CT Meeting 2012

Phase-Correlated Perfusion Imaging of Free-Breathing Rodents

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FRIEDRICH-ALEXANDER-UNIVERSITÄT ERLANGEN-NÜRNBERG

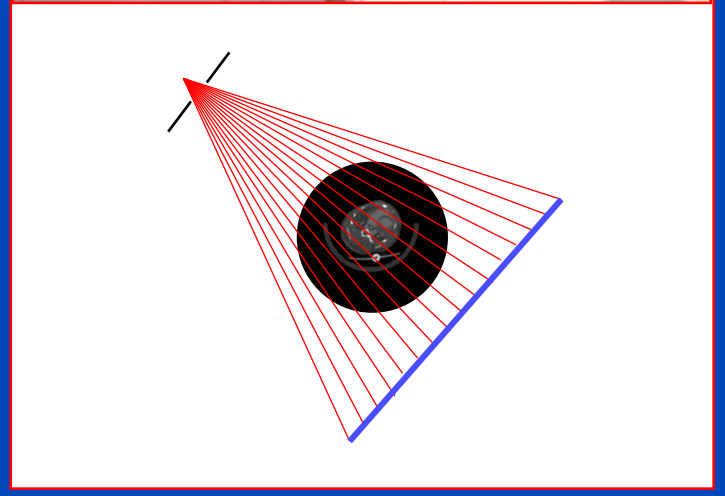
DEUTSCHES KREBSFORSCHUNGSZENTRUM IN DER HELMHOLTZ-GEMEINSCHAFT

Aim

- Perfusion studies are already a common tool in clinical practice.
- Although many animal models for cardiac diseases exist **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.

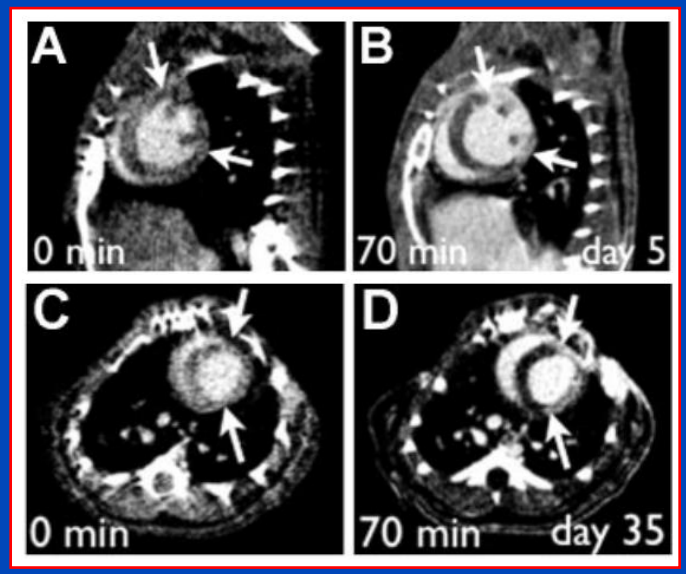
VolumeCT (VCT)

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



Cardiac Perfusion of Small Animals Prior Art

- High resolution (100 µm) imaging of the thoracic region.
- No phase-correlation and thus motion artifacts occur.
- Administration of more than 1 mL of contrast agent within 70 min.

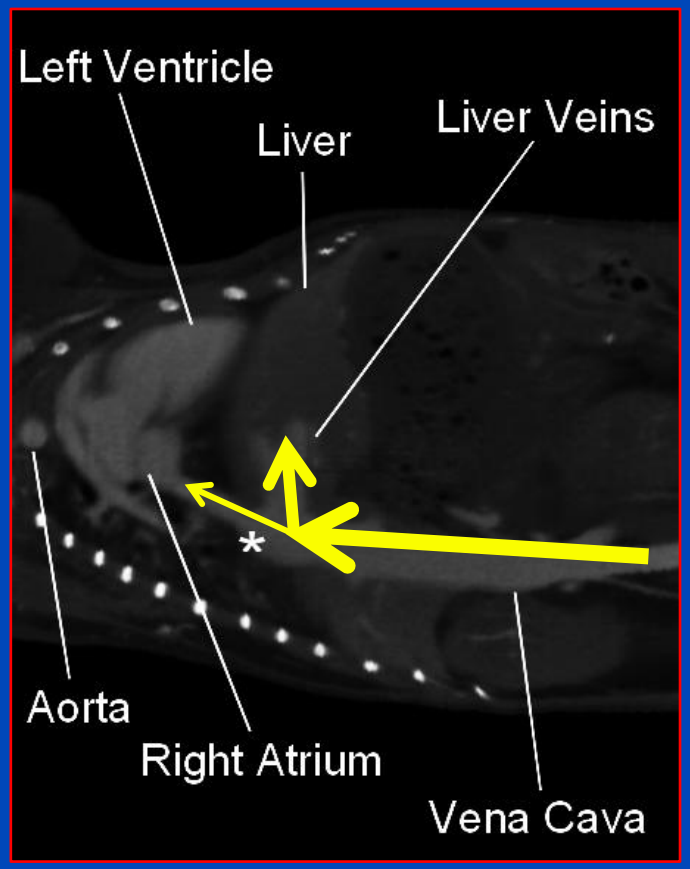


Nahrendorf M, Badea C, Hedlund LW, Figueiredo JL, Sosnovik DE, Johnson GA, Weissleder R. High–resolution imaging of murine myocardial infarction with delayed-enhancement cine micro-CT. American Journal of Physiology: Heart and Circulatory Physiology. 2007; 292:H3172–H3178.

