

Low-Dose Cardiac- and Respiratory Gated Myocardial Perfusion Imaging of Free-Breathing Mice

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Disclosures

- Nothing to disclose

Cardiovascular Micro-CT Today

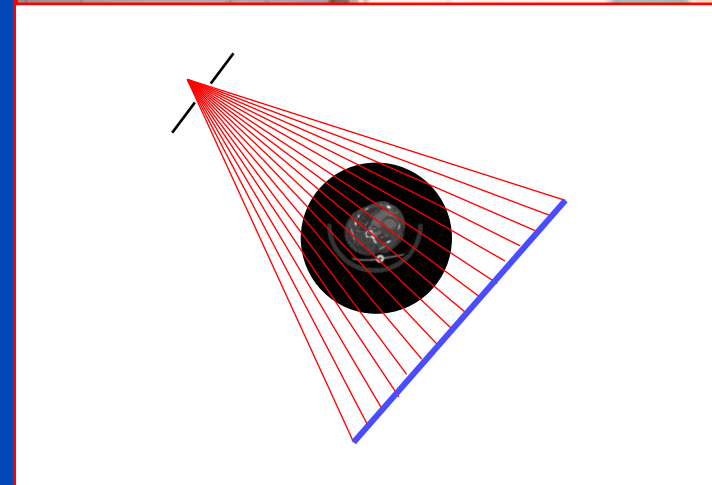
- High dose (>2 Gy) respiratory and cardiac correlated micro-CT: **Available.**
- Low dose (<0.2 Gy) respiratory and cardiac correlated micro-CT: **Available.**
- Dual energy CT of the heart: **Available.**
- Cardiac perfusion imaging: **This presentation.**
- Imaging of coronary arteries: **Not available.**

Aim

- Although many animal models of cardiac diseases are available **cardiac perfusion** is difficult in small animals due to the high cardiac and respiratory rates of up to 400 bpm and 250 rpm, respectively.
- We aim at providing a scan and acquisition protocol and dedicated reconstruction method that allows to perform perfusion studies of free breathing small animals at reasonable dose.

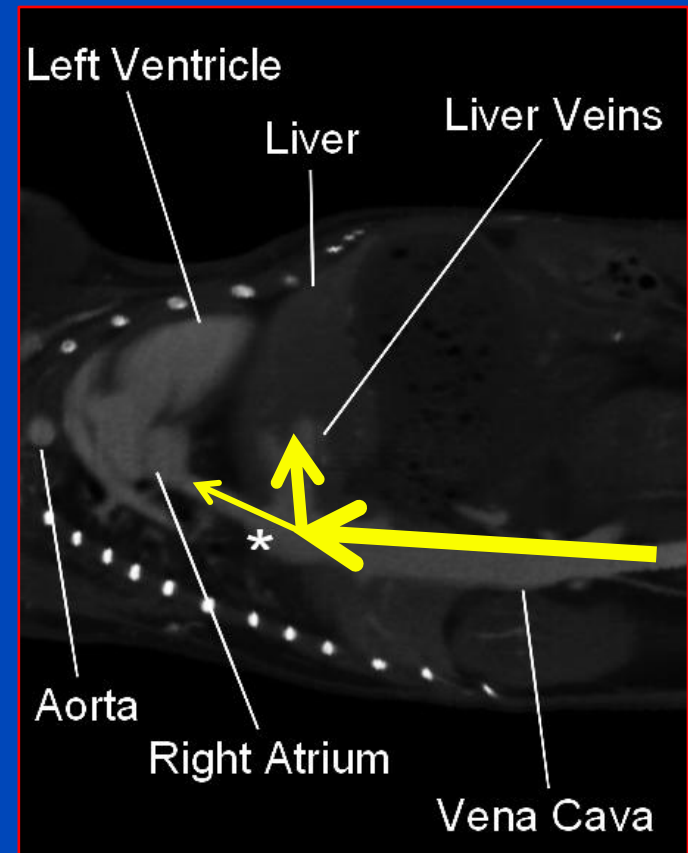
VolumeCT (VCT)

- VolumeCT (Siemens Healthcare, Forchheim, Germany)
- X-ray source:
 - Focal spot size: $400\ \mu\text{m} \times 400\ \mu\text{m}$
 - Tube voltage range: 80 kV – 140 kV
 - Tube current range: 10 mA – 50 mA
- Detector:
 - Varian flat panel detector
 - 1024×768 pixel (2x2 binning)
 - 1024×192 @ **100 fps**
 - $388\ \mu\text{m}$ pixel size
 - Spatial sampling: $238\ \mu\text{m}$
 - 10 ms integration time
- Protocol:
 - Scan time: 20 s
 - Rotation speed: $18\ ^\circ/\text{s}$
 - Number of projections: 2000
 - Estimated dose: 50 mGy



