

Basics of X-Ray-Based Tomographic Imaging for IGRT 3: Motion Management with CT

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Electrocardiogram-correlated image reconstruction from subsecond spiral computed tomography scans of the heart

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Subsecond computed tomography (CT) scanning offers potential for improved heart imaging. We therefore developed and validated dedicated reconstruction algorithms for imaging the heart with subsecond spiral CT utilizing electrocardiogram (ECG) information. We modified spiral CT z -interpolation algorithms on a subsecond spiral CT scanner. Two new classes of algorithms were investigated: (a) 180°CI (cardio interpolation), a piecewise linear interpolation between adjacent spiral data segments belonging to the same heart phase where segments are selected by correlation with the simultaneously recorded ECG signal and (b) 180°CD (cardio delta), a partial scan recon-

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Noninvasive Coronary Angiography by Retrospectively ECG-Gated Multislice Spiral CT

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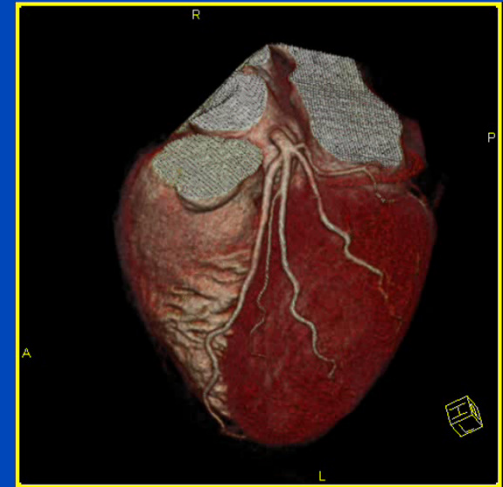
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Imaging the Heart with CT

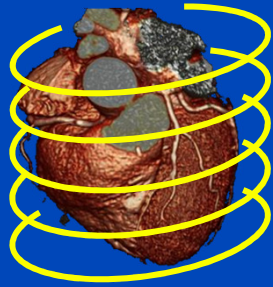
(Cardiac-CT = phase-correlated CT)



- Periodic motion
- Synchronisation (ECG, Kymogram, ...)
- Phase-correlated scanning = Prospective Gating
 - Used in the 80s and 90s with little success.
 - Came recently into use again due to large cone-angles.
- Phase-correlated reconstruction = Retrospective Gating
 - Single-phase (partial scan) approaches, e.g. 180°MCD
 - Bi-phase approaches, e.g. ACV (Flohr et al.)
 - Multi-phase Cardio Interpolation methods, e.g. 180°MCI (gold-standard)
 - Generations
 - » Single-slice spiral CT: 180°CD, 180°CI (introduced 1996¹)
 - » Multi-slice spiral CT: 180°MCD, 180°MCI (introduced 1998²)
 - » Cone-beam spiral CT: ASSR CD, ASSR CI (introduced 2000³)
 - » Wide cone-beam CT: EPBP (introduced 2002⁴)
 - » Multi-source CBCT: EPBP (introduced 2005⁵)

¹Med. Phys. 25(12):2417-2431 (1998), ²Med. Phys. 27(8):1881-1902 (2000), ³Proc. Fully 3D-2001:179-182 (2001),

⁴Med. Phys. 31(6): 1623-1641 (2004), ⁵Med. Phys. 33(7): 2435-2447 (2006)



Retrospective Gating

=

Standard scan + ECG-correlated recon

Standard spiral scan with low pitch value ($p \leq f_H \cdot t_{\text{rot}}$)

Phase-correlated reconstruction

$p \cdot T_{\text{rot}} / 2 \leq \text{Temp. resolution} \leq T_{\text{rot}} / 2$

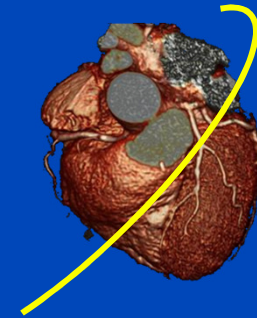
Works also at high heart rates

Dose management: ECG-based TCM

Full phase selectivity

Highly robust (also with arrhythmia)

Good dose usage



Prospective Gating

=

ECG-triggered scan + standard recon

ECG-triggered sequence- or spiral scan with high pitch value

Standard image reconstruction

Temporal resolution = $T_{\text{rot}} / 2$

Good at low heart rates

Dose management: inherent

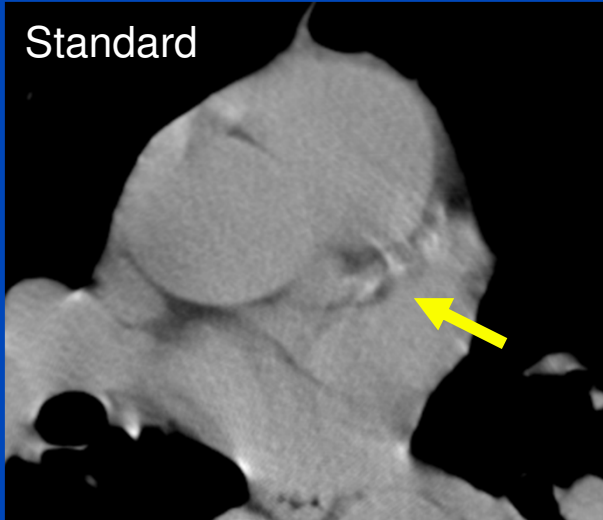
No phase selectivity

Sufficiently robust (not with arrhythmia)

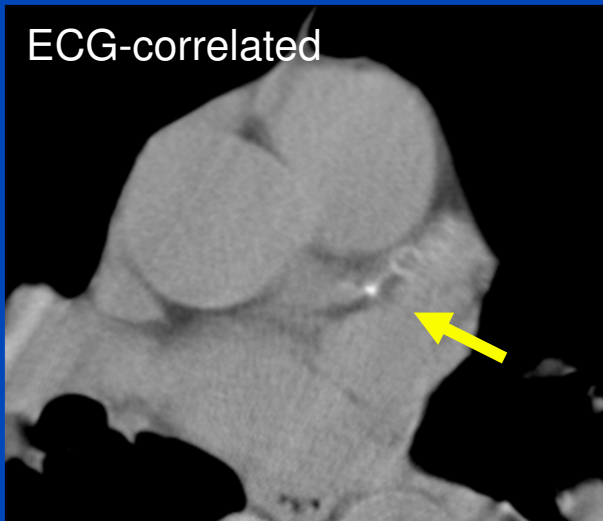
Very good dose usage

Single Slice CT (RSNA 1997)

Standard



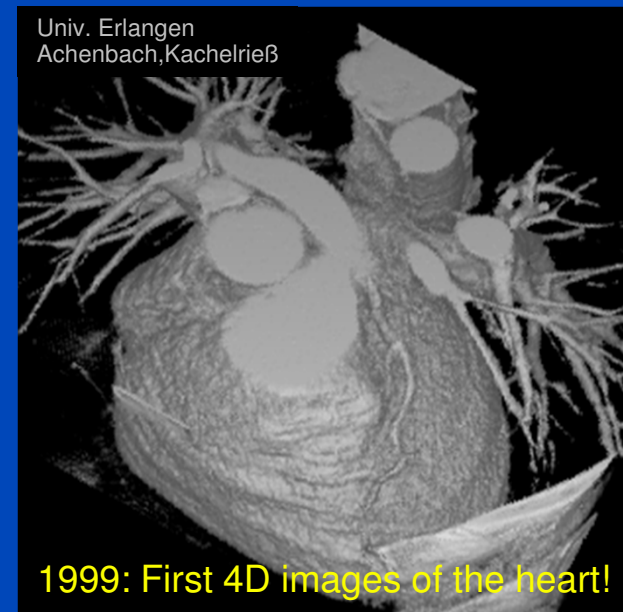
ECG-correlated



Kachelrieß et al. Electrocardiogram-correlated image reconstruction from subsecond spiral computed tomography scans of the heart. Med. Phys., 25(12):2417-2431, December 1998.