CONTRAST INJECTION PROTOCOL

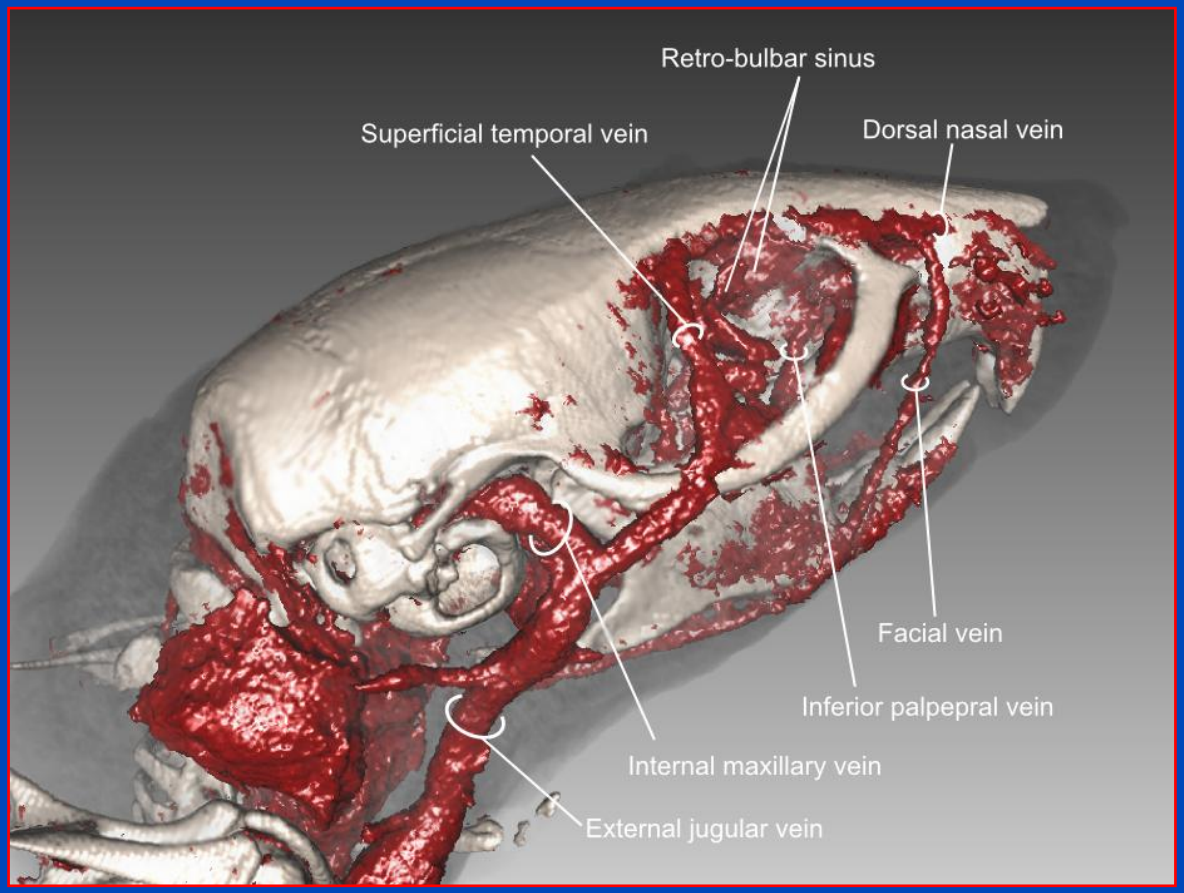
Contrast Injection

- 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 throught the vena cava of a mouse obtained from a high resolution micro-CT scan.

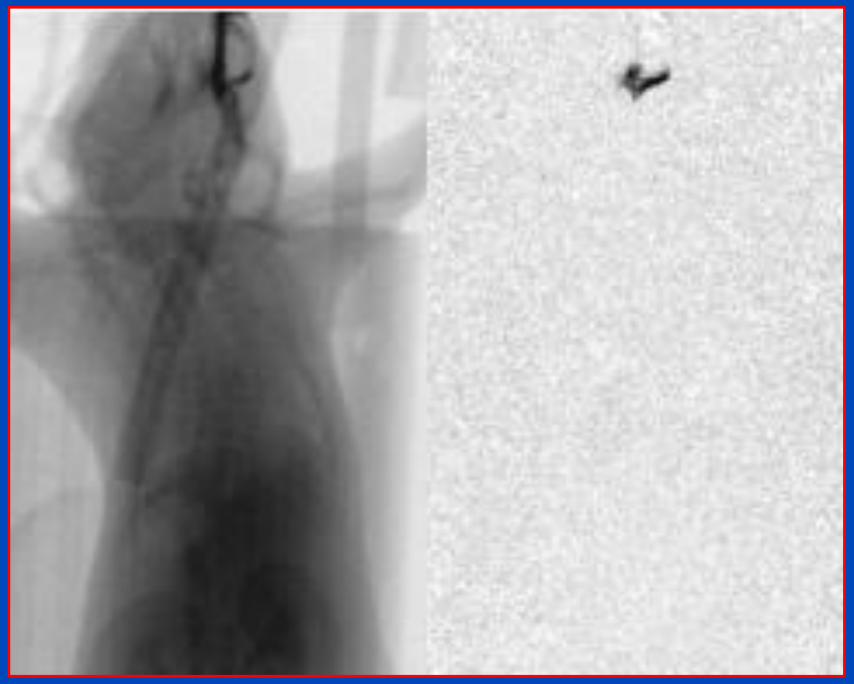
Contrast Injection



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.

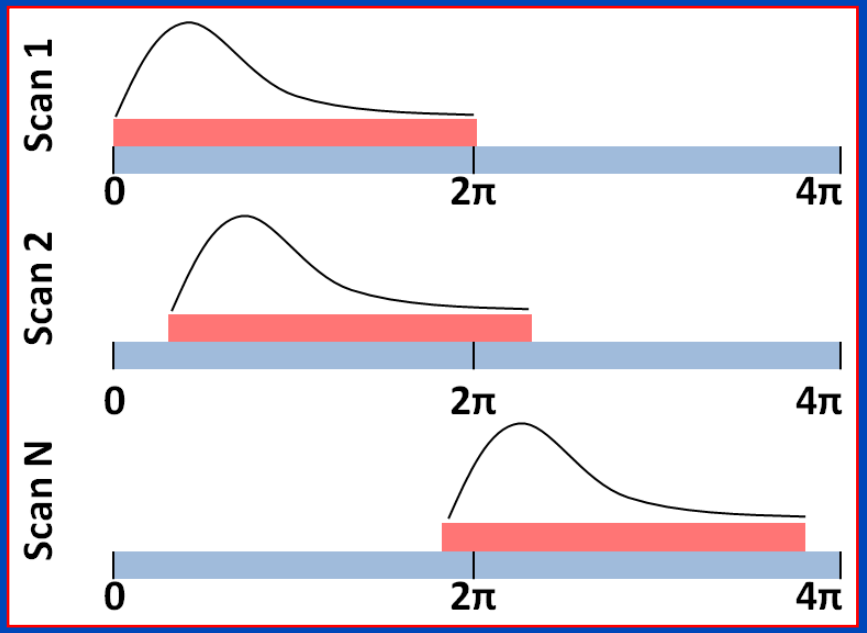


Left figure: acquired projection images.
Right figure : subtraction angiography.