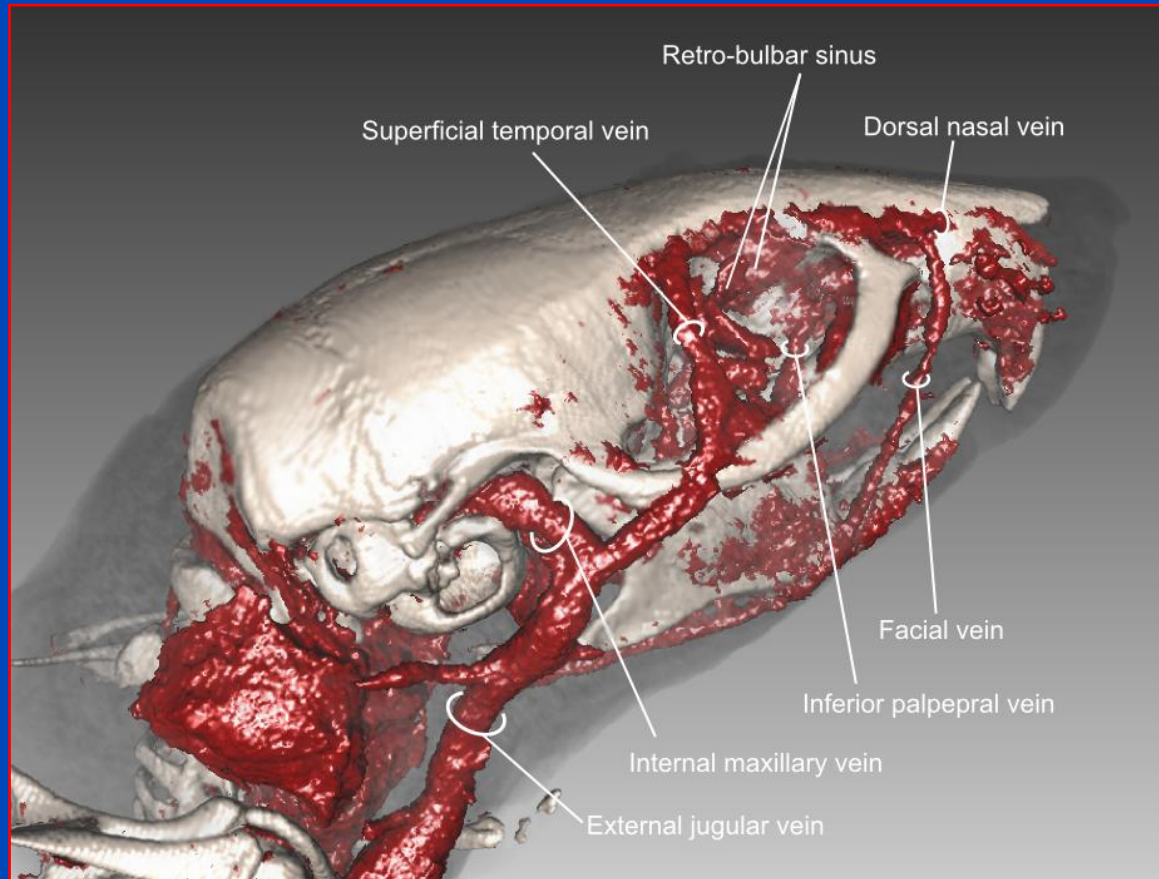
Contrast Injection

- We wish to inject boli of 25 μL .
- Clinical contrast agents are highly viscous (up to 8.7 mPa·s).
- Retrograd blood flow from the vena cava to the liver veins near the diaphragm.
- Bolus is dissolved before it arrives in the heart.
- Another route for contrast injection is required.
- We propose to inject into the **retro-bulbar sinus**.



Curved MPR through the vena cava of a mouse obtained from a high resolution micro-CT scan.