Early Cardiac Spiral CT

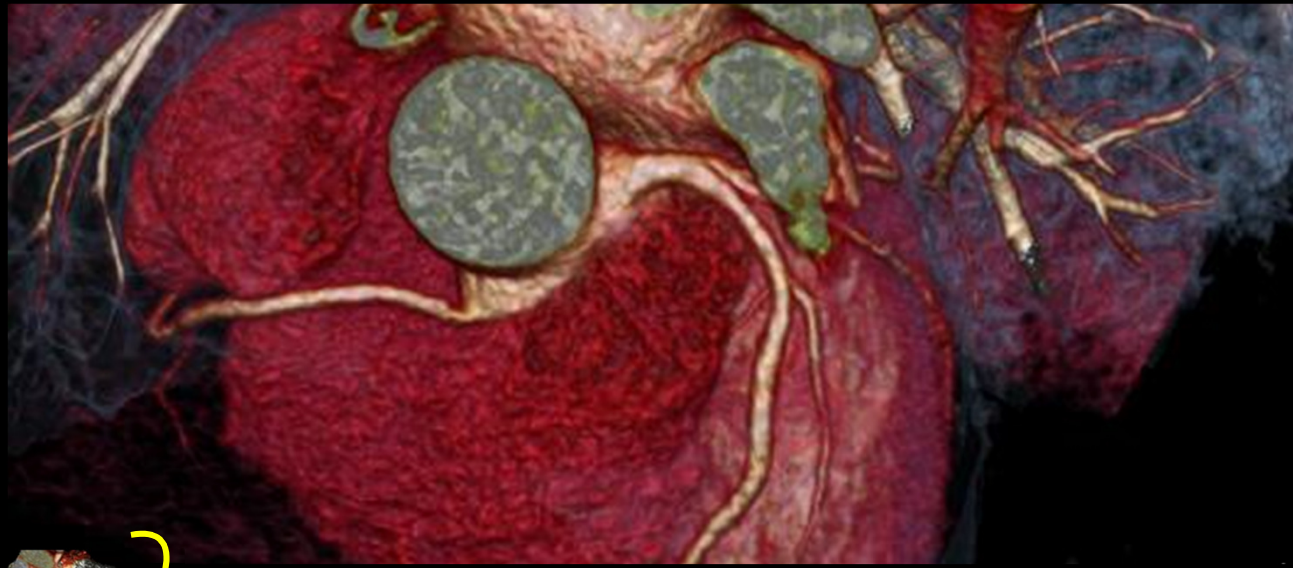
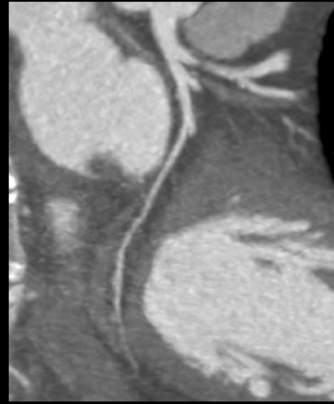
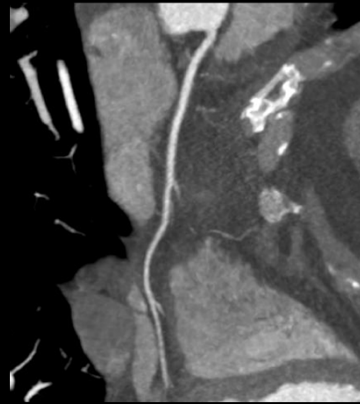
4-Slice CT (RSNA 1999)



1999: First 4D images of the heart!

Kachelrieß et al. ECG-correlated imaging of the heart with subsecond multislice spiral CT. IEEE TMI, 19(9):888-901, September 2000.

Cardiac Spiral CT Today



Adult

Temporal resolution: 75 ms

Collimation: 2.64×0.6 mm

Spatial resolution: 0.6 mm

Scan time: 0.28 s

Scan length: 128 mm

Rotation time: 0.28 s

80 kV, 300 mAs / rotation

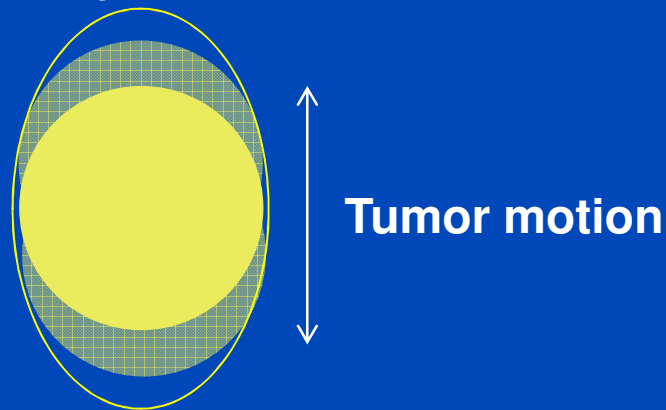
Flash Spiral

Eff. dose: 0.36 mSv

Courtesy of Sir Run Run Shaw University HongKong / HongKong, China

Target Motion

- During radiation treatment the patient's tumor will move due to respiratory (and cardiac) motion
- Tumor motion can be significant: up to several centimeters for diaphragm, liver, kidney, pancreas, thorax, ...
- To avoid missing the tumor:
 - Clinical target volume (CTV) needs to be significantly larger than the gross tumor volume (GTV)
 - Increase portal size
 - Increase irradiation to healthy tissue



Motion Management

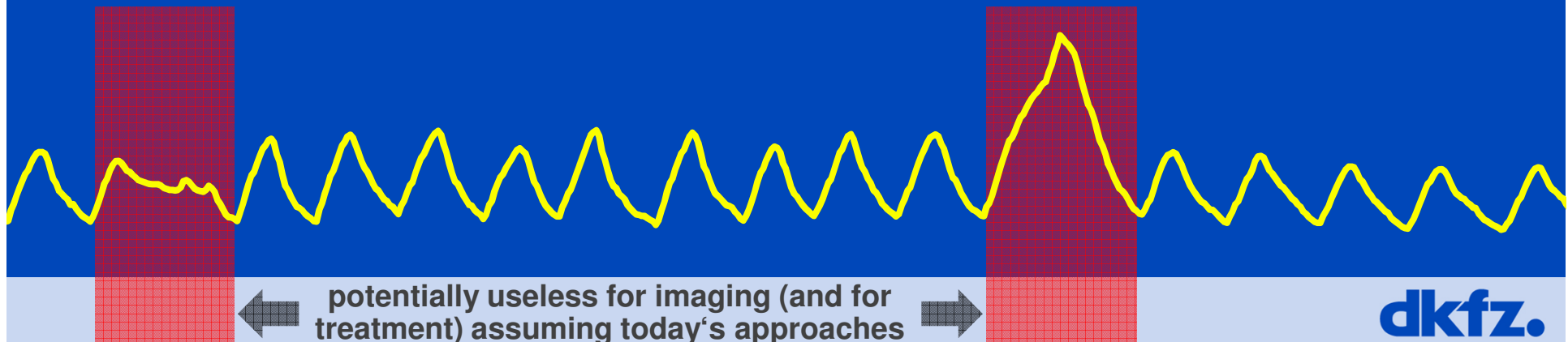
- **Motion surrogate signals**
 - Motion belts (Anzai, Mayo, ...)
 - Optical signal (RPM, ...)
 - Intrinsic rawdata-based signals (kymogram, radar, ...)
- **Quantifying motion due to respiration**
 - Oblique x-ray image pairs (fiducial markers may be required)
 - 4D CT scan (low pitch spiral or multiple rotation sequence)
 - Several CT scans
 - 4D CBCT scan (slow circle, preferably with motion compensation)
- **Accounting for motion during treatment**
 - Breath-hold (with patient coaching, no 4D CT required)
 - Gating (4D CT or 4D CBCT advantageous)
 - Tracking (4D CT or 4D CBCT required)

3D Planning CT

- Spiral acquisition is fast
- Only a snapshot of the patient is shown
- No information about organ or tumor motion
- Impossible to measure the amount of tumor motion

4D Planning CT

- Either conduct a very low pitch spiral CT $p \leq f_R t_{\text{rot}}$
- or a sequence scan, comprised of several circle scans.
- Scan needs to be slow enough to cover a full motion cycle at each z-position.
- Reconstruction applies retrospective gating, i.e. phase-correlated reconstruction algorithms are used.
- Problems, such as data gaps, may occur with irregular breathers.