SCAN PROTOCOL & GATING

Scan Protocol

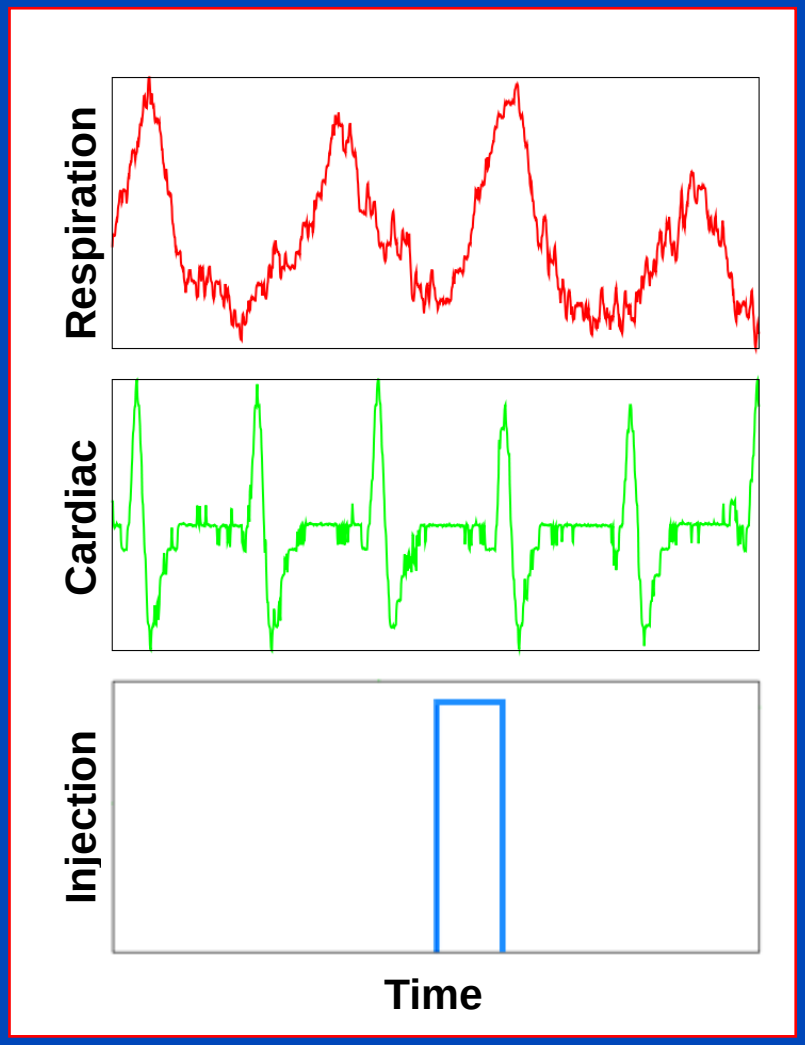
- We perform N=10 scans each over 360° within 20 s.
- 2000 projections are acquired in every scan.
- Each scan starts at a different angle. We thus ensure to cover the complete angular range.
- We inject 25 µL per scan and 250 µL in total.



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 retro-spectively correlated to the acquired projections.
- Phase windows for image reconstruction are defined by c, r, p and corresponding window widths Δc, Δr, Δp.



Extrinsic Gating

- Three gating signals require the reconstruction to be correlated to all of these signals.
- Example:
  - 10×2000 projections in total
  - Cardiac window: 20 %
  - Respiratory window: 20 %
  - Perfusion window: 1 s (5 %)
  - Only 0.2 % of all acquired projections contribute to a reconstruction.