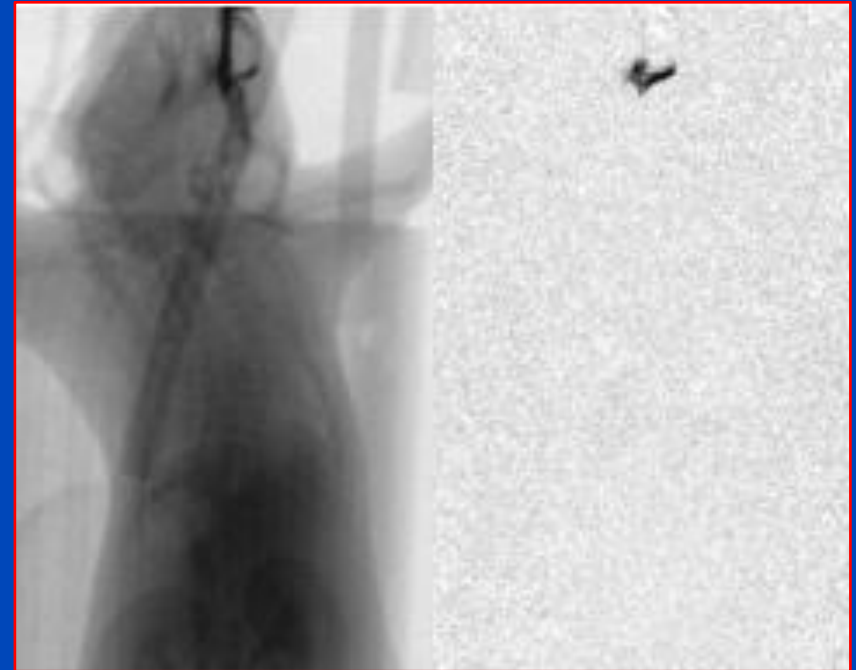
Contrast Injection



Volume rendering of a high resolution micro-CT scan with a spatial resolution of about 40 μm .

Contrast Injection

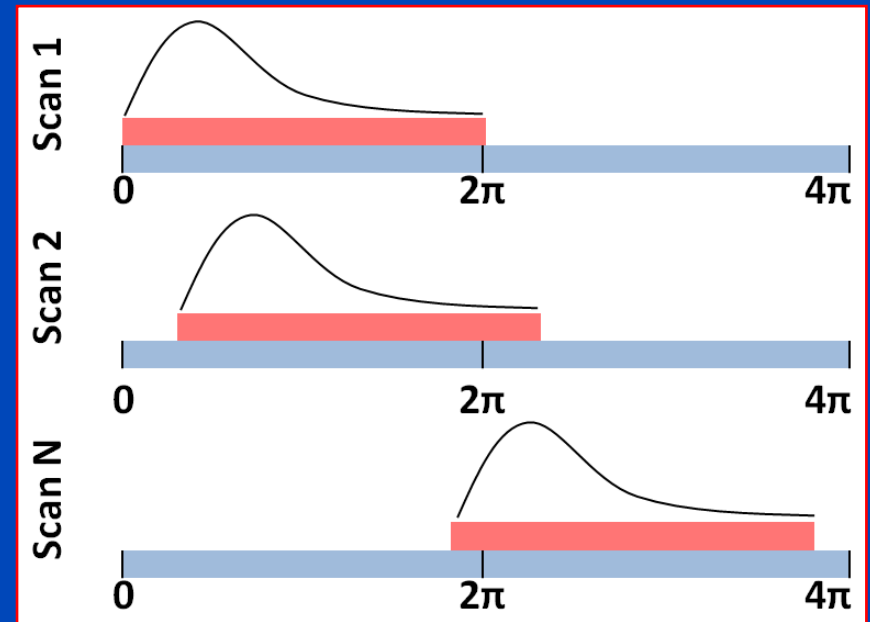
- Injection into the retro-bulbar sinus is verified using digital subtraction angiography.
- Imeron 300 is used as contrast agent.
- Contrast agent arrives in the right ventricle 1.5 s after the injection.
- Contrast agent is in the left ventricle after about 2.0 s.
- Enhancement of the aorta visible after about 2.5 s.



Left figure: acquired projection images.
Right figure : subtraction angiography.

Scan Protocol

- We perform $N=10$ scans each over 360° within 20 s.
- 2000 projections are acquired in every scan.
- Each scan starts at a different angle. We thus ensure to cover the complete angular range.
- We inject $25 \mu\text{L}$ per scan and $250 \mu\text{L}$ in total.



Schematic illustration of the used scan protocol. This is inspired by *Badea CT, Johnston SM, Subashi E, Qi Y, Hedlund LW, Johnson GA. Lung perfusion imaging in small animals using 4D micro-CT at heartbeat temporal resolution. Medical Physics. 2010; 37:54–62.*

Extrinsic Gating

- Respiration (r) is monitored using a pneumatic pillow.
- Information on cardiac motion (c) are obtained using electrodes attached to the paws.
- Timestamp of contrast injection/start of the perfusion (p) is recorded.
- All signals are retrospectively correlated to the acquired projections.
- Phase windows for image reconstruction are defined by c, r, p and corresponding window widths Δc , Δr , Δp .

