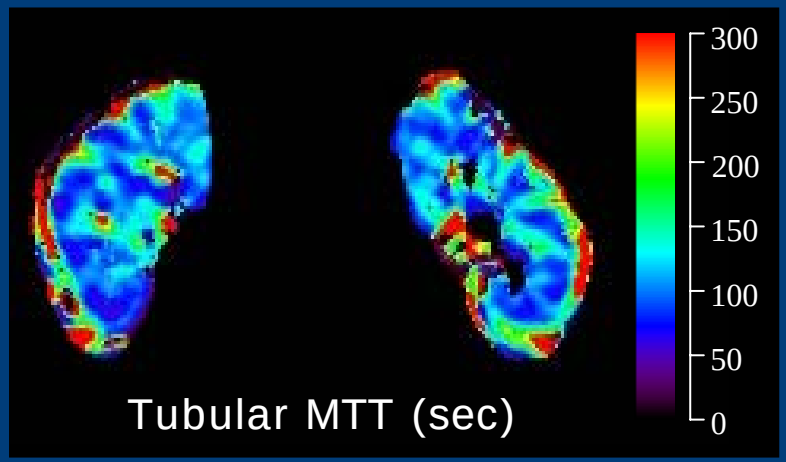
First Results

Pixel data (volunteer)



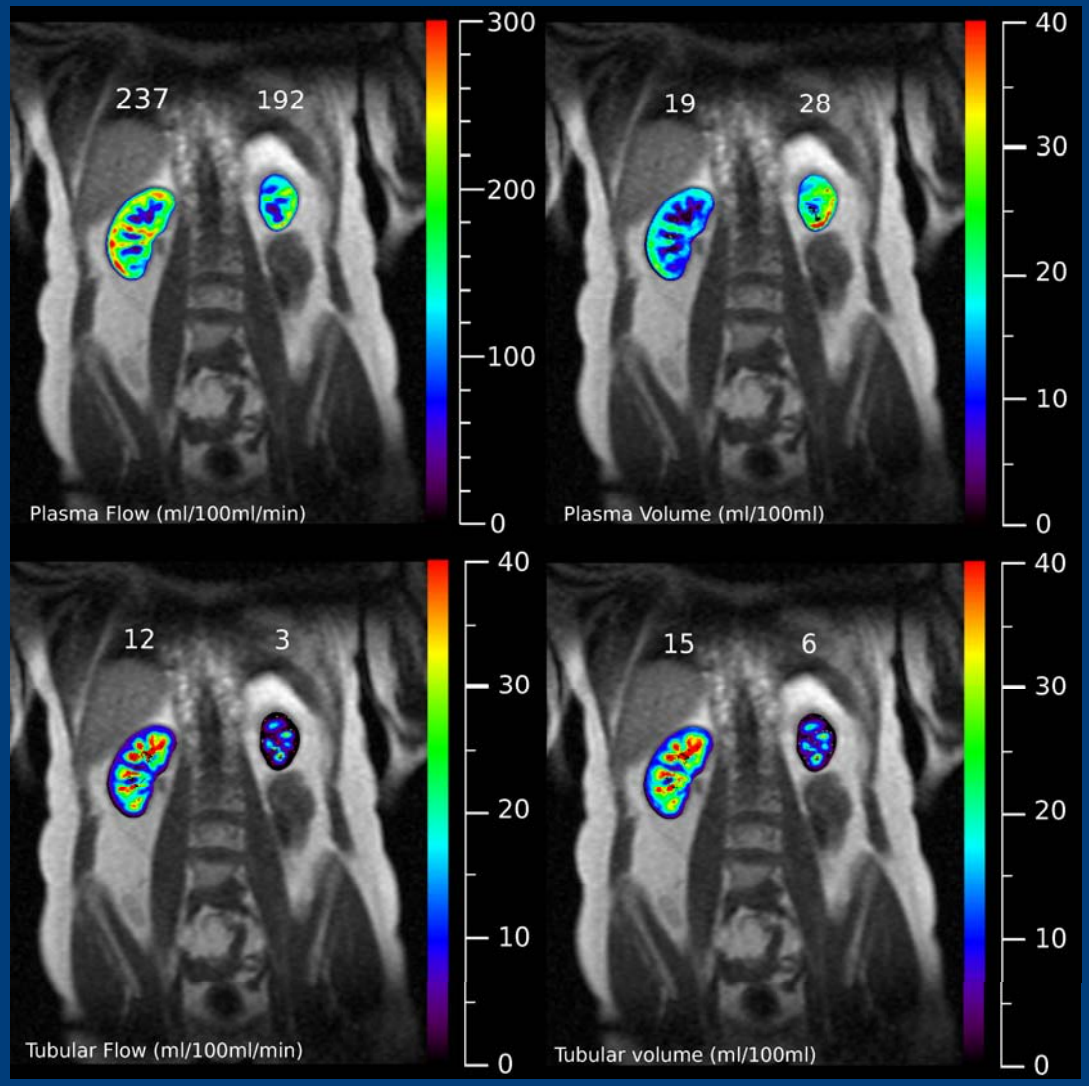






First Results

Pixel data (patient)