External Motion Surrogates

Respiratory:

Cardiac:

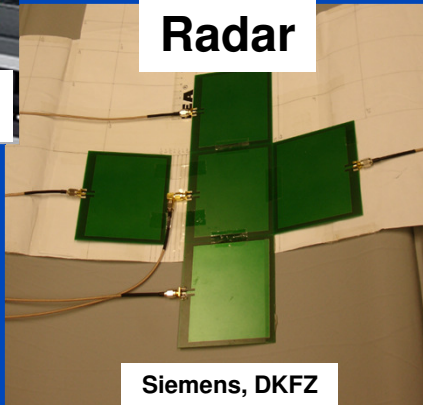
RPM system



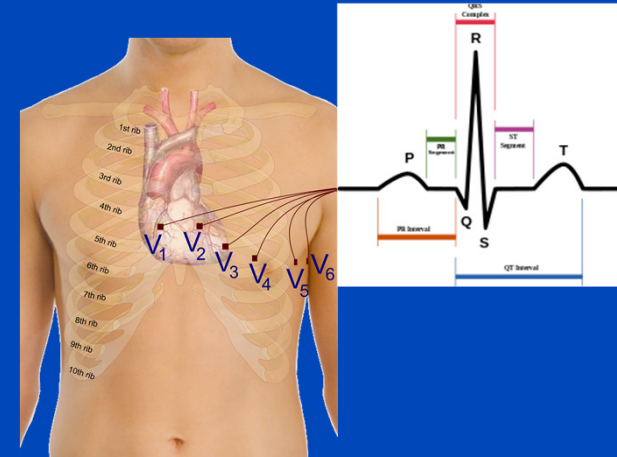
Respiration Belt



Radar



ECG



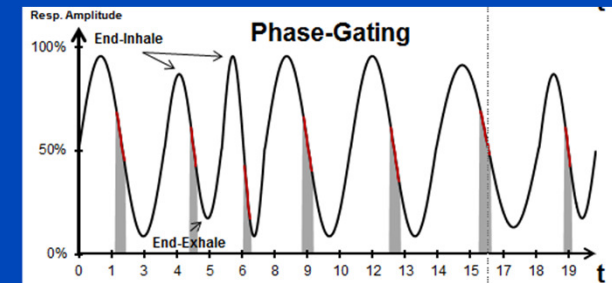
Pulse Oximeter



Phase- and Amplitude Gating

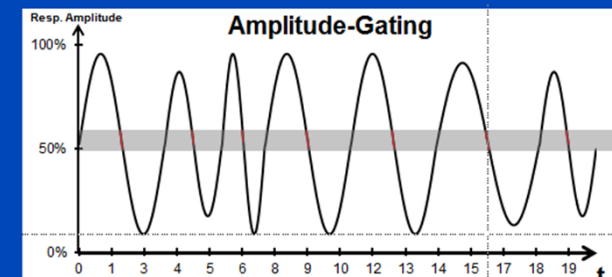
- **Phase gating**

- Assumes periodicity in time and amplitude
- Used in cardiac 3D CT (pro- and retrospective)
- Used in cardiac 4D CT (retrospective)
- Assumptions well-justified apart from extrasystoles



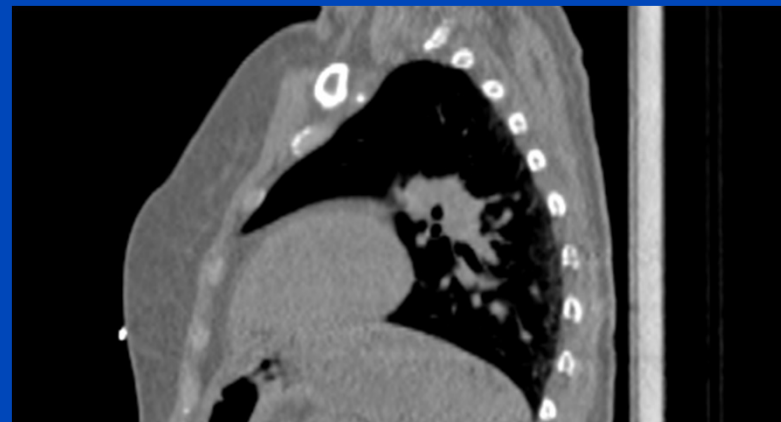
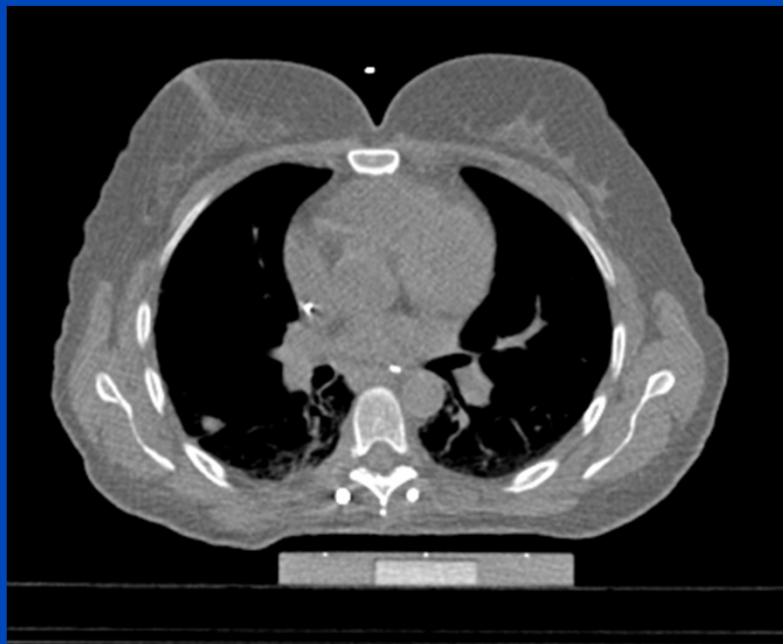
- **Amplitude gating**

- Assumes periodicity in time
- More robust against amplitude variations
- Used for respiratory 3D CT (prospective)
- Used for respiratory 4D CT (retrospective)
- Assumptions not really justified because motion patterns change with changing amplitude



4D CT Scan

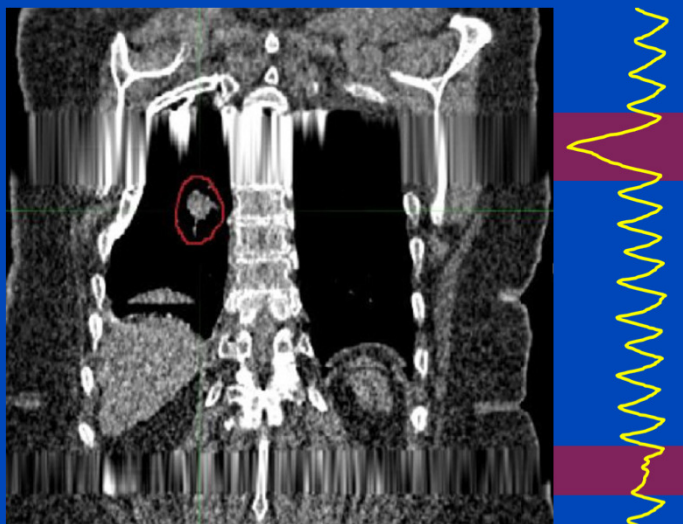
Siemens Somatom Definition Flash



C = 0 HU, W = 1000 HU

Problems with 4D Respiratory-Correlated CT

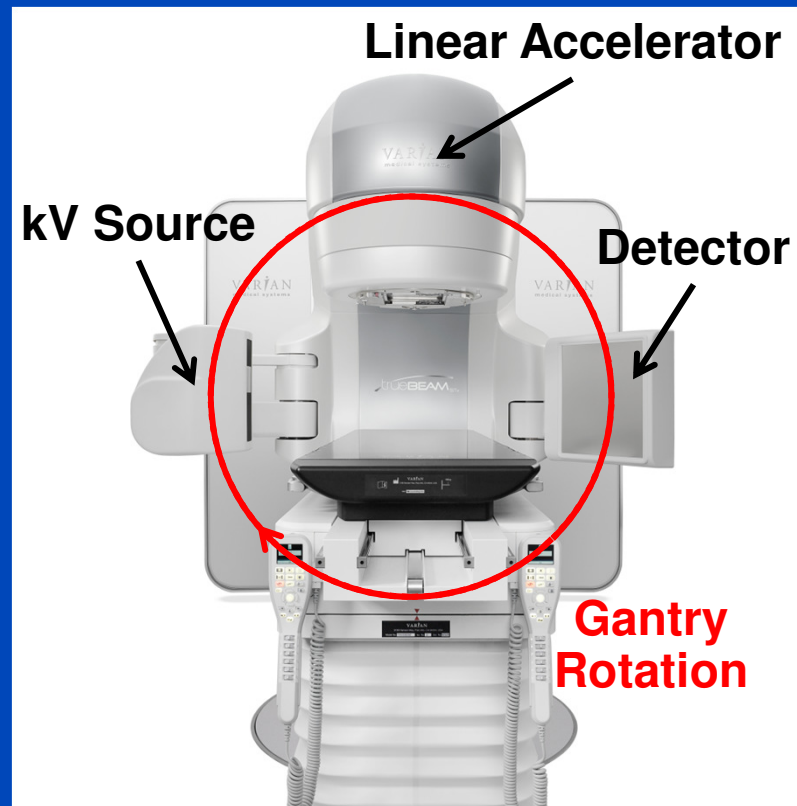
- Pitch value must be low enough $p \leq f_R t_{\text{rot}}$
- Irregular respiration may yield data gaps
 - these are typically filled by interpolating adjacent images
 - and not by advanced reconstruction techniques