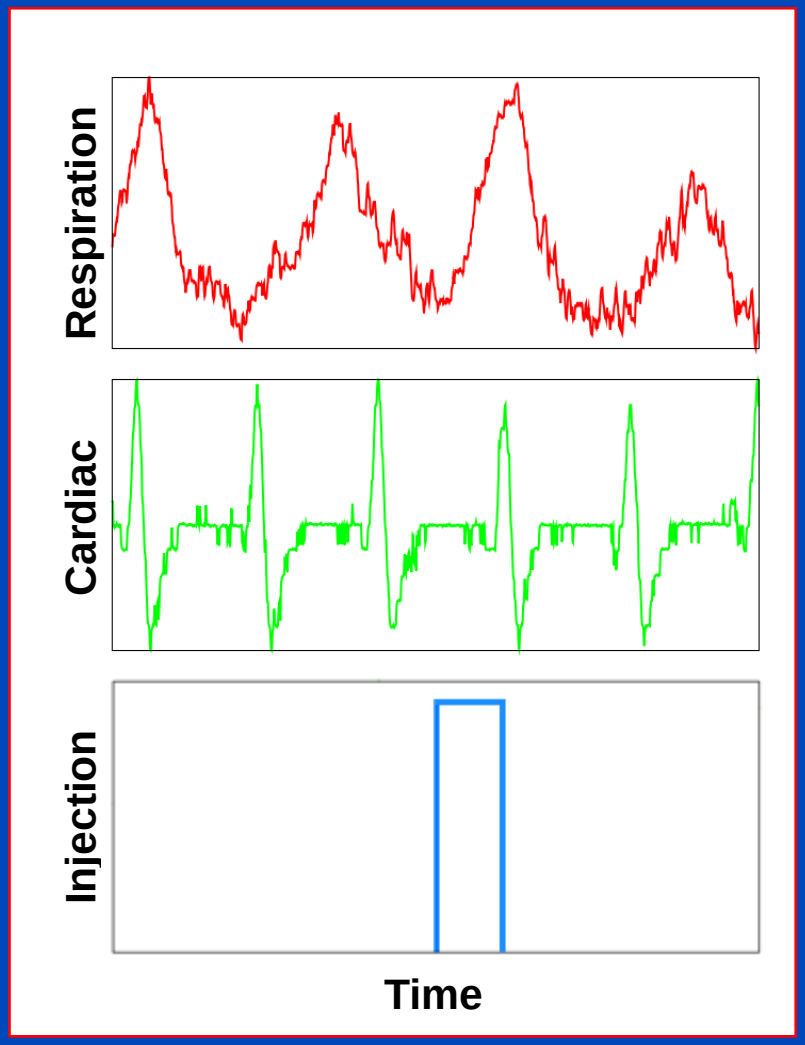
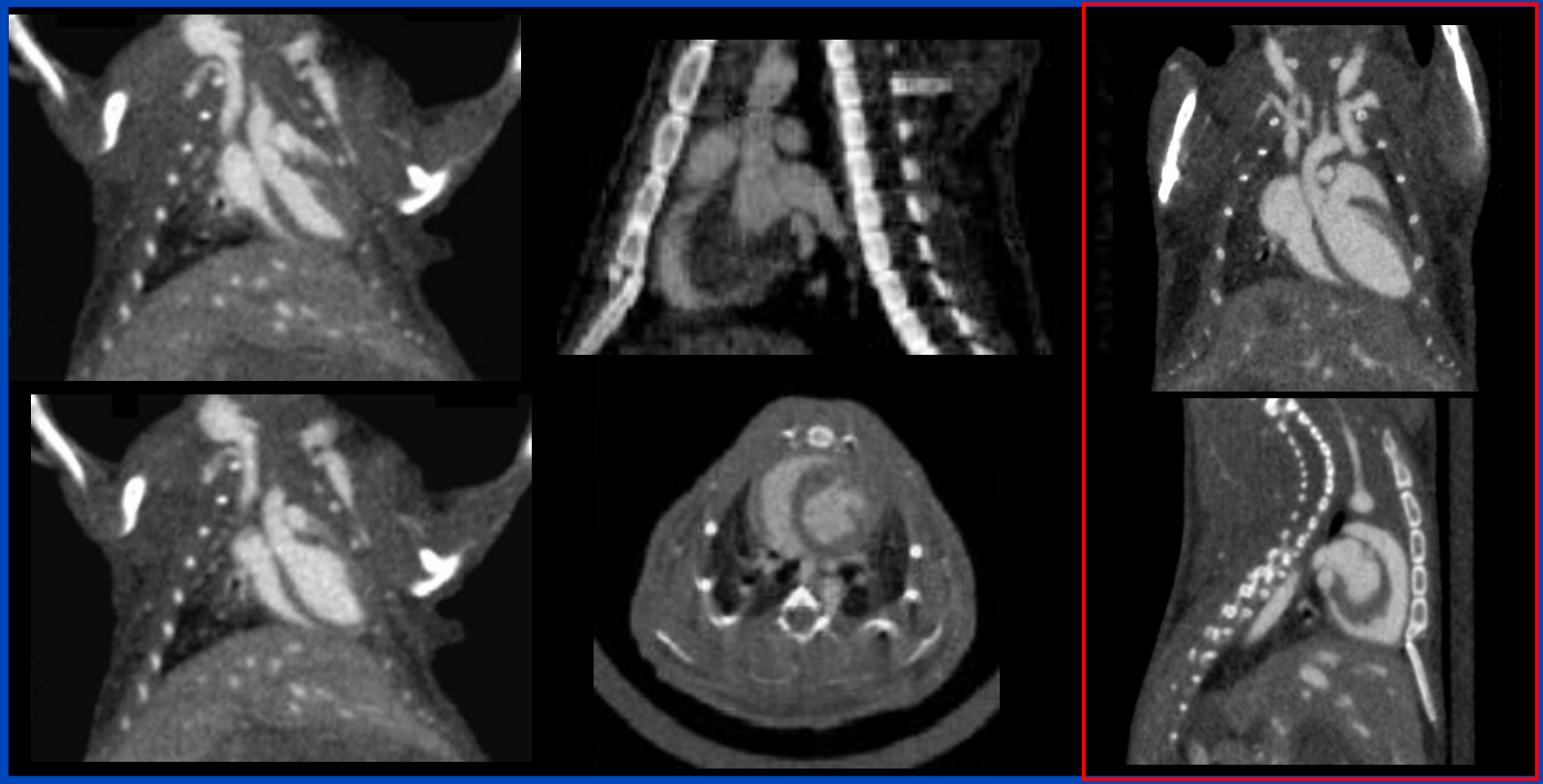