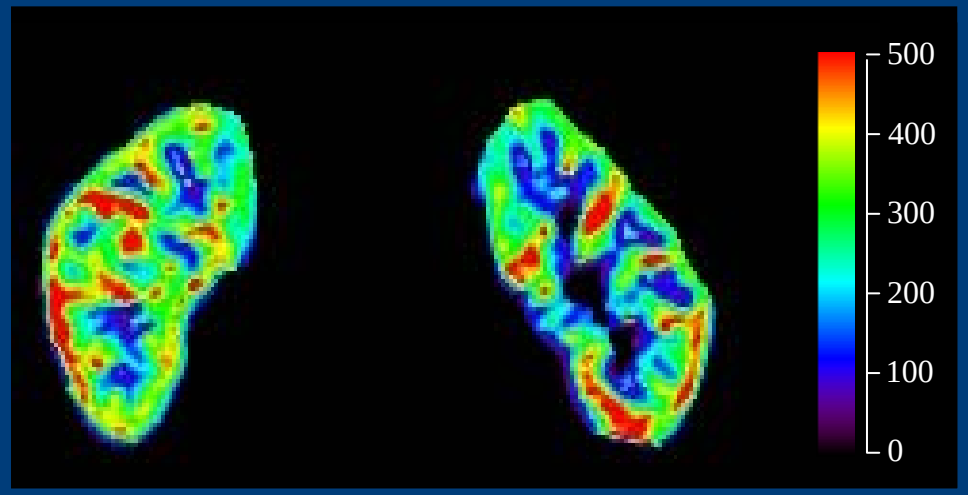


First Results

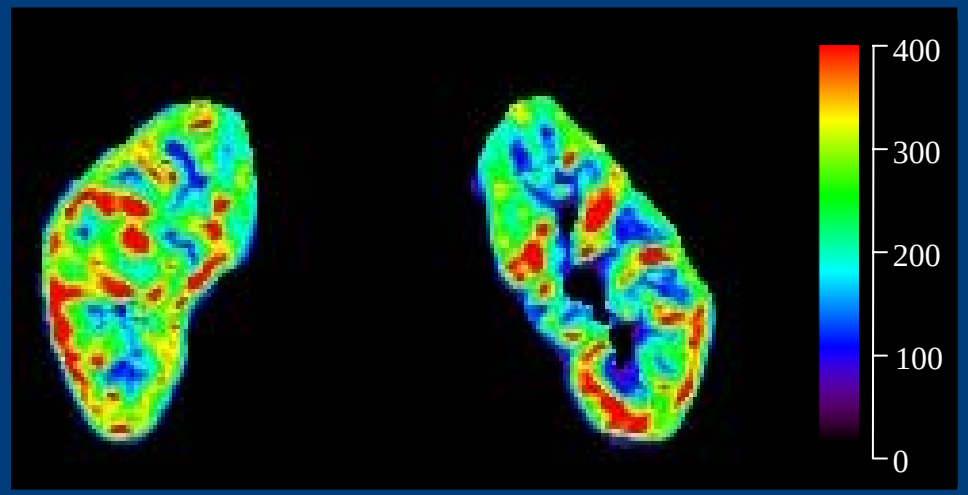
Comparison to deconvolution (volunteer)

Plasma Flow (ml/100ml/min)

2-compartment model

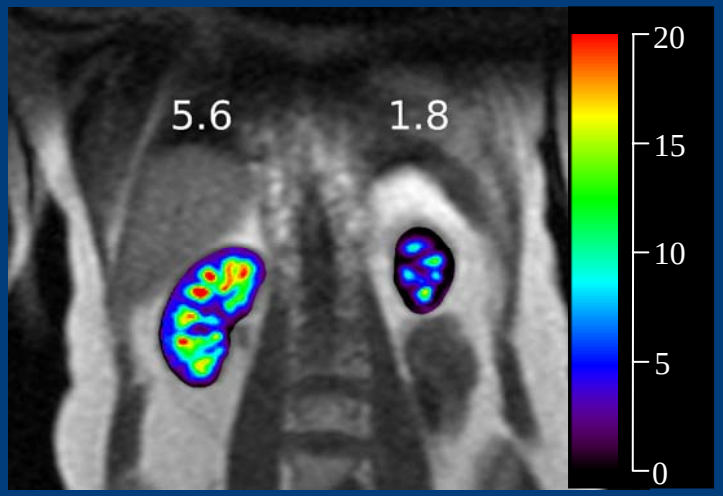
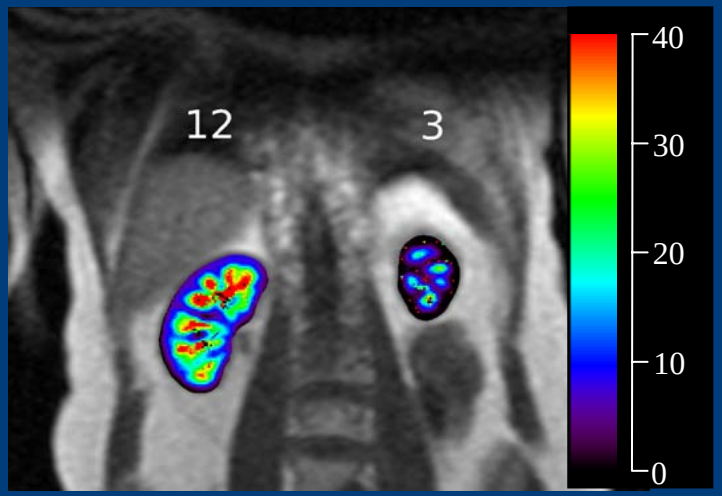
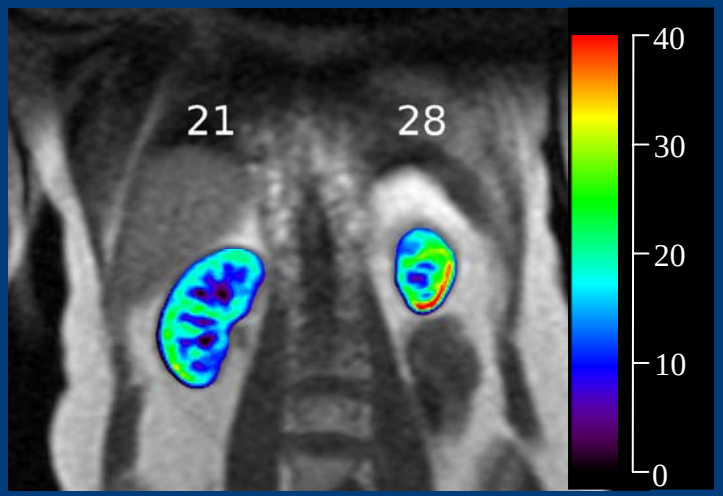
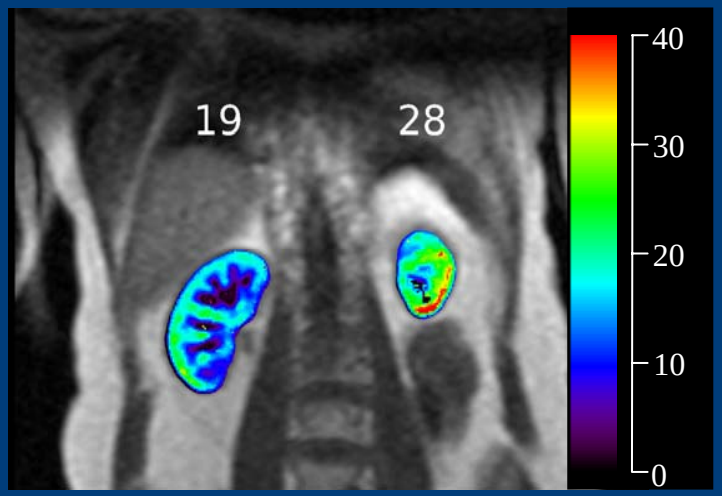