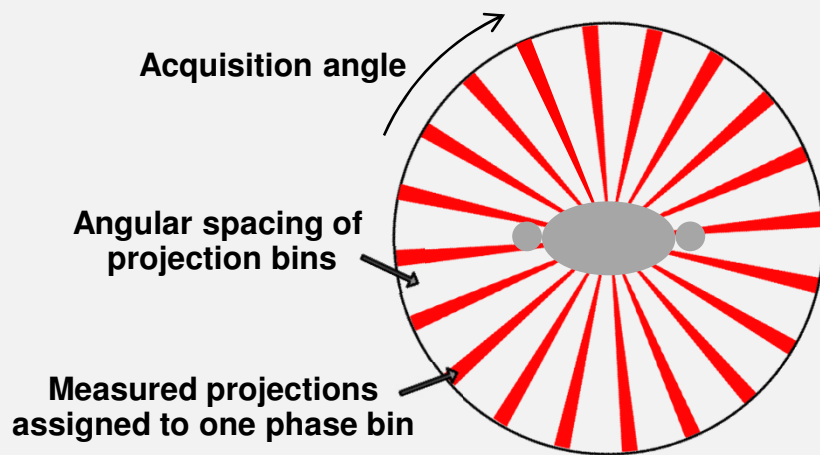
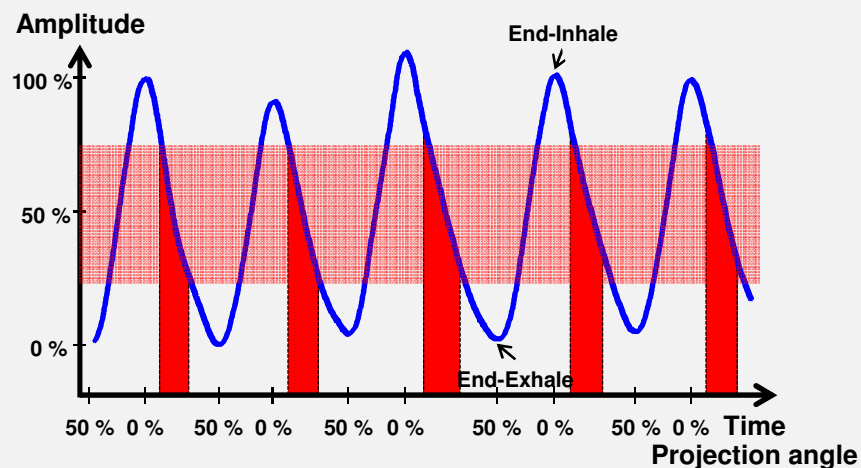
- Only a fraction of data is used for each frame

Motion Modelling is the Future!

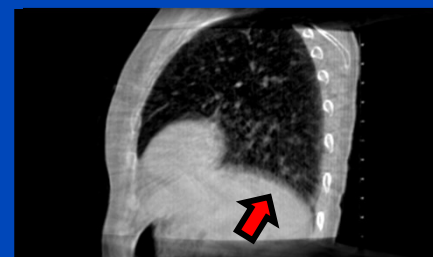
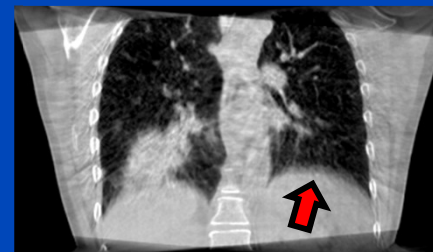
Motion Management for CBCT in IGRT



4D CBCT Scan with Retrospective Gating



Without gating (3D):
Motion artifacts



With gating (4D):
Sparse-view artifacts

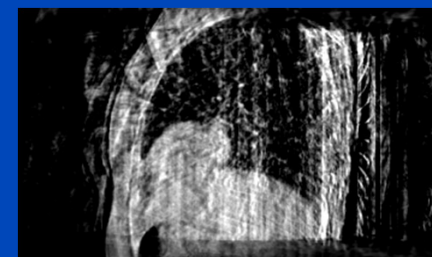
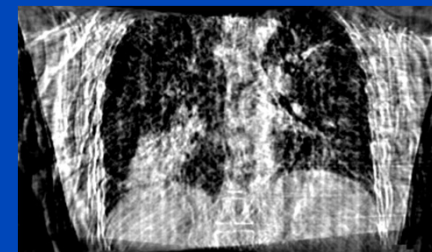
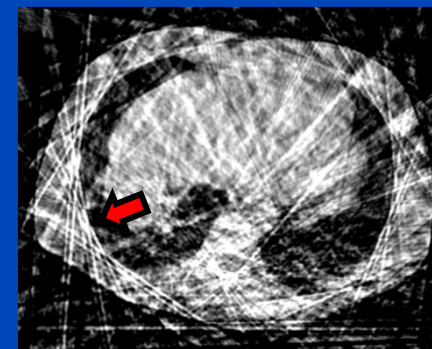
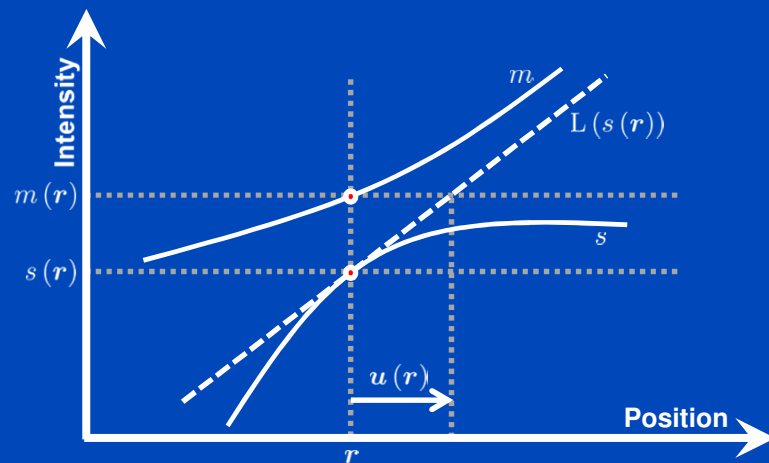


Image Registration

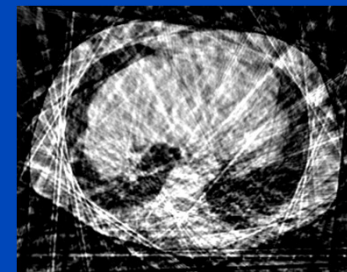
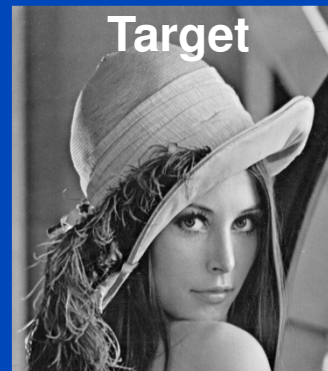
- Static target image s
- Model to be deformed m
- Find transformation vector field T , i.e. $s = m \circ T$
- **Demons algorithm**
 - Displacement update u by intensity matching on linear approximation

$$u = \frac{m - s}{\|\nabla s\|^2 + (m - s)^2} \nabla s$$



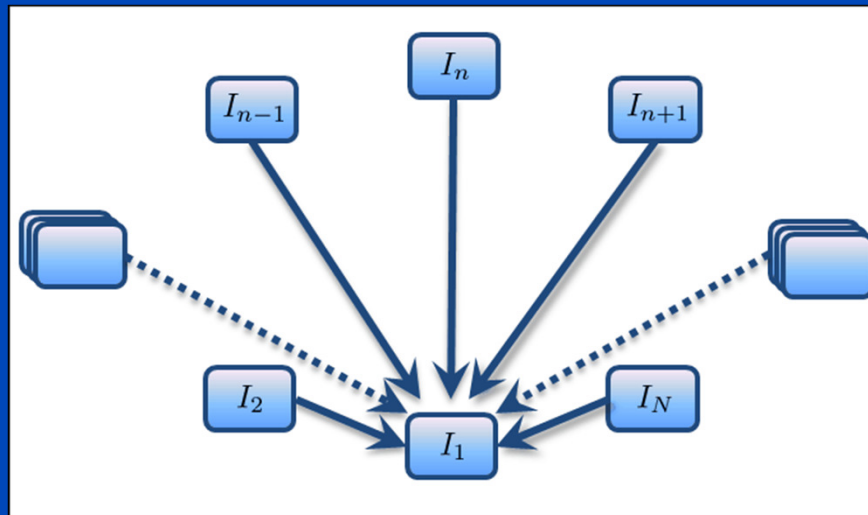
- Regularization
 - Two Gaussian convolution kernels $G_{\text{fluid}}, G_{\text{diffusion}}$
 - $T \leftarrow G_{\text{diffusion}} * (T \circ \exp(G_{\text{fluid}} * u))$