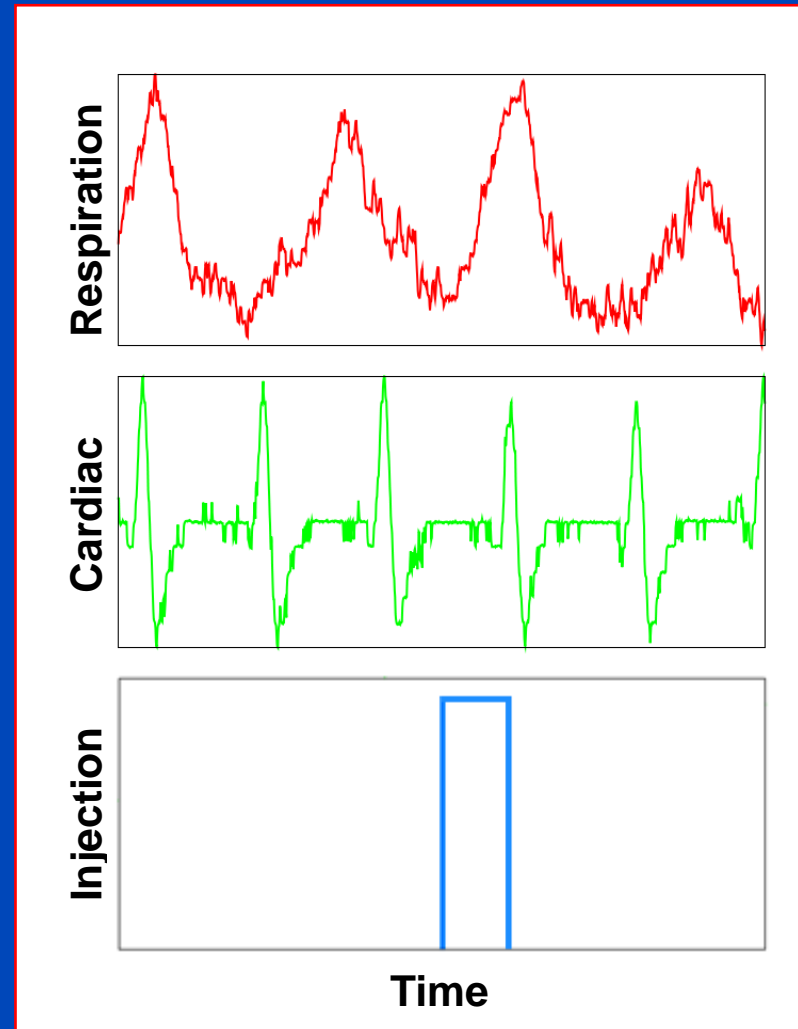
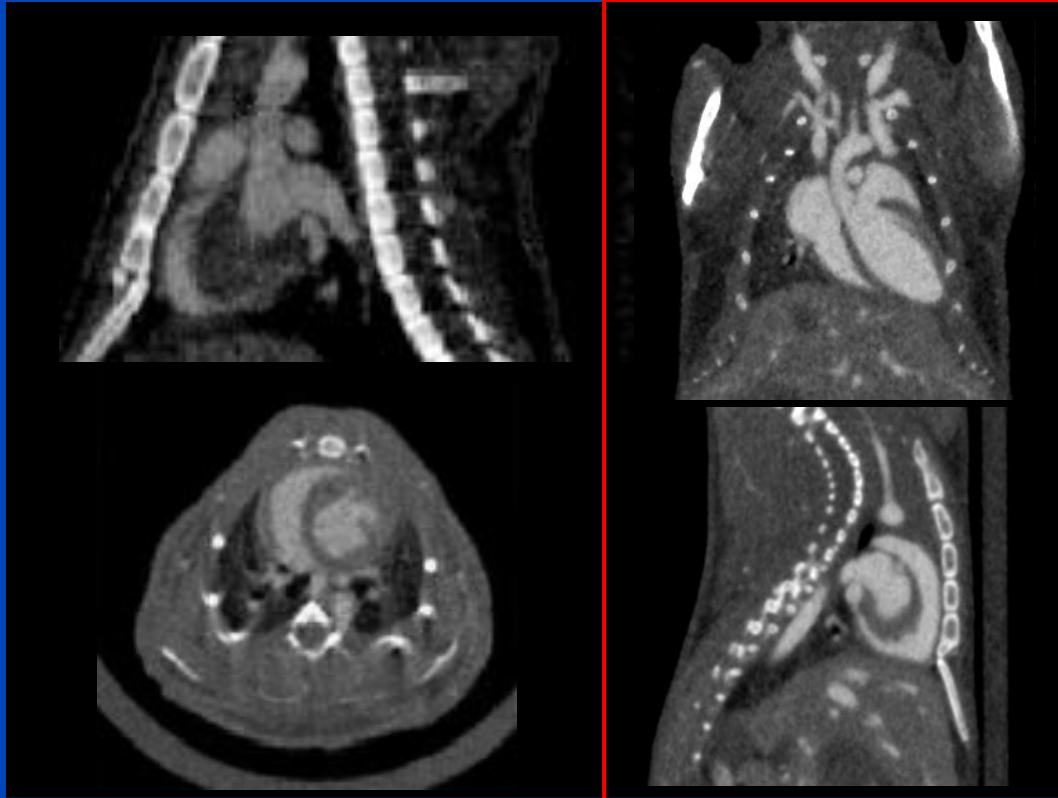