Deconvolution



First Results

Comparison to Patlak (patient)

	Patlak	2-compartment model
Tubular Flow (ml/100ml/min)		
Plasma Volume (ml/100ml)		

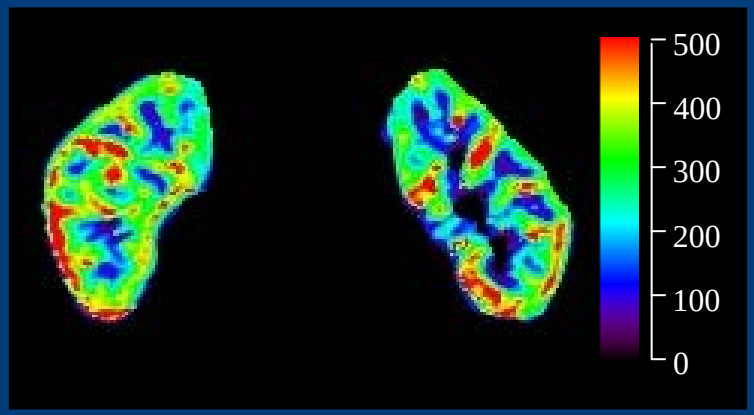
First Results

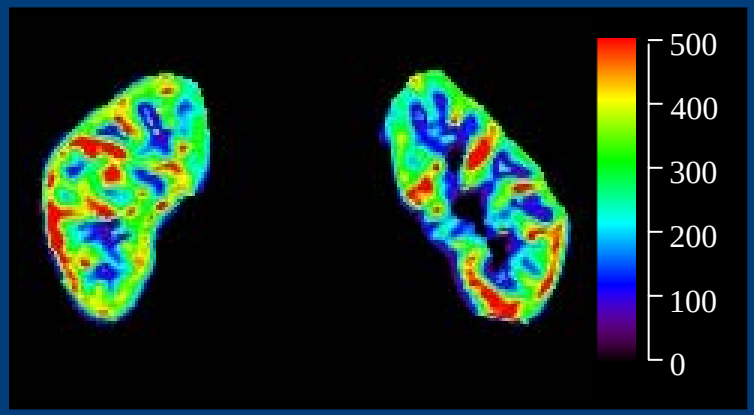
Temporal constraints (volunteer)

Measurement time
8 min

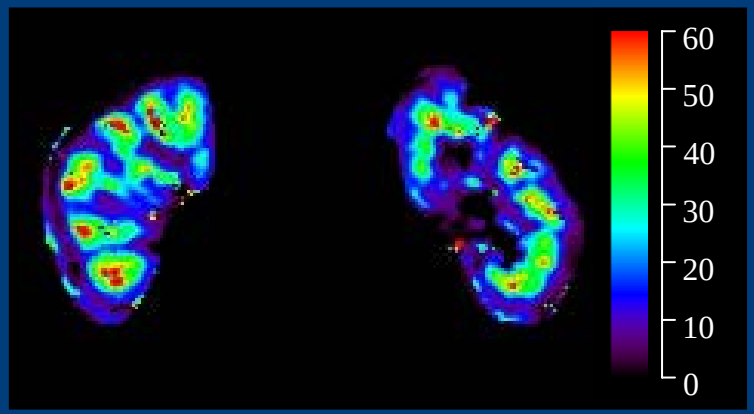
Measurement time
1 min

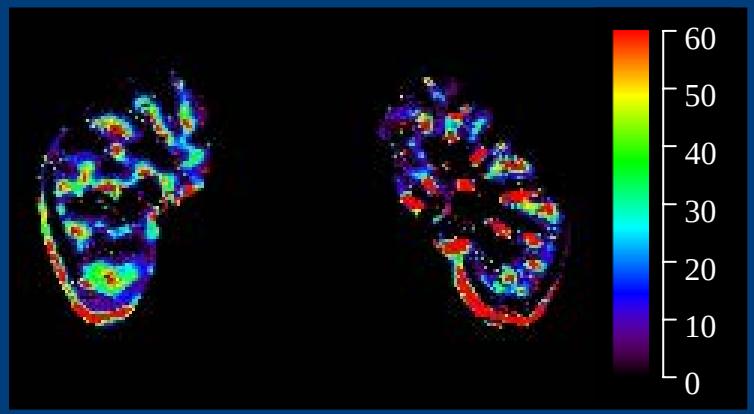
Plasma Flow
(ml/100ml/min)





Tubular Flow
(ml/100ml/min)