IMAGE RECONSTRUCTION

THE PLDPC ALGORITHM

Image Reconstruction Prior Art

280 mGy, 150 µm, 10 phases	1840 mGy, 90 µm, 12 phases	500 mGy, 80 µm, 50 phases

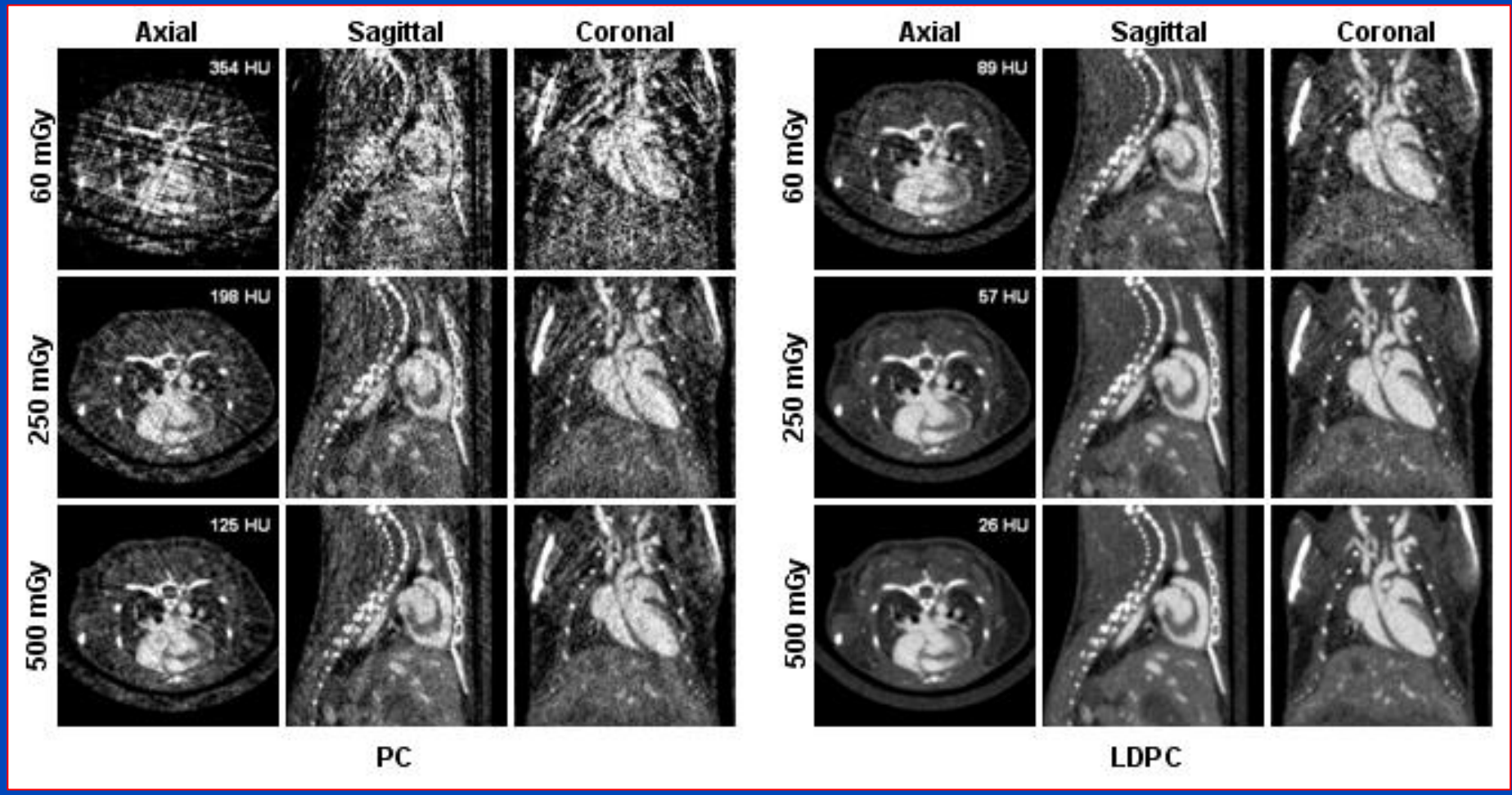


M. Drangova, N. L. Ford, S. A. Detombe, A. R. Wheatley, and D. W. Holdsworth, "Fast retrospectively gated quantitative four–dimensional (4D) cardiac micro computed tomography imaging of free–breathing mice," *Investigative Radiology*, vol. 42, no. 2, pp. 85–94, Feb. 2007.

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 Prior Art



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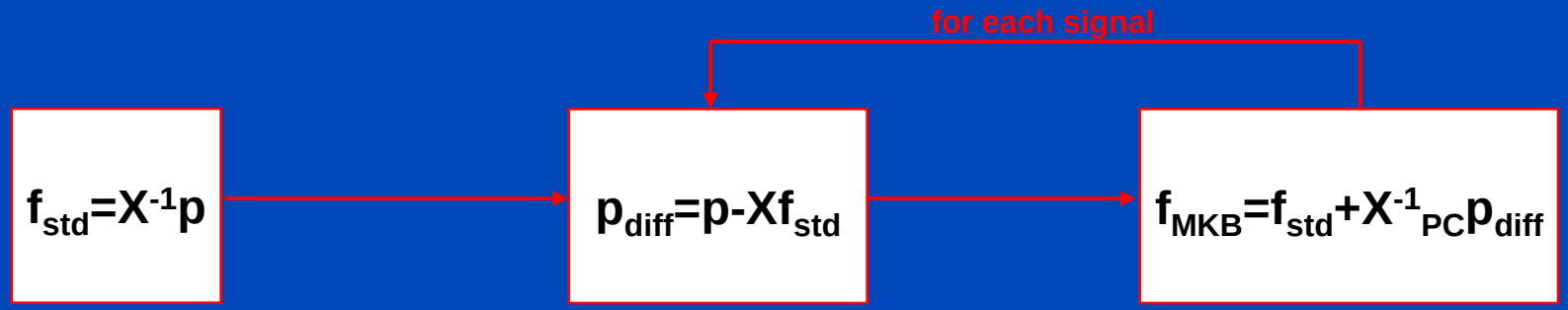
Modified McKinnon-Bates Algorithm



- Use image based on all projections as prior (standard image)
- Calculate rawdata difference for desired motion phases
- Perform correction

Standard image f_{std} reconstructed from all projections.

McKinnon-Bates reconstruction f_{MKB}.

G. C. McKinnon and R. Bates, "Towards imaging the beating heart usefully with a conventional CT scanner," *IEEE Transactions on Biomedical Engineering*, vol. BME-28, no. 2, pp. 123–127, Feb. 1981.

Edge Preserving Spatio-Temporal Postprocessing

Five-dimensional bilateral filtering (three spatial and two temporal dimensions)

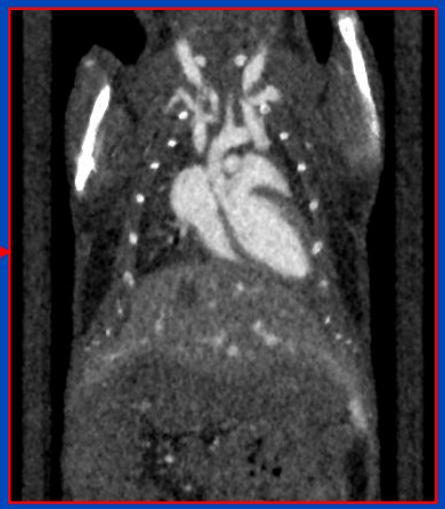
$$f_{\mathrm{LDPC}} = B f_{\mathrm{MKB}} = \frac{\int dt^5 D(x,t) R(x,t) f(t)}{\int dt^5 D(x,t) R(x,t)}$$

Standard image reconstructed from all projections.

Modified MKB

Modified McKinnon-Bates reconstruction.

5D Filter



Final low-dose phase-correlated (LDPC) image.

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.

Edge Preserving Spatio-Temporal Postprocessing

Six-dimensional bilateral filtering (three spatial and three temporal dimensions)

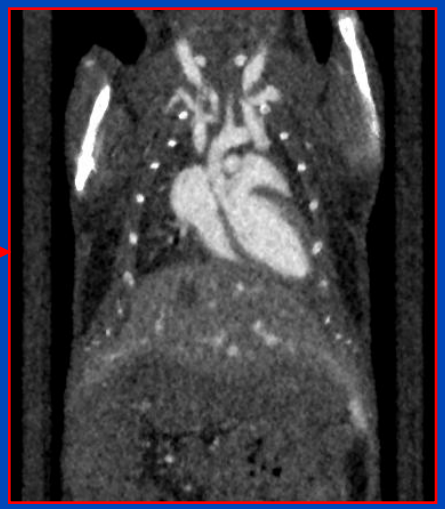
$$f_{\mathrm{PLDPC}} = B f_{\mathrm{MKB}} = \frac{\int dt^6 D(x,t) R(x,t) f(t)}{\int dt^6 D(x,t) R(x,t)}$$

Standard image reconstructed from all projections.

Modified MKB

Modified McKinnon-Bates reconstruction.

6D Filter



Final low-dose phase-correlated (PLDPC) image.