Image Reconstruction Prior Art

1840 mGy, 90 μm , 12 phases 500 mGy, 80 μm , 50 phases

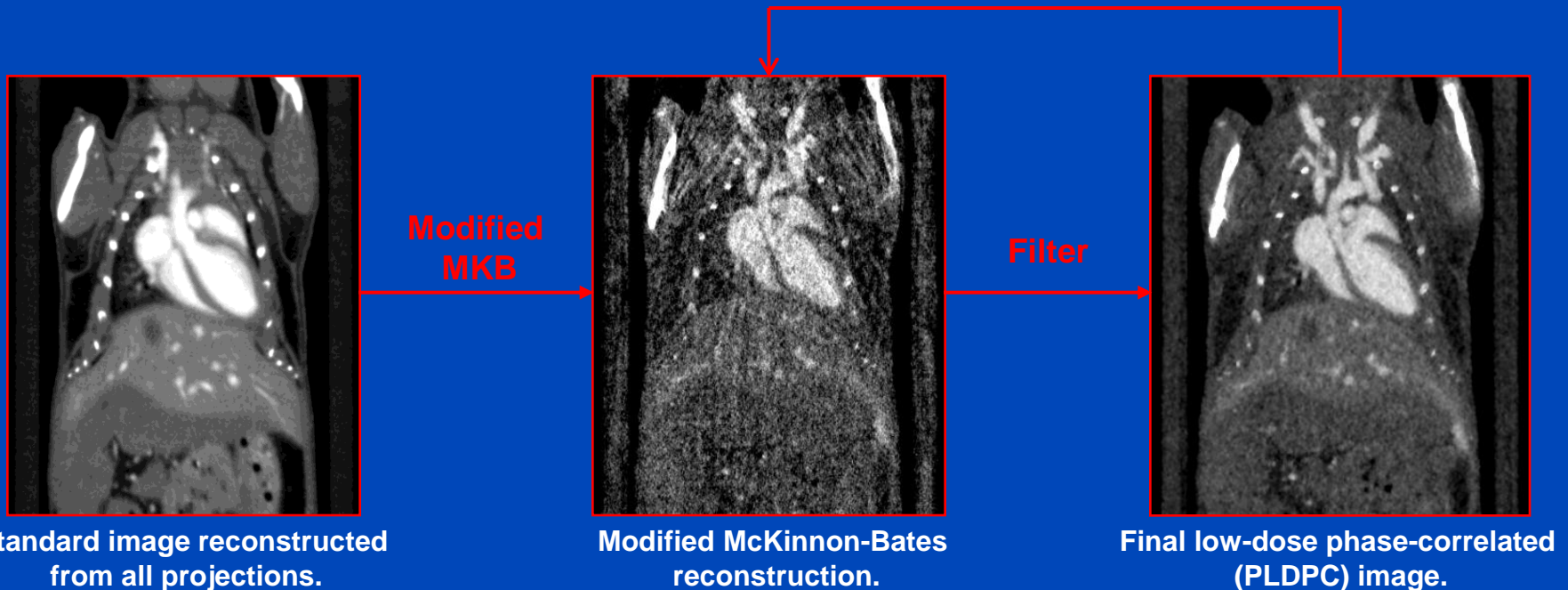


C. Badea, B. Fubara, L. Hedlund, and G. Johnson, "4D micro-CT of the mouse heart," *Molecular Imaging*, vol. 4, no. 2, pp. 110–116, Apr./Jun. 2005.