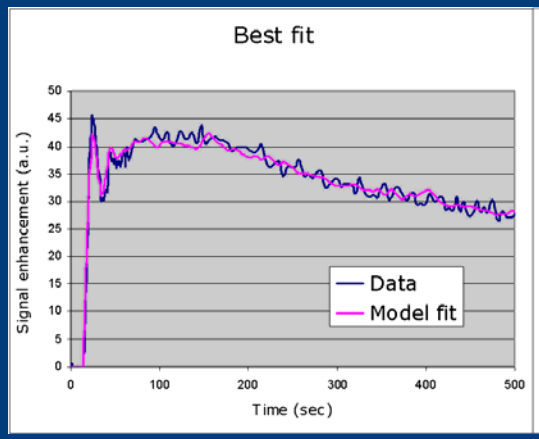
Results

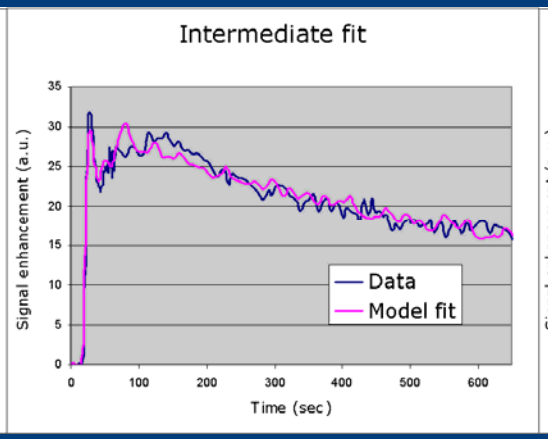
15 volunteers

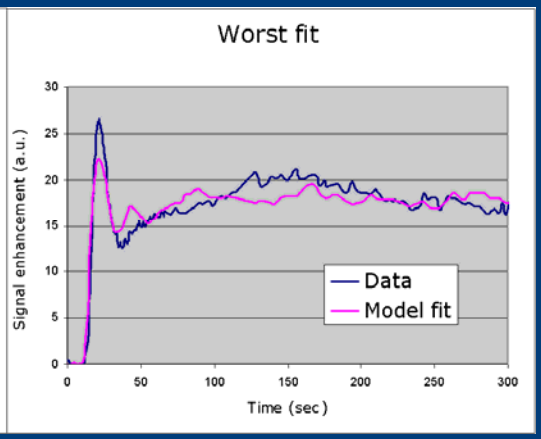
Results

ROI data (15 volunteers)

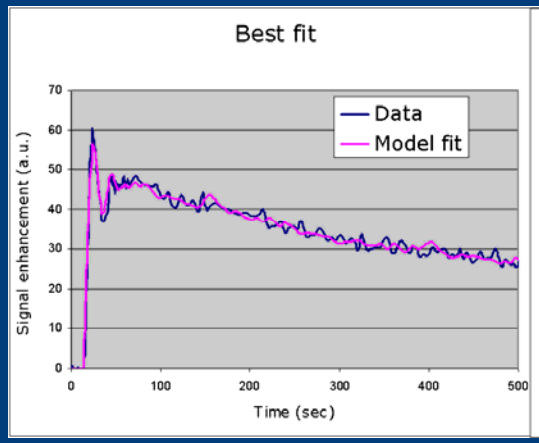
KIDNEY

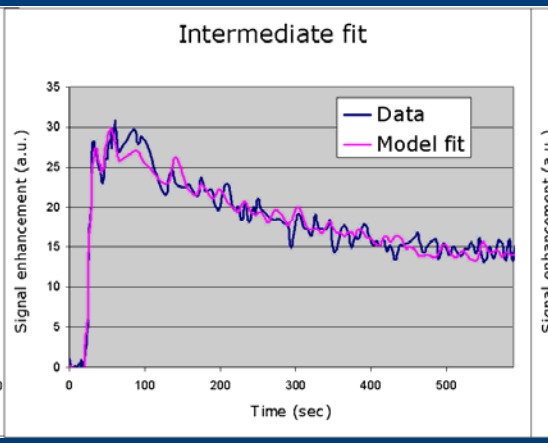


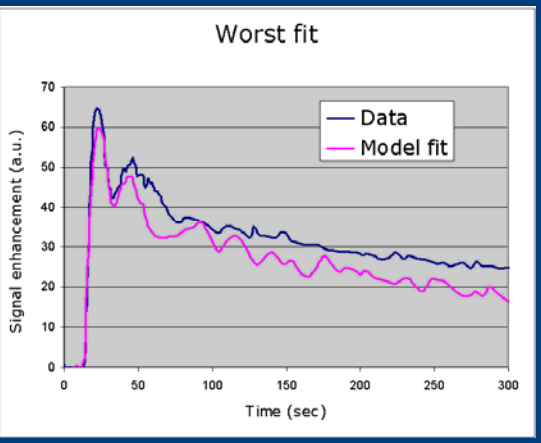




CORTEX







Results

ROI data (15 volunteers)

4-Parameter fit	KIDNEY		CORTEX	
	Mean	Stddev	Mean	Stddev
Plasma Flow (ml/100ml/min)	229	57	340	86
Plasma Volume (ml/100ml)	24	3.4	36	4.7
Tubular Flow (ml/100ml/min)	15	3.6	10	5.4
Tubular Volume (ml/100ml)	31	12	19	7.7
Plasma Mean Transit Time (sec)	6.5	1.3	6.6	1.2
Tubular Mean Transit Time (sec)	125	55	123	62
Root-Mean-Square Error (%)	0.5	0.2	0.8	0.8

Table 1: Mean and standard deviations of the fitted model parameters and the relative root-mean-square error of the fit. The mean transit times of both compartments can be obtained from the four fit parameters using the central volume theorem.

Note: „Typical“ values

TF: (120 ml/min) / 400g
= 30 ml/min/100g

PF: 220-275 ml/100g/min (cortex)

PV: 15 ml/100g (cortex)