Deformed model matching target



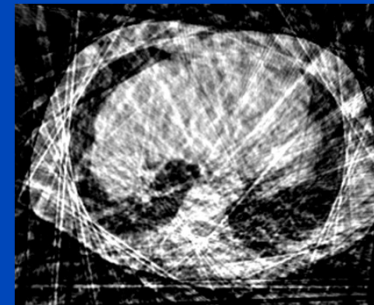
A Standard Motion Estimation and Compensation Approach (sMoCo)

- Motion estimation via standard 3D-3D registration

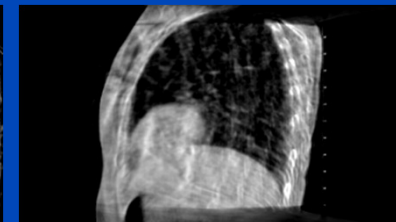
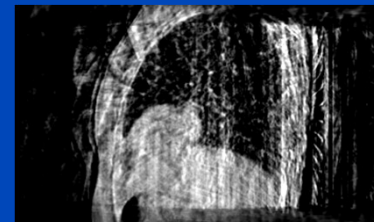
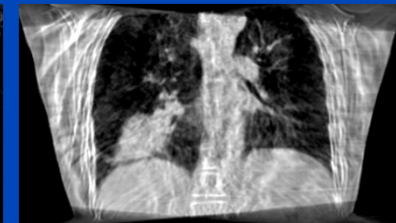
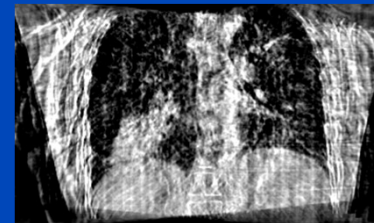
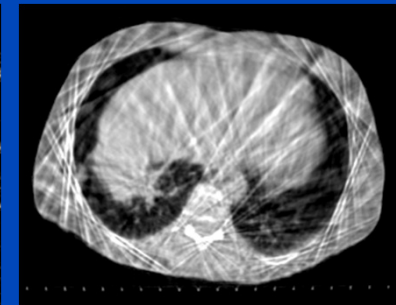


- Has to be repeated for each reconstructed phase
- Streak artifacts from gated reconstructions propagate into sMoCo results

Gated 4D CBCT

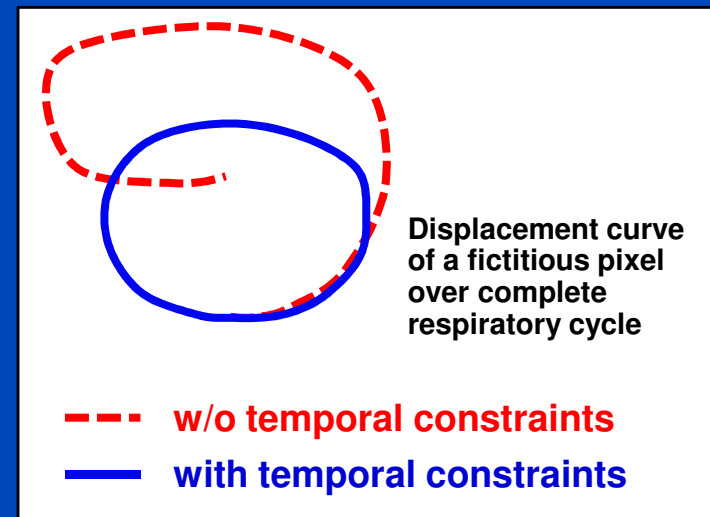
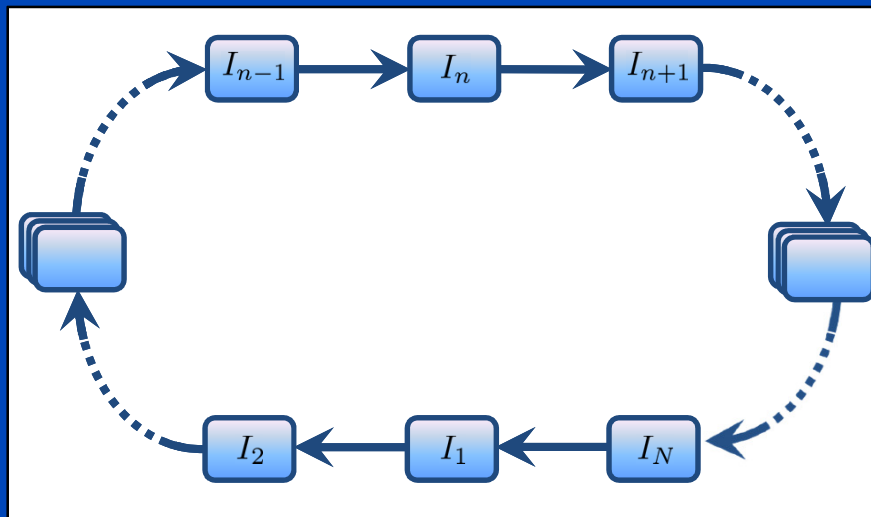


sMoCo



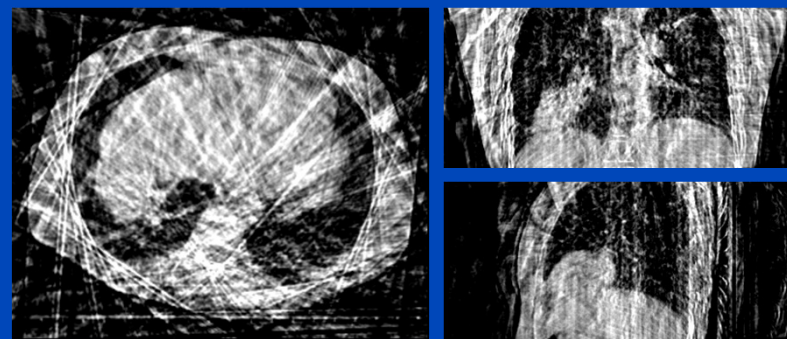
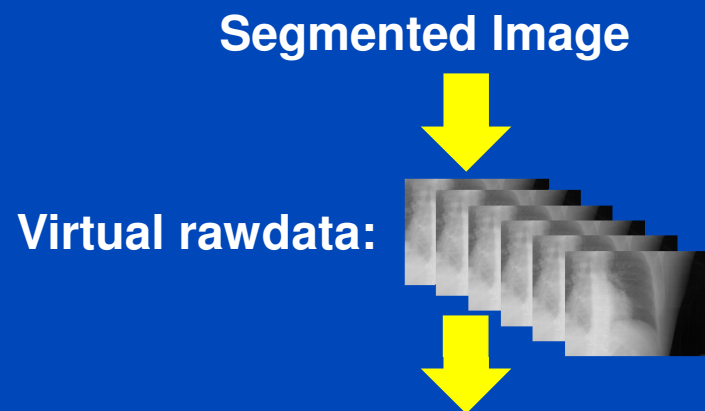
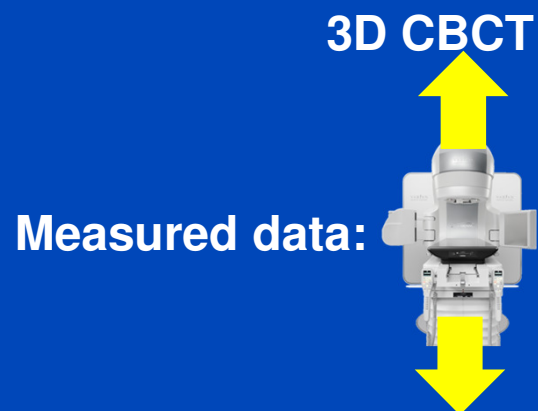
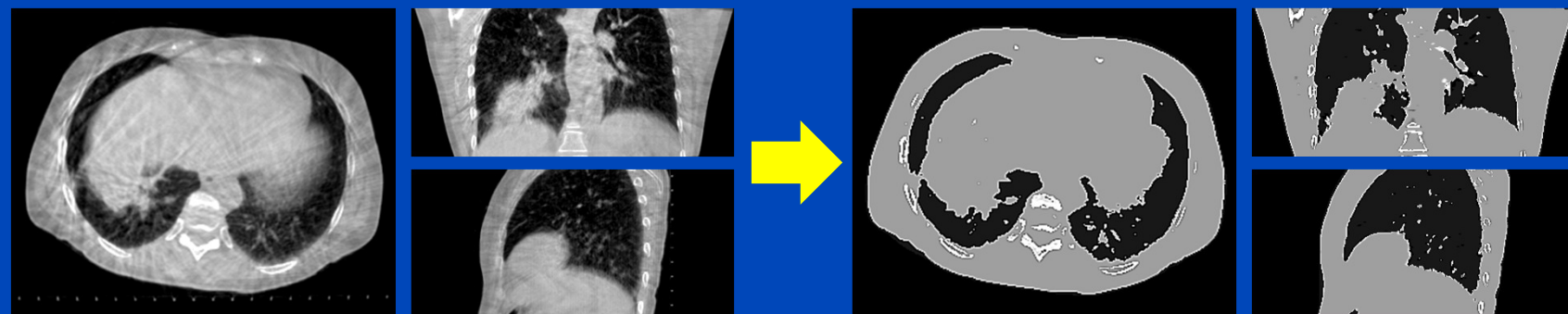
A Cyclic Motion Estimation and Compensation Approach (cMoCo)