S. Sawall, F. Bergner, R. Lapp, M. Mronz, M. Karolczak, A. Hess, and M. Kachelrieß, "Low-dose cardio-respiratory phase-correlated cone-beam micro-CT of small animals," *Medical Physics*, vol. 38, no. 3, pp. 1416-1424, Feb. 2011.

Image Reconstruction

- Iterative reconstruction method
- Based on a modified McKinnon-Bates algorithm
- Refined by a high-dimensional edge-preserving filter



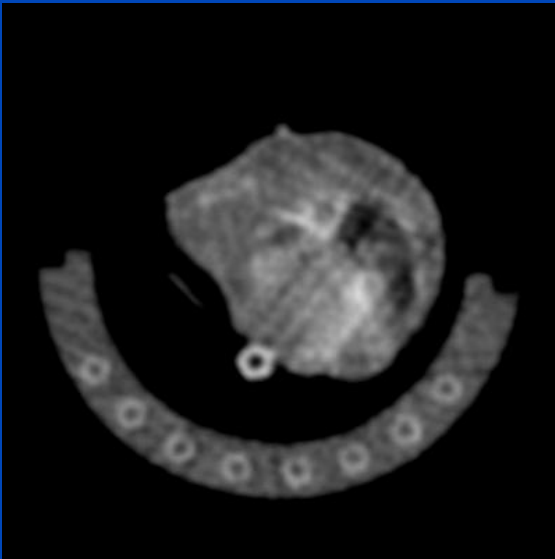
RESULTS

Results

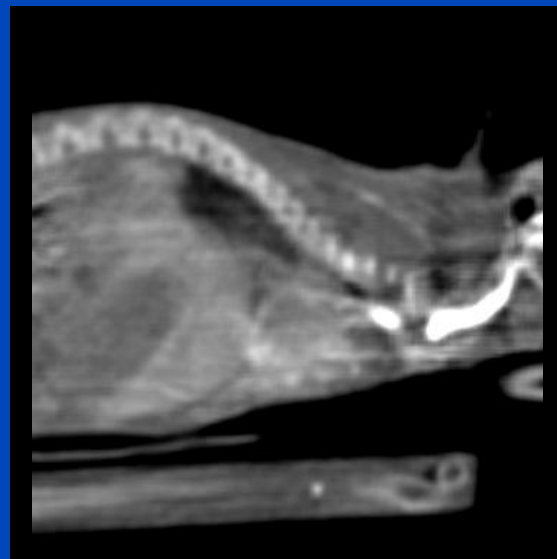
	Mouse 1	Mouse 2
Respiratory rate	120 rpm	115 rpm
Cardiac rate	265 bpm	250 bpm
Contrast agent	Imeron 300	Imeron 300
Administered volume	10x25 μ L	10x25 μ L