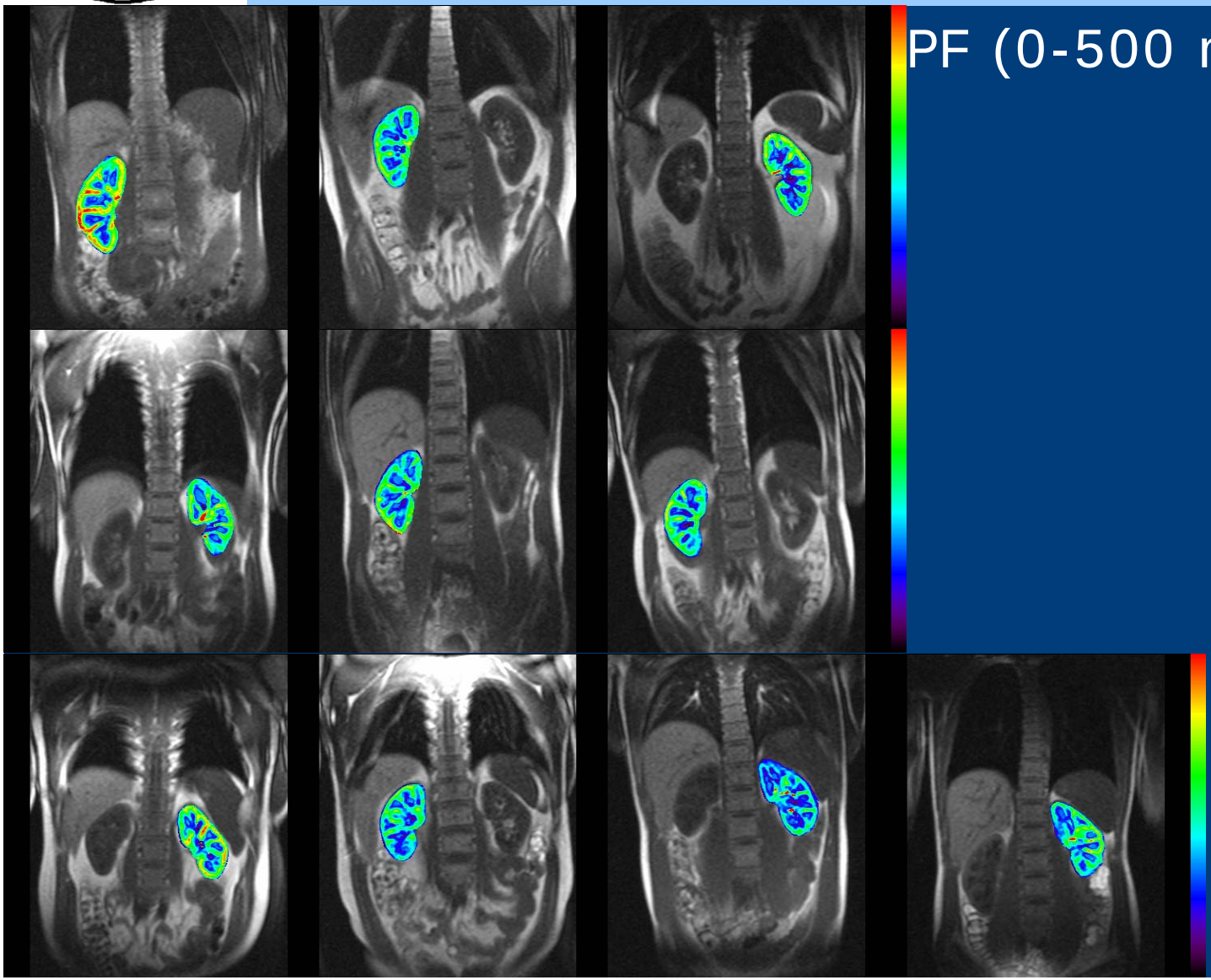
PT: 3-5 sec (capillary bed)

TT: 1-3 min

??