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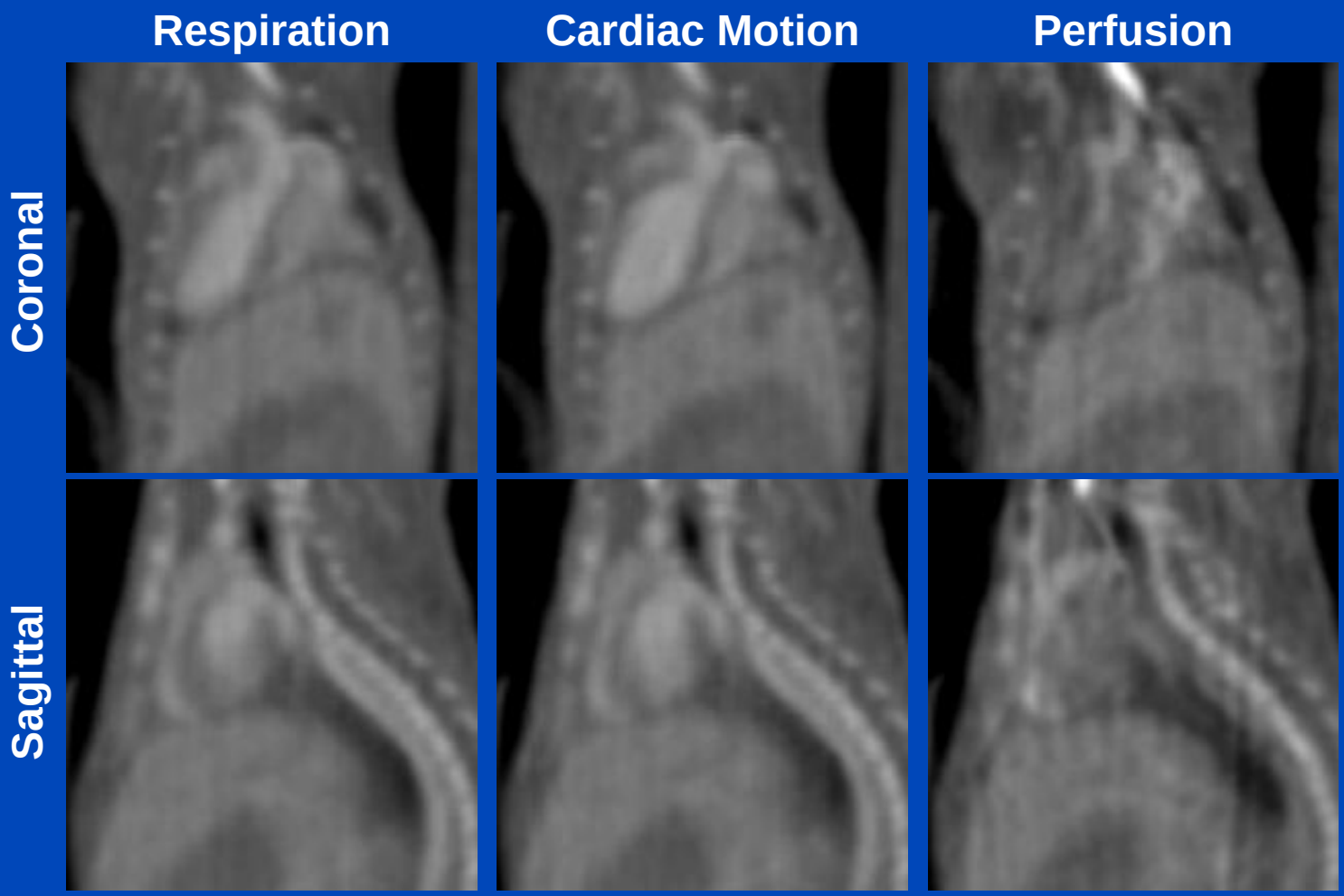
RESULTS