Results Mouse 1

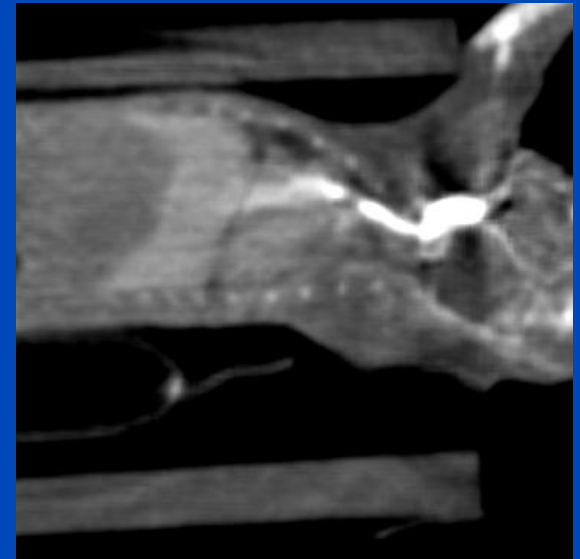
Axial



Sagittal

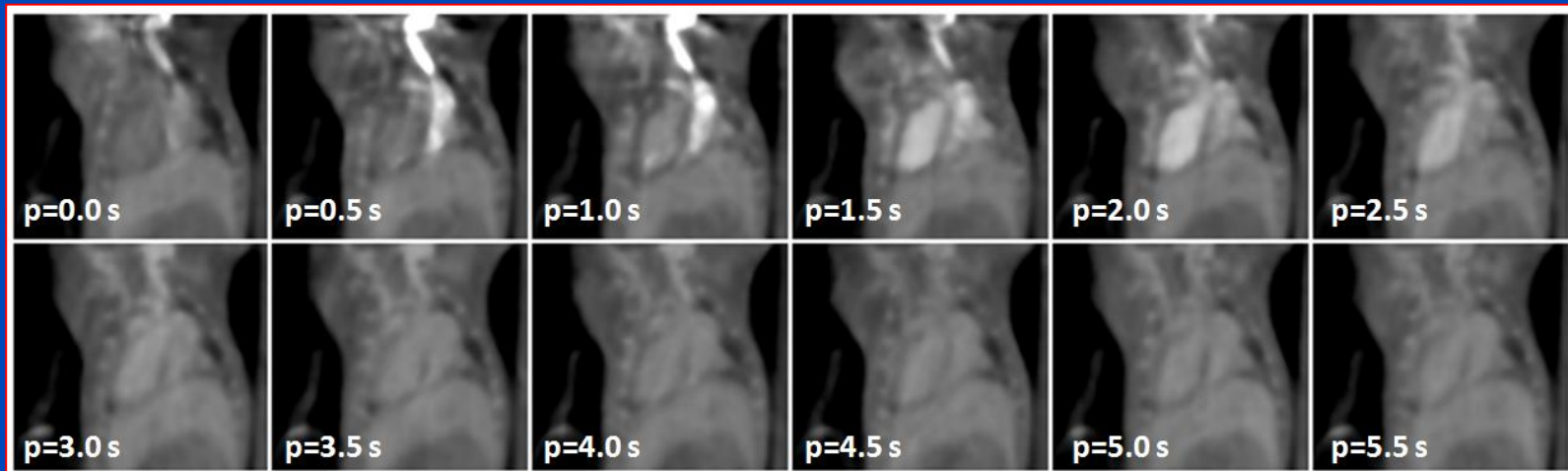


Coronal



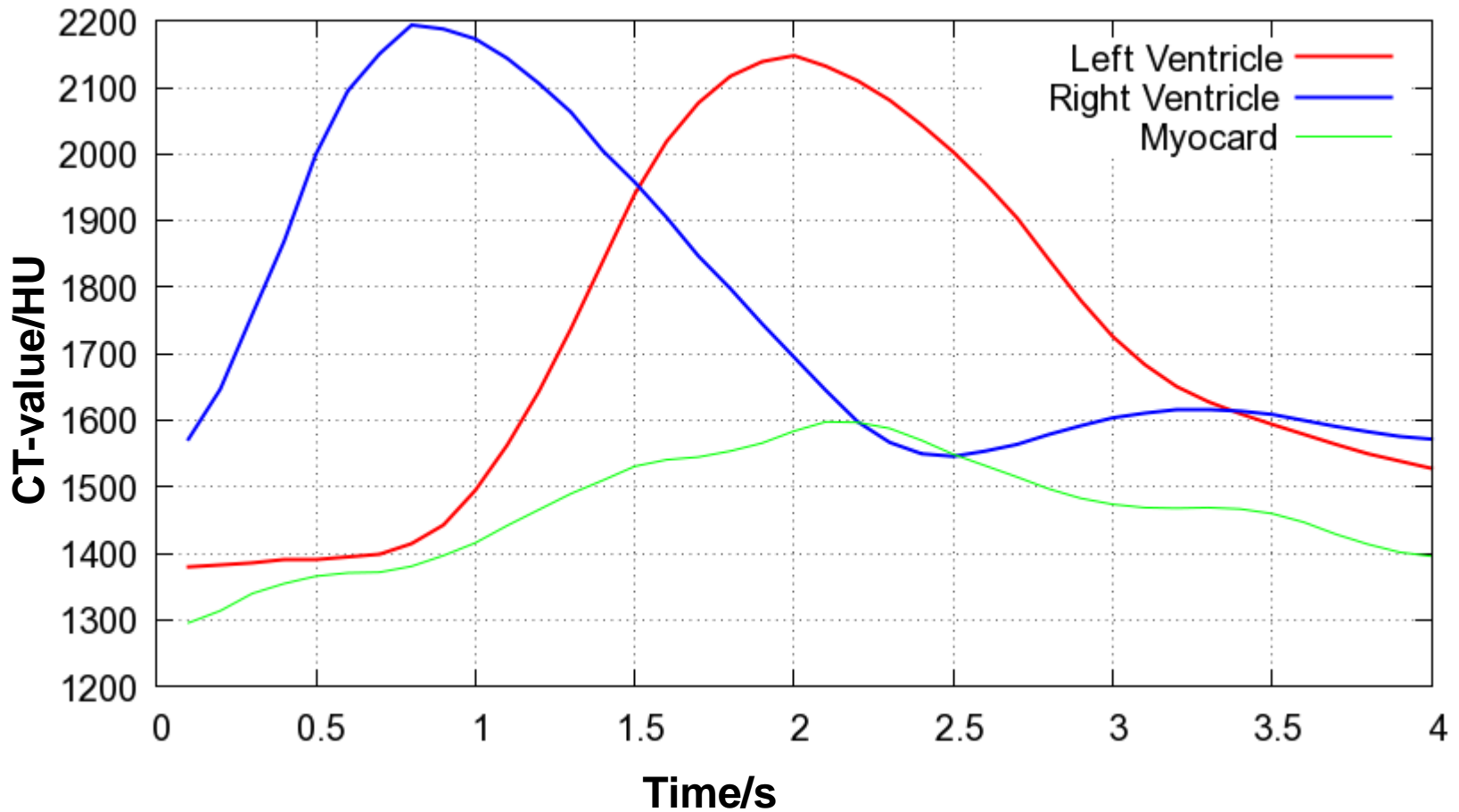
Gating: $\Delta c=20\%$, $c=0\%$, $\Delta r=25\%$, $r=0\%$, $\Delta p=5\%$ (1.25 s)
Windowing: C=500 HU, W=800 HU