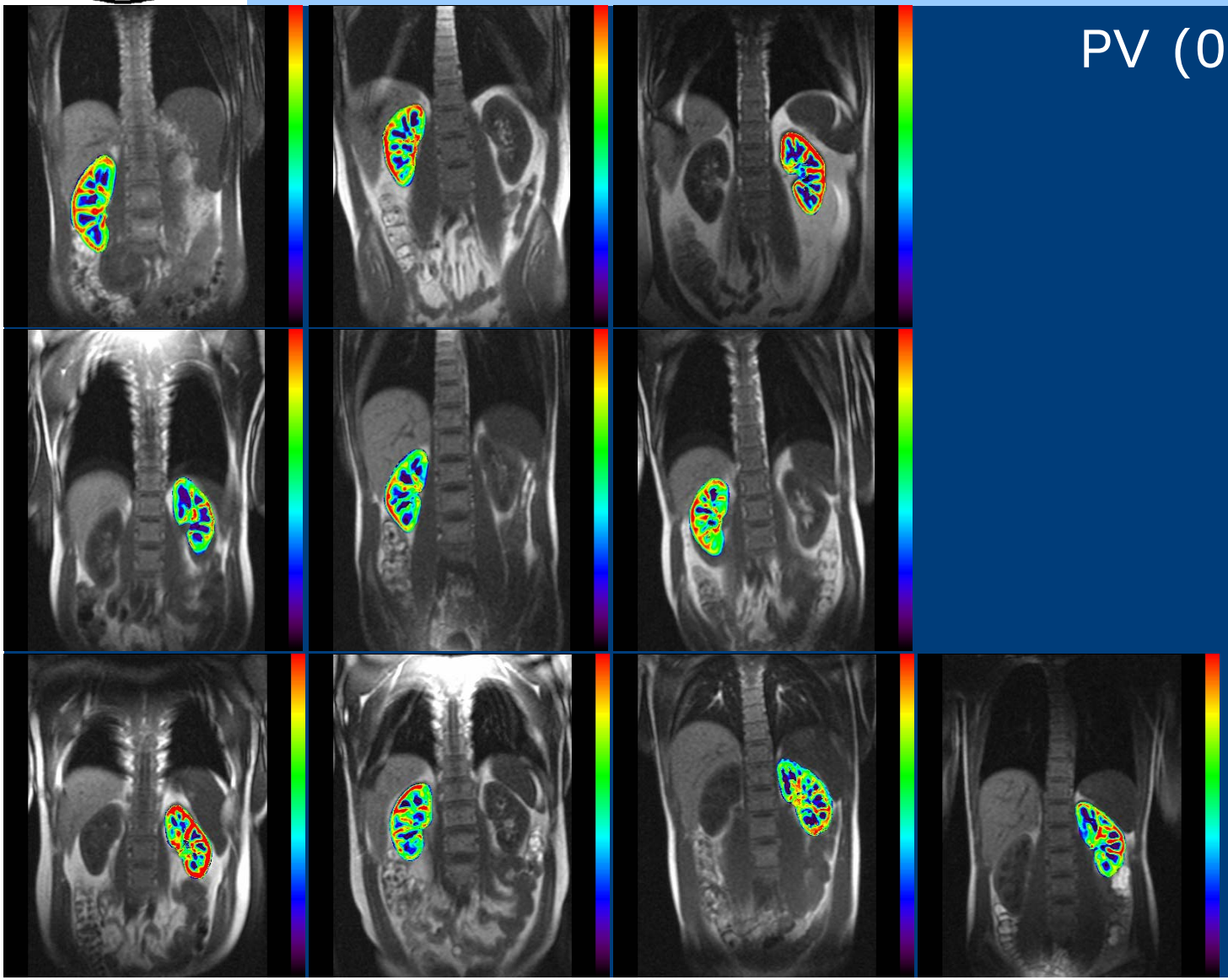
Results

Pixel data (10/15 volunteers)



Results

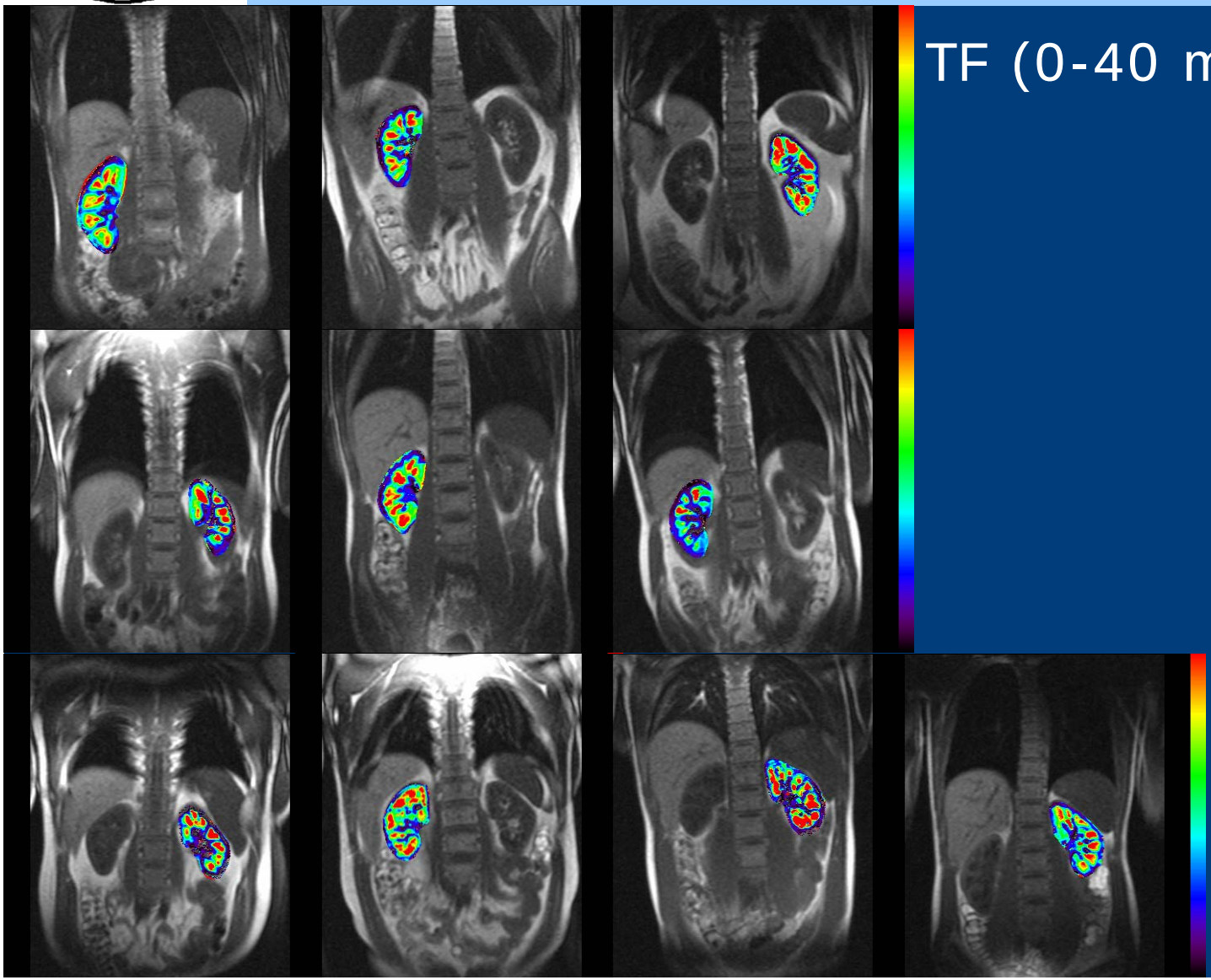
Pixel data (10/15 volunteers)



PV (0-40ml/100ml)