- Motion estimation only between adjacent phases
 - All other MVFs given by concatenation

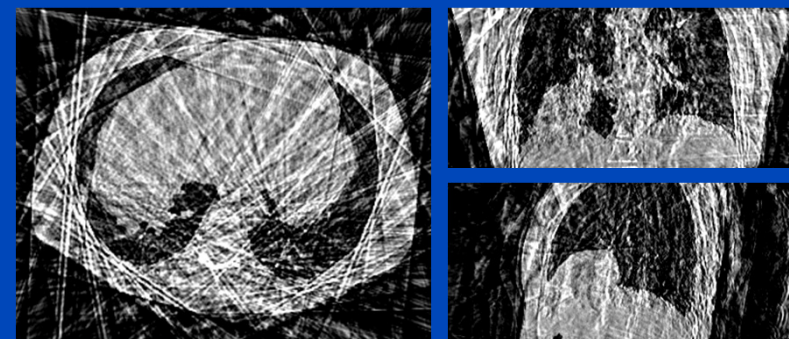


- Incorporate additional knowledge
 - A priori knowledge of quasi periodic breathing pattern
 - Non-cyclic motion is penalized
 - Error propagation due to concatenation is reduced

Artifact Model-Based MoCo (aMoCo)



Gated 4D CBCT



4D Artifact Images

Propagation of Respiratory Motion

- Respiratory motion propagates into 3D reconstruction even if the image is stationary.
- Perform segmentation before forward projection.

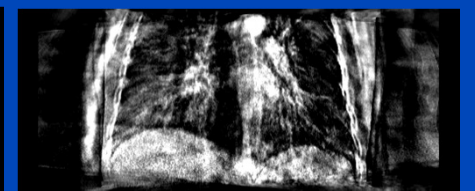
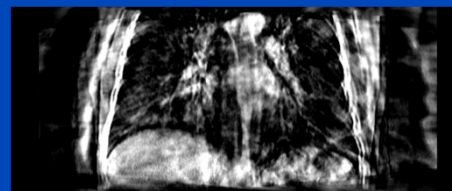
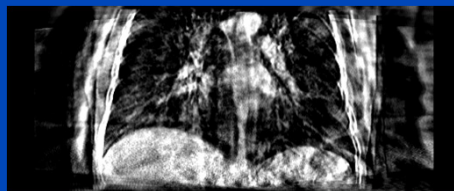
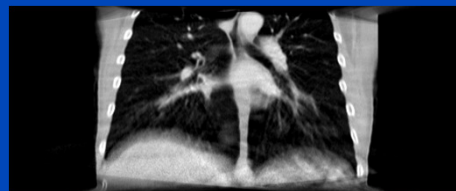
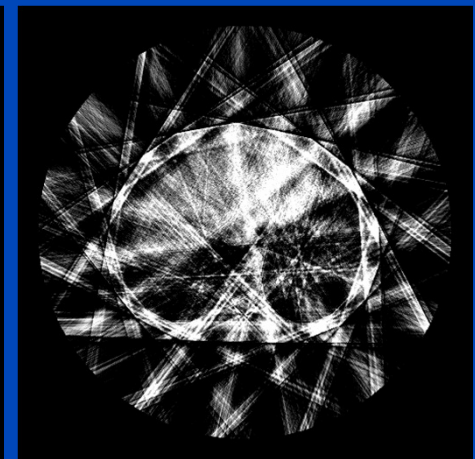
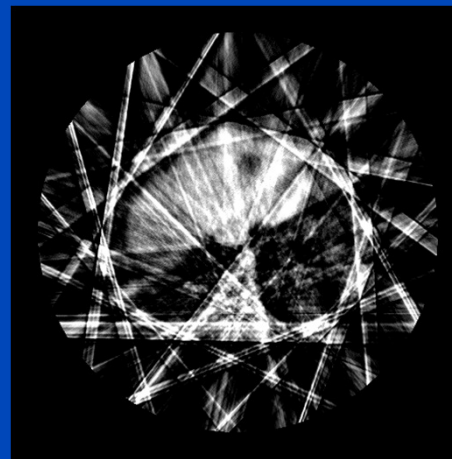
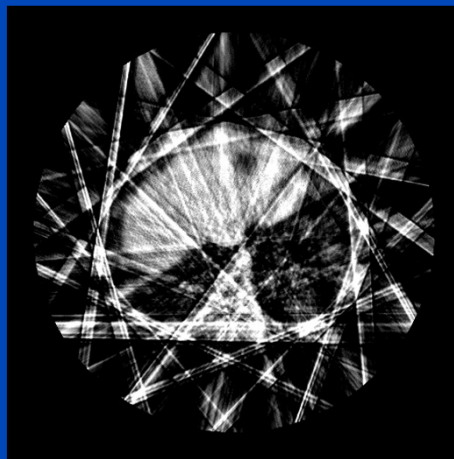
Artifact Image:

$$X^{-1}p$$

$$X_{PC}^{-1}p$$

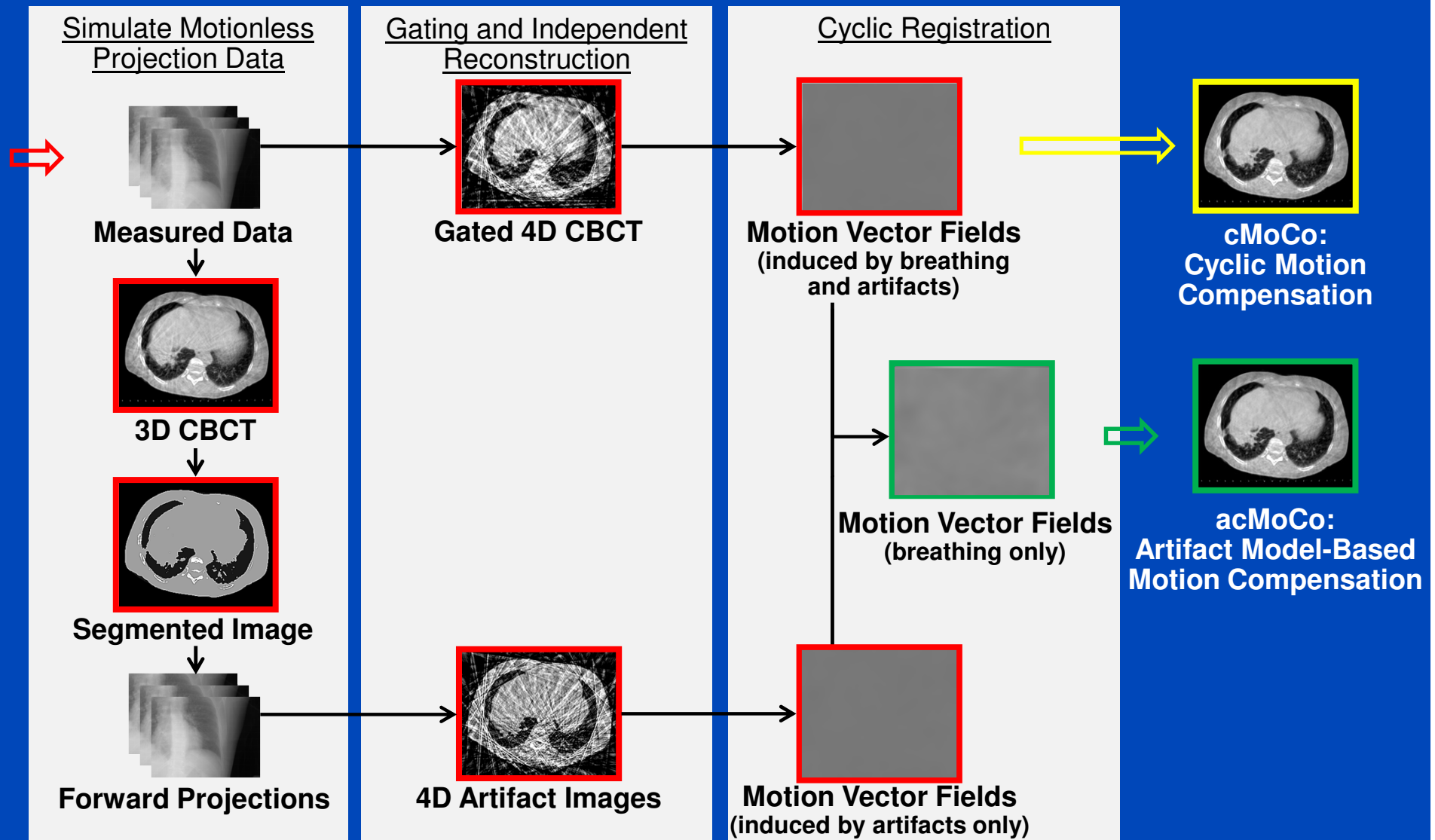
$$X_{PC}^{-1}(X(X^{-1}p))$$

$$X_{PC}^{-1}(X(\text{Segm. Im.}))$$



PC = phase-correlated reconstruction = gated reconstruction (CT or MR). $C = -200$ HU, $W = 1400$ HU

Motion Estimation using an Patient-Specific Artifact Model



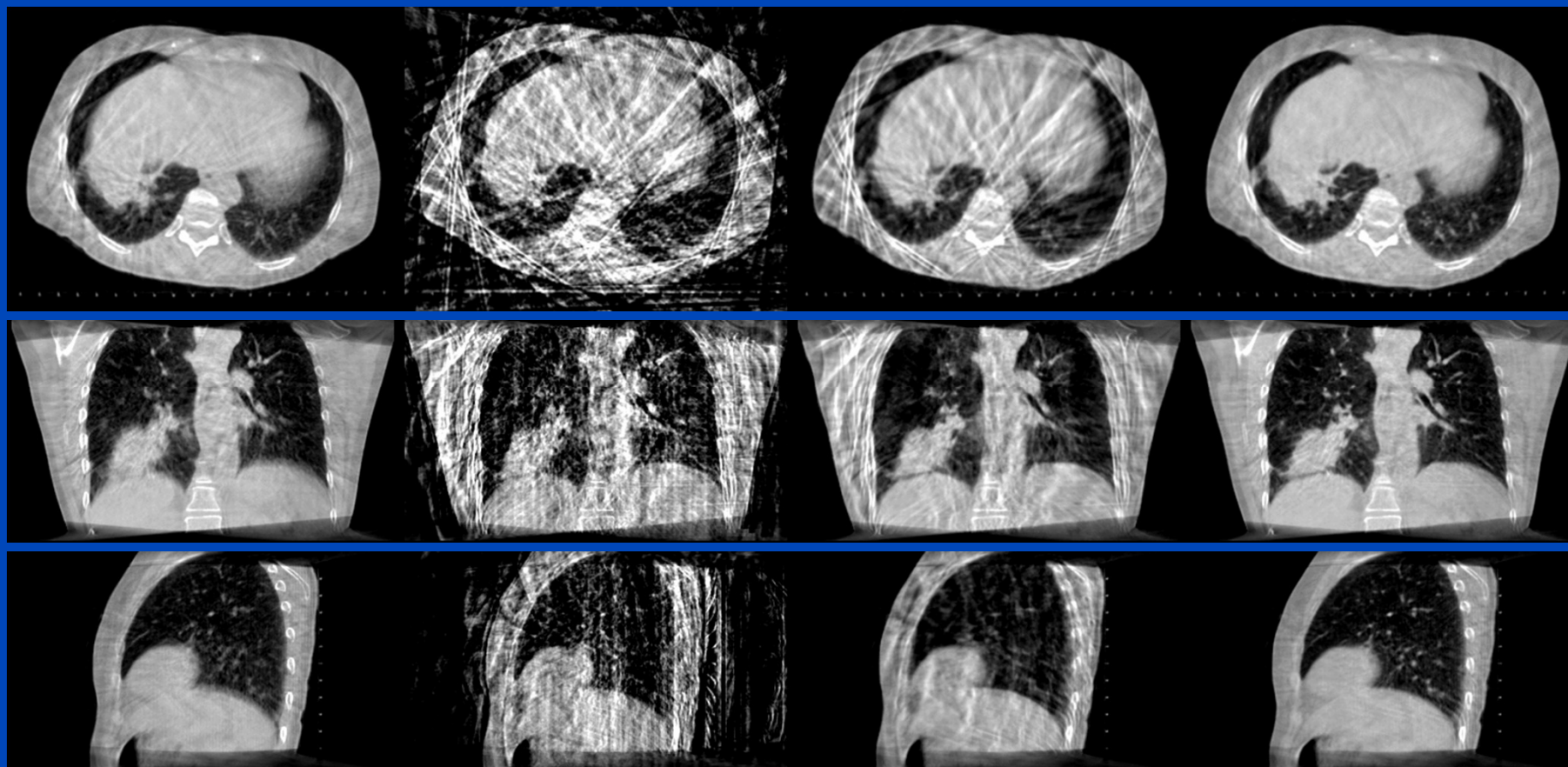
Patient Data – Results

3D CBCT
Standard

Gated 4D CBCT
Conventional
Phase-Correlated

sMoCo
Standard Motion
Compensation

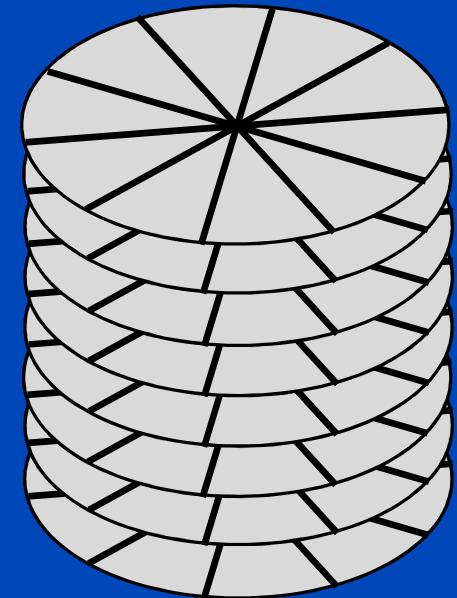
acMoCo
Artifact Model-Based
Motion Compensation



Spin-Off Effects?

What about MoCo in MR, in PET/MR, or in MR-guided RT?

- MR acquisition is slow
- 4D MR acquisition is even slower
- Thus:
Develop a framework for MR-MoCo
- Use motion vector fields
 - to compensate the motion from clinical sequences
 - to compensate the motion from other modalities
 - for tracking the tumor position
- Using dedicated image reconstruction and registration techniques, allows to cope with highly undersampled data.¹

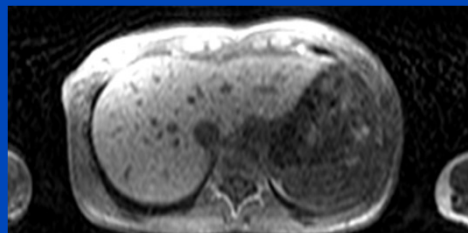


¹ Rank, Heußner, Buzan, Wetscherek, Freitag, Dinkel, Kachelrieß. 4D respiratory motion-compensated image reconstruction of free-breathing radial MR data with very high undersampling. *Magn Reson Med*, in press.