Results Mouse 2



Gating: $\Delta c=20\%$, $c=0\%$, $\Delta r=25\%$, $r=0\%$, $\Delta p=5\%$ (1.25 s)
Windowing: C=500 HU, W=800 HU

Time-Density-Curve



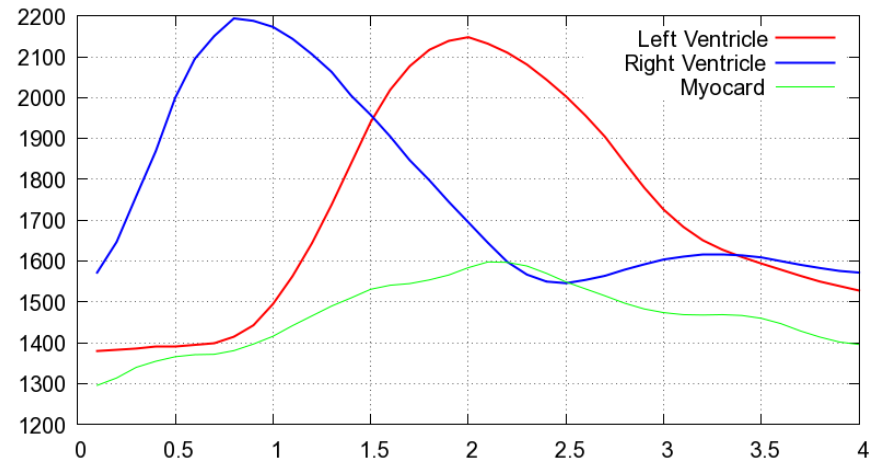
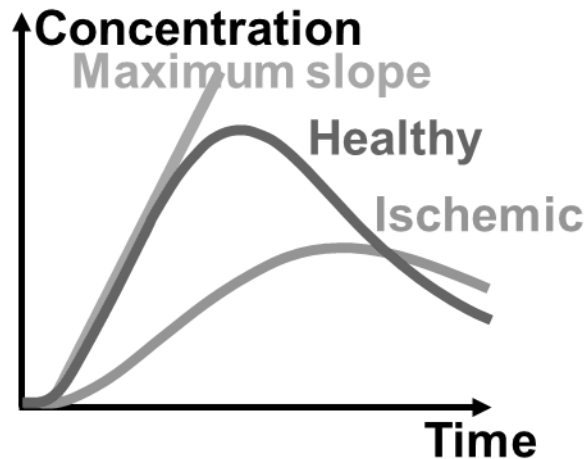
Clinical Case

Clinical Examinations

SOMATOM Definition Flash
Flash Speed. Lowest Dose.



Preclinical Examinations



Summary & Conclusions

- Cardiac- and respiratory-correlated reconstructions come at no additional cost allowing for the quantification of ejection fraction etc.
- The dose per imaging study is about 500 mGy, what is far below the LD₅₀ of 5-7 Gy.
- The injection technique is minimally invasive allowing for longitudinal studies.
- The quantitative results correspond well to what is known from clinical practice.
- Overall results show that **cardiac perfusion studies in small rodents are possible**.
- This boosts preclinical research with a lot of new possibilities.

Thank you!

This presentation will shortly be available at www.dkfz.de/ct.

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