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	10×25 µL	10×25 µL

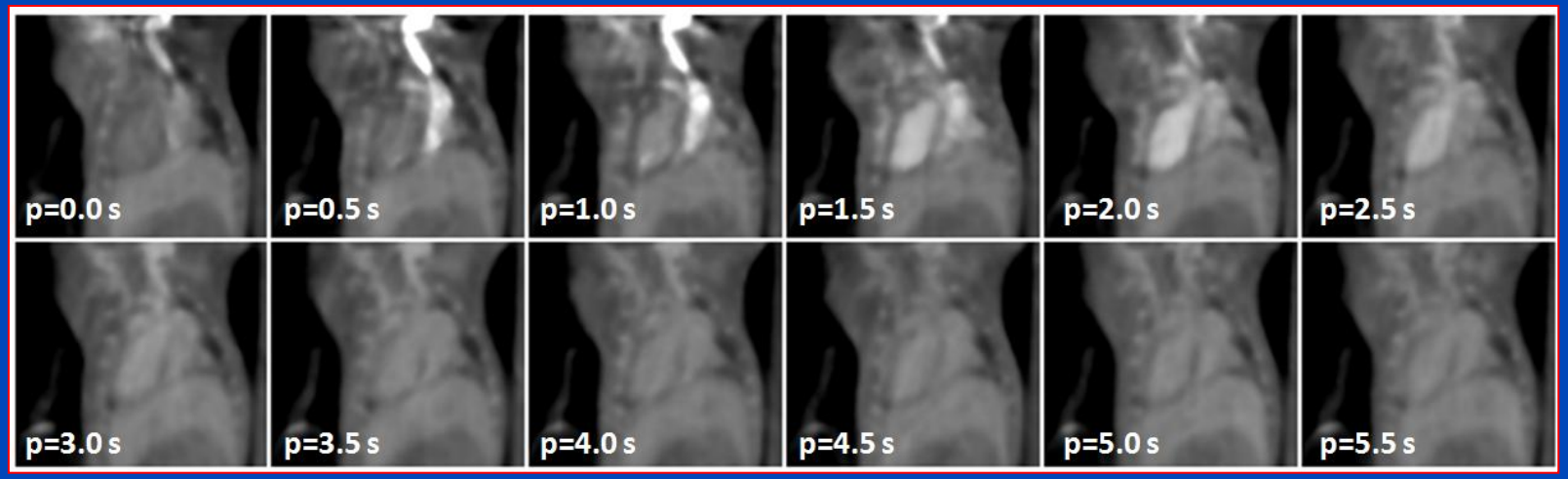
Mouse 1



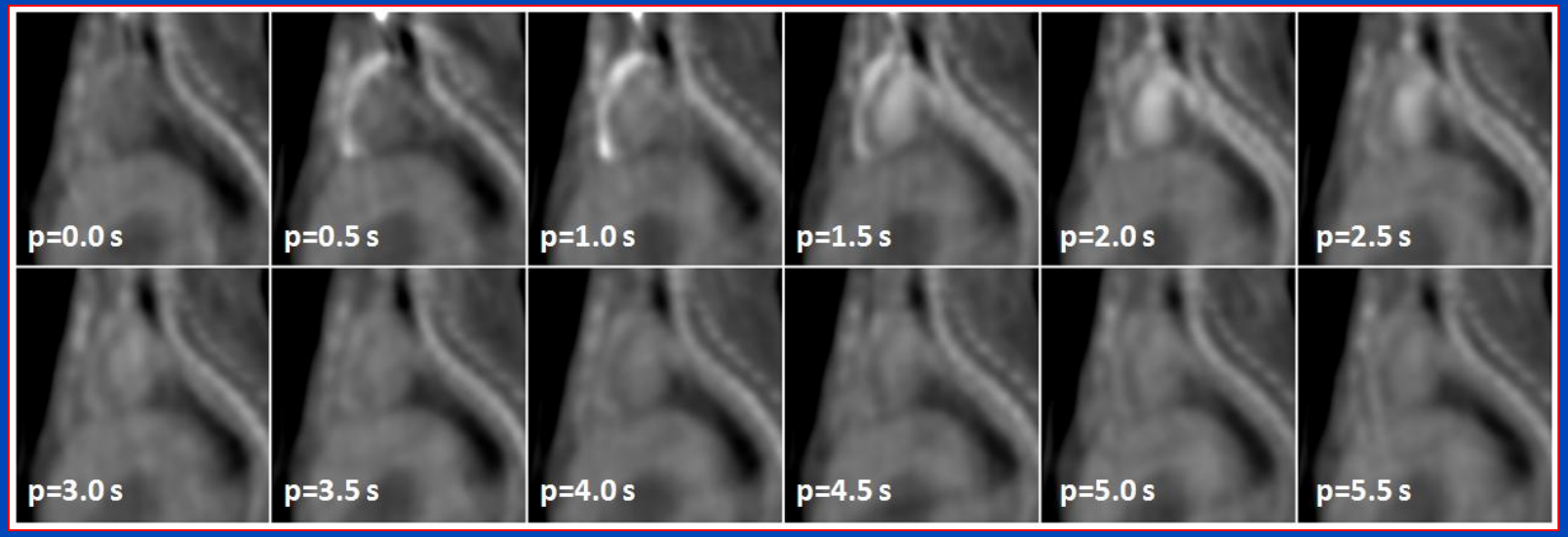
Δr=20, Δc=20%, Δp=0.5 s (600 HU / 700 HU)