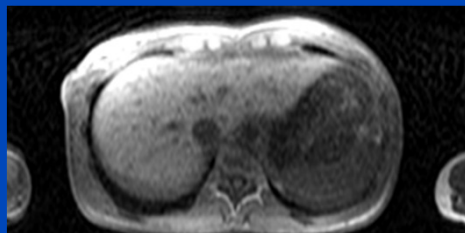
4D MR Motion Compensation

Results Volunteer p8

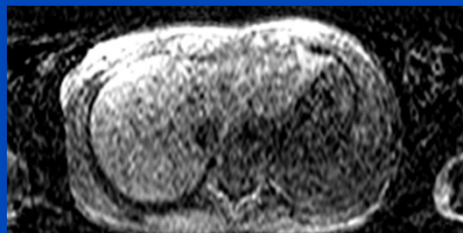
4D gridding
6 min 51 s



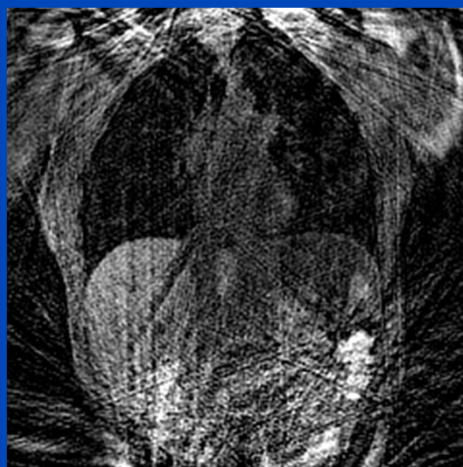
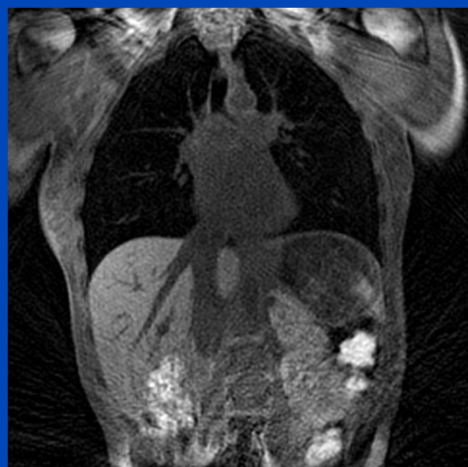
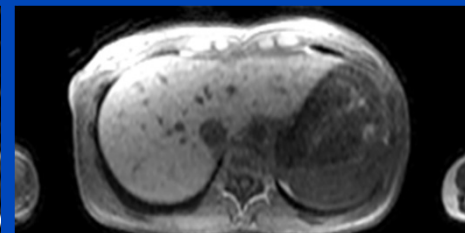
3D gridding
37 s



4D gridding
37 s



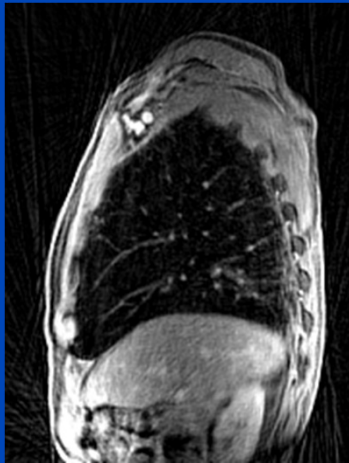
4D joint MoCo-HDTV
37 s



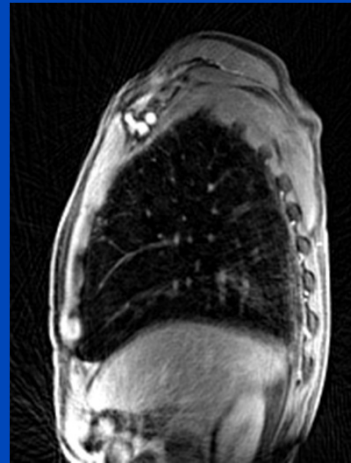
4D MR Motion Compensation

Results Patient c24

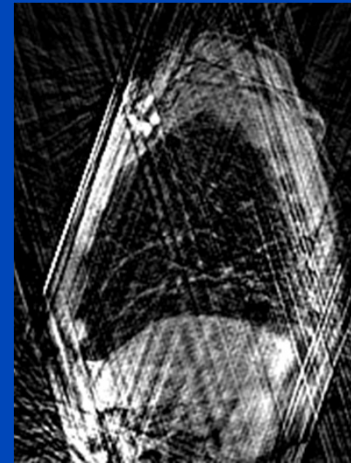
4D gridding
5 min 50 s



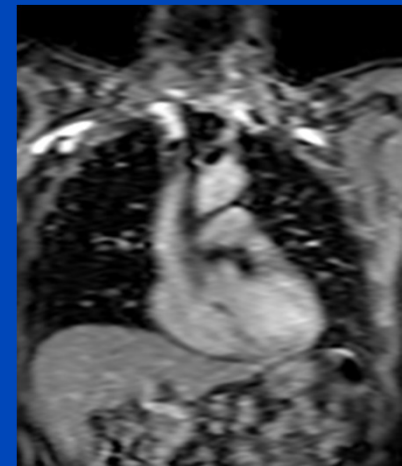
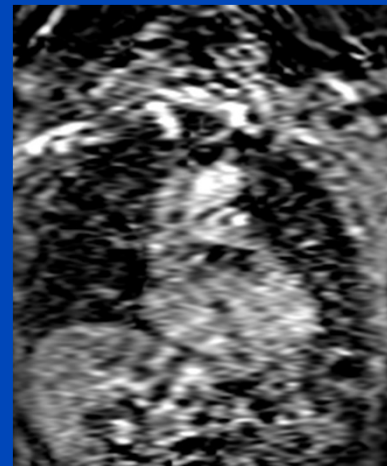
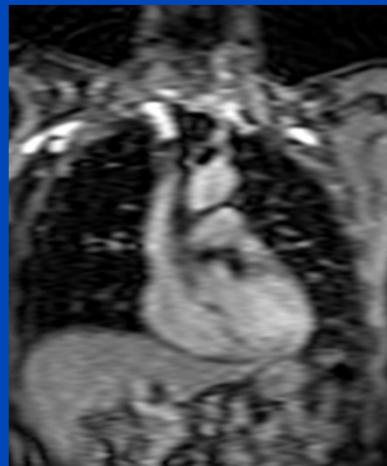
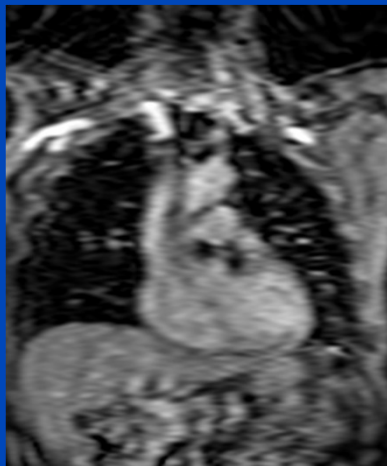
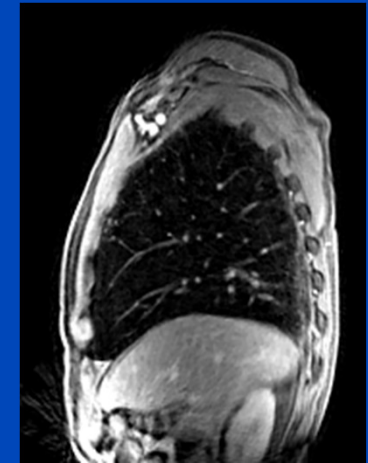
3D gridding
41 s



4D gridding
41 s



4D joint MoCo-HDTV
41 s



Magnetom Aera at Thoraxklinik, Radial VIBE WIP 528K
 $R = 20$, $\Delta r = 10\%$

4D PET/MR Motion Compensation

Data Acquisition and Processing

- Simultaneous PET/MR acquisition at Siemens Biograph mMR at DKFZ
 - number of subjects: 5 (thorax), 2 (abdomen)
 - tracer: fluorodeoxyglucose (^{18}F -FDG)
 - acquisition time per bed: 5 min
 - MR sequence: 3D-encoded gradient echo sequence with radial stack-of-stars sampling scheme and golden angle radial spacing
 - pre-processing of PET list-mode data
 - » sorting of list-mode data into sinograms for different motion phases with binning tools
 - » scatter estimation with e7-tools
 - in-house MoCo OSEM algorithm for reconstruction



Related Work