Results

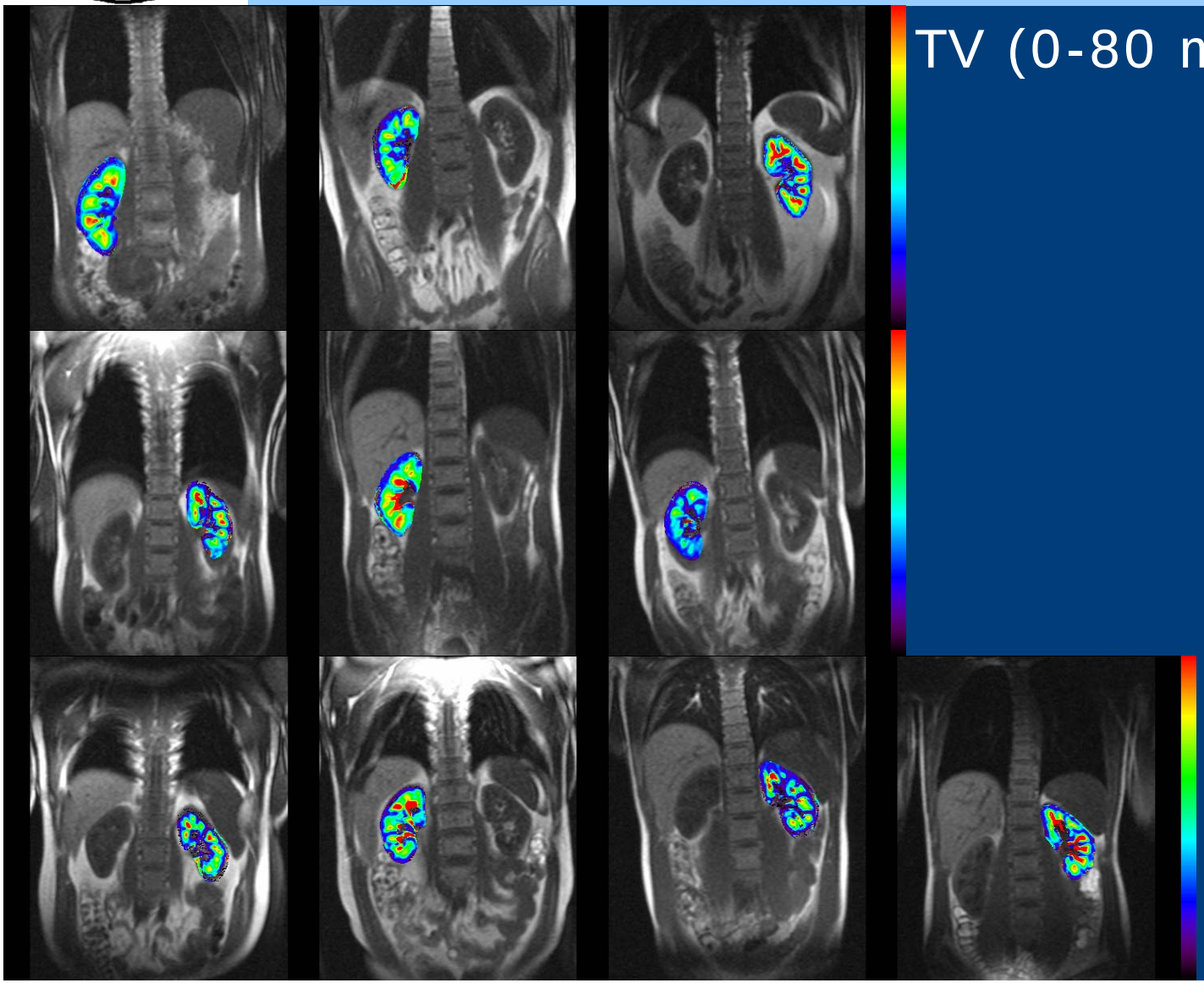
Pixel data (10/15 volunteers)



TF (0-40 ml/100ml/min)

Results

Pixel data (10/15 volunteers)



TV (0-80 ml/100ml/min)

Results

Pixel data (10/15 volunteers)

Cortex ROI	PF (ml/100ml/min)	PV (ml/100ml)	TF (ml/100ml/min)	TV (ml/100ml)
ROI analysis	309 (45)	35 (4.0)	11 (5.3)	21 (6.5)
Pixel Analysis	309 (43)	35 (4.2)	11 (5.3)	21 (7.1)

Results

Comparison of methods (15 volunteers)

Kidney ROI	PF (ml/100ml/min)	PV (ml/100ml)	TF (ml/100ml/min)	TV (ml/100ml)	Chi-Square (%)
4-Parameter model	229 (57)	24 (3.4)	**15 (3.6)**	*31 (12)*	0.47 (0.23)
5-Parameter model	**337 (68)**	*22 (3.3)*	**18 (4.8)**	*33 (11)*	0.29 (0.14)
Deconvolution / Patlak	210 (50)	24 (6.2)	12 (3.2)	30 (8.7)	N/A

Note: Arterial delay 1.5s (0.5s)

Cortex ROI	PF (ml/100ml/min)	PV (ml/100ml)	TF (ml/100ml/min)	TV (ml/100ml)	Chi-Square (%)
4-Parameter model	340 (86)	36 (4.7)	10 (5.4)	*19 (7.7)*	0.80 (0.83)
5-Parameter model	**496 (136)**	*33 (4.6)*	**15 (7.8)**	*23 (5.8)*	0.39 (0.19)
Deconvolution / Patlak	331 (70)	38 (10)	7.3 (5.5)	18 (8.5)	N/A

Note: Arterial delay 1.4s (0.5s)

Results

Comparison to Tofts model (15 volunteers)

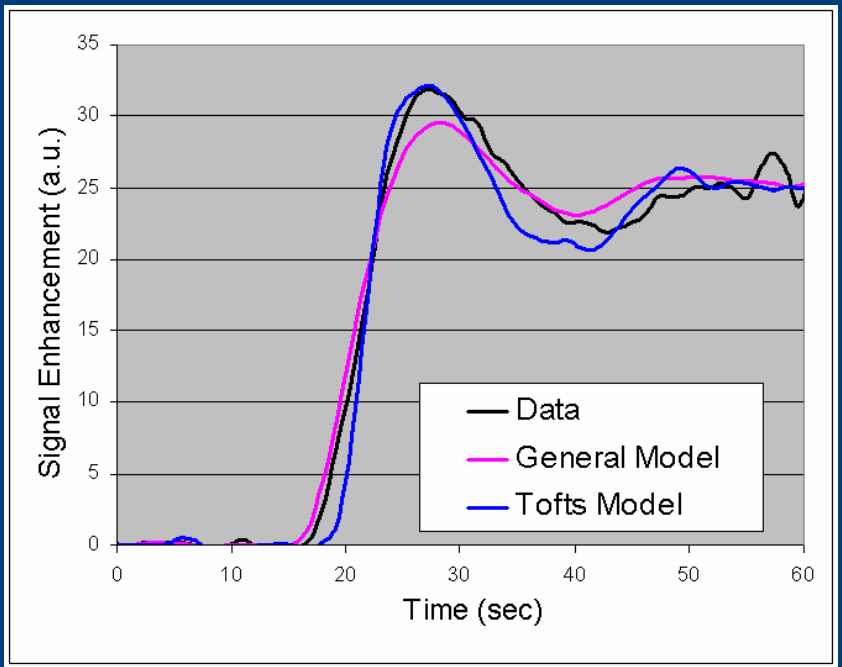


Figure 1. A plot of the data and both model fits for the first 60 sec in a typical case. Note that the arterial peak in the Tofts-fit is narrower than that of the General model since the Tofts model does not allow for intravascular dispersion. The fits in later phases of the contrast passage (>1min) show no obvious differences.