Mouse 2

Coronal

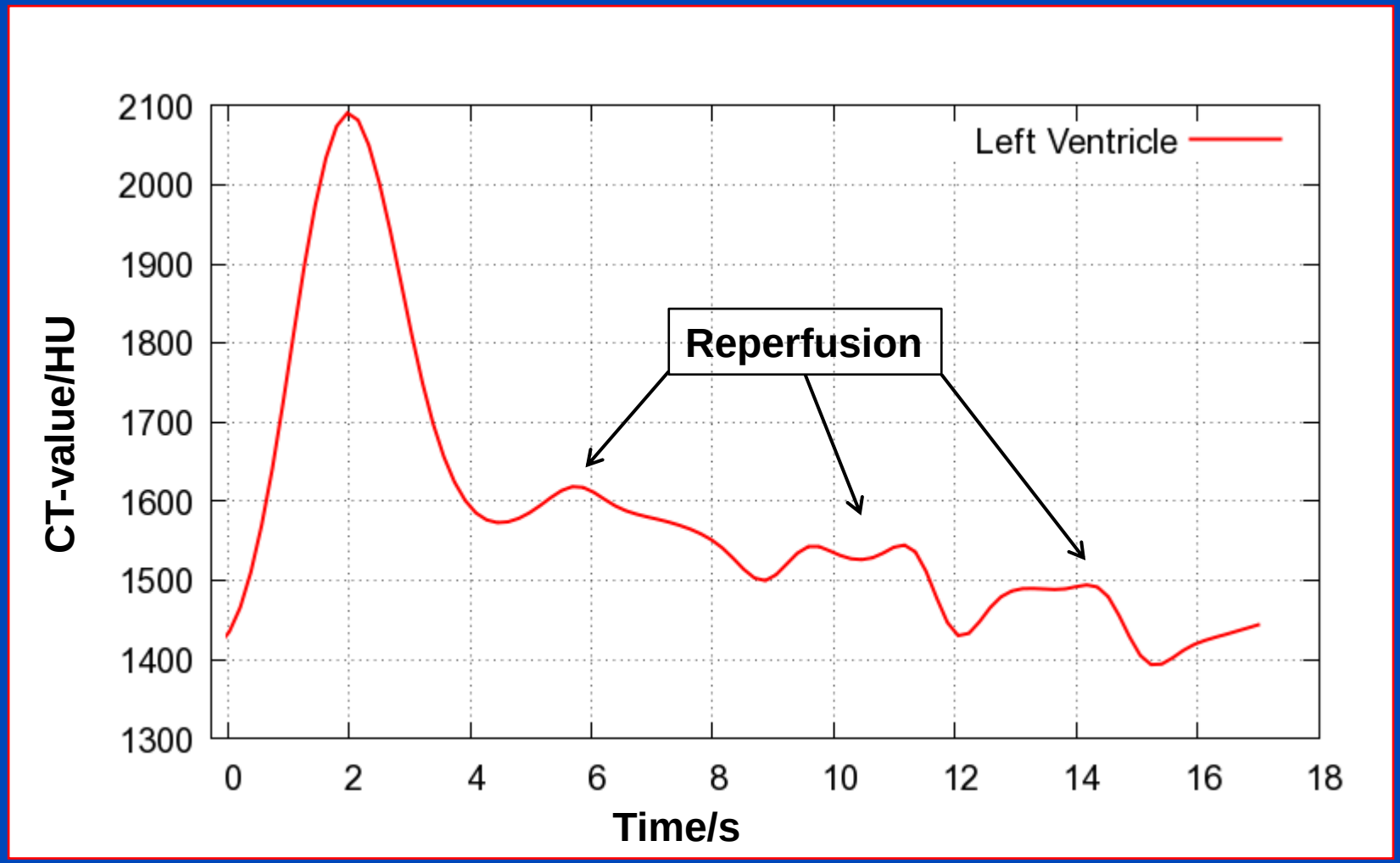


Sagittal

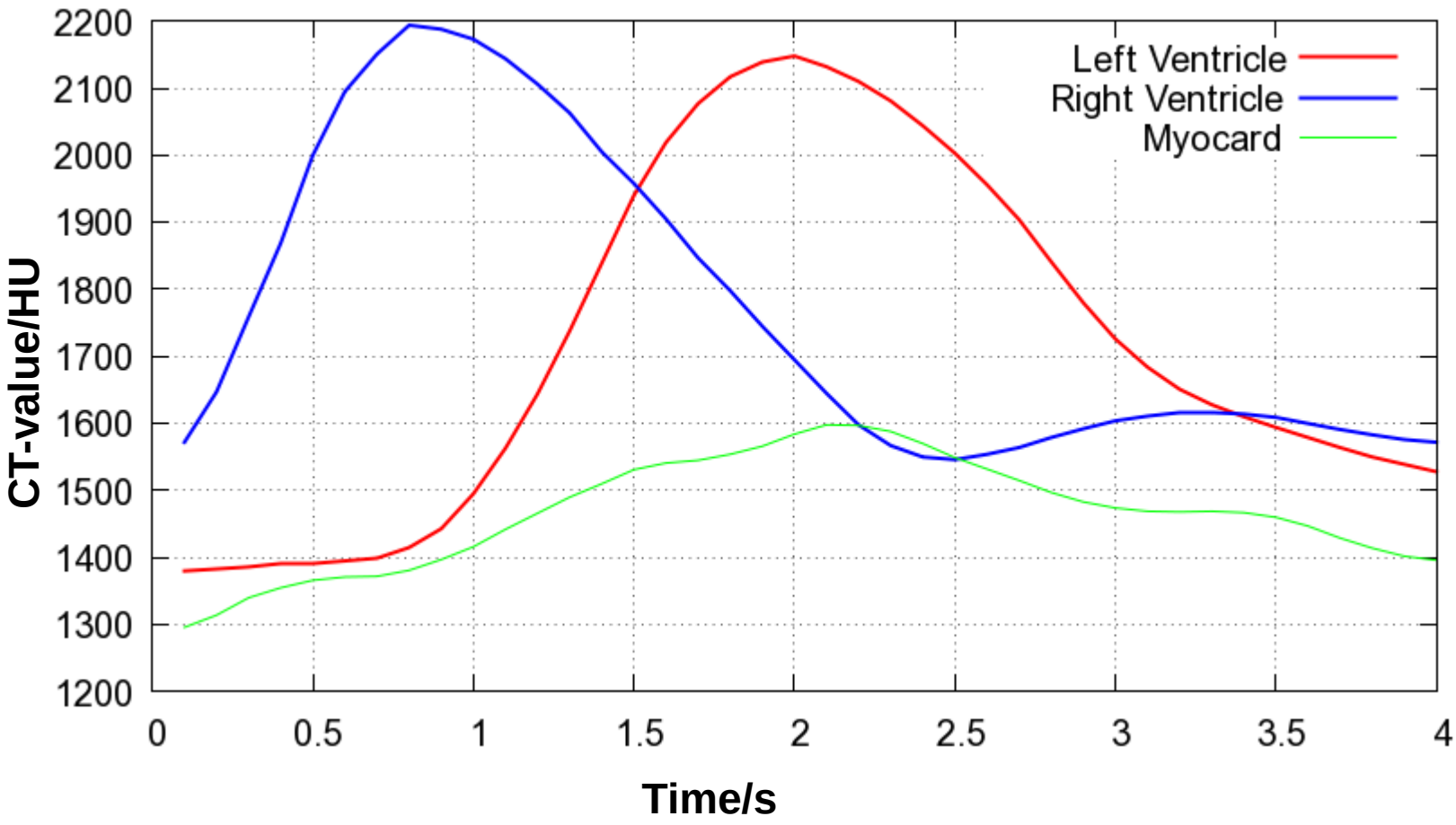


r=0%, Δr=20%, c=20%, Δc=20%, Δp=0.5 s (600 HU / 900 HU)

Time-Density-Curve

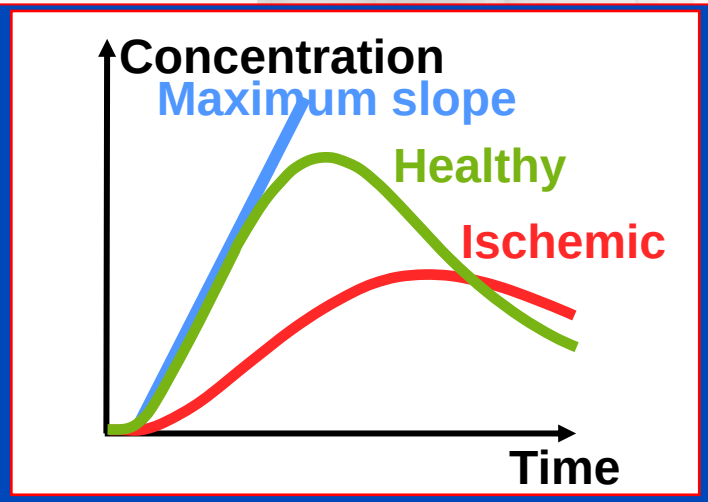


Time-Density-Curve

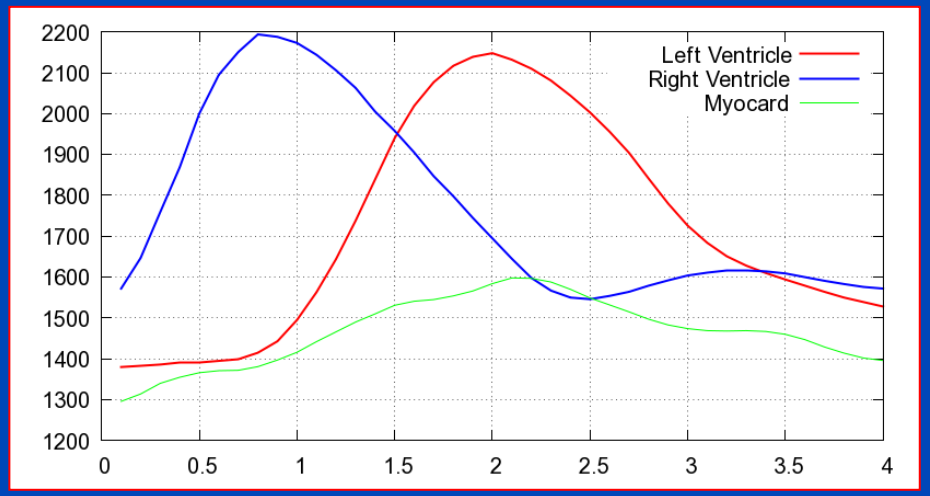


Clinical Case

Clinical Examinations



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 LD_{50} 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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