Fitted Parameters		KIDNEY		CORTEX	
		Mean	Stddev	Mean	Stddev
PV	General Model	24	3.4	36	4.7
	Tofts Model	17	2.8	24	4.2
	Patlak	*24*	*6.2*	*38*	*10*
TF	General Model	15	3.6	10	5.4
	Tofts Model	28	8.3	49	40
	Patlak	*12*	*3.2*	*7.3*	*5.5*
TT	General Model	125	53	123	60
	Tofts Model	84	37	48	19
RMS	General Model	0.5	0.2	0.8	0.8
	Tofts Model	0.8	0.7	0.9	0.3

Table 1. Values of the fitted parameters Plasma Volume (ml/100ml), Tubular Flow (ml/100ml/min) and Tubular Mean Transit Time (sec). The bottom two rows give the relative Root-Mean-Square error of the fit (%). The values in red are significantly different from those obtained with the Patlak model.

4-parameter Tofts model *versus* 4-parameter separable model

Results

Temporal constraints (15 volunteers)

Requirements

Temporal resolution

PV 9s

PF 4s

TV 9s

TF 5s

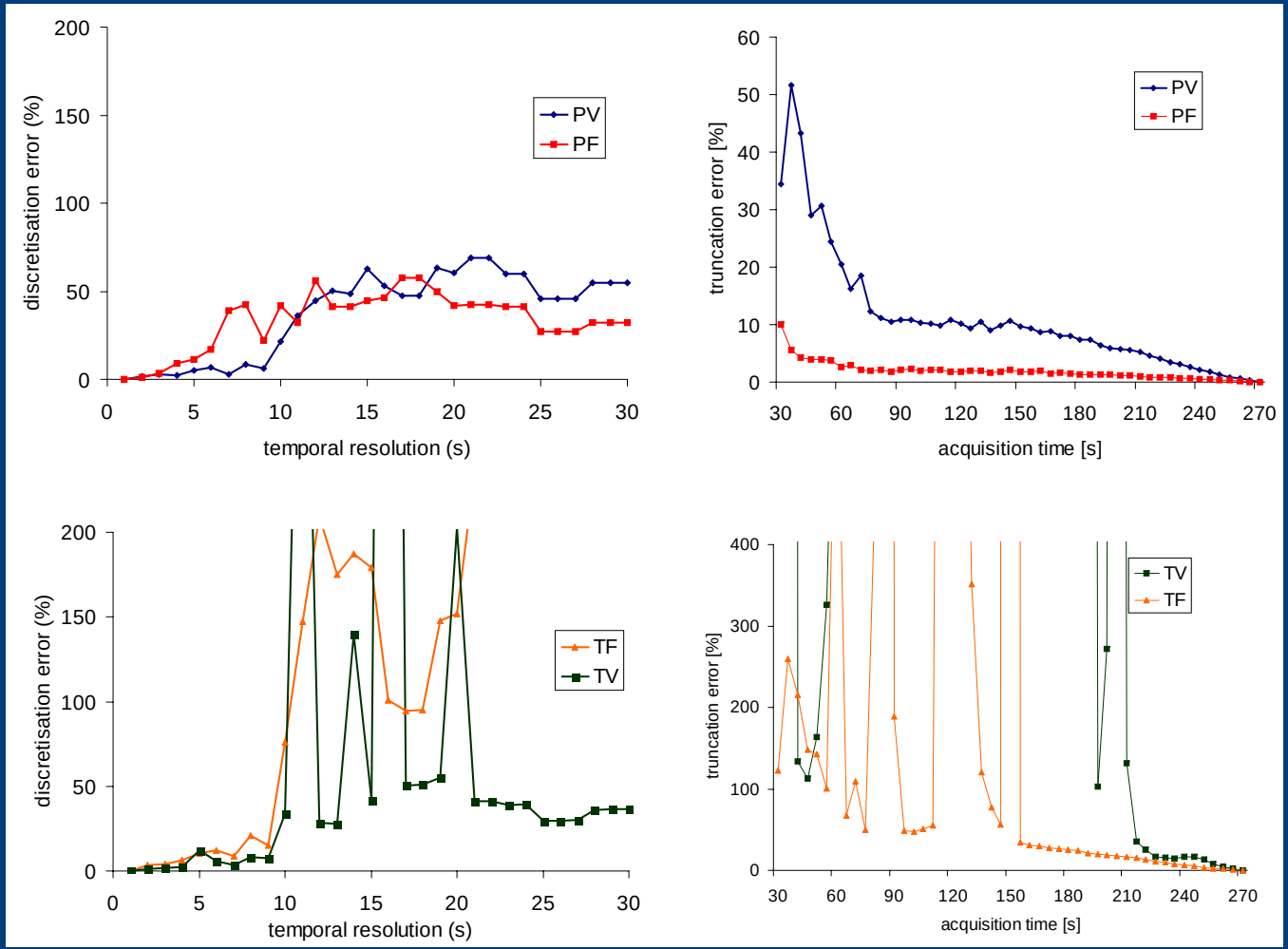
Measurement time

PV 85s

PF 35s

TV 250s

TF 220s



Future research

- Motion correction!!
  - Acquisition (3D?)
  - Post-processing
    - Retrospective triggering
    - Deformable registration
- Improve robustness with hybrid methods?
  - Initial values from deconvolution/Patlak
  - Fix selected parameters to deconvolution/Patlak values
- Signal optimization & Dynamic T1-quantification
- Clinical evaluation

Thank you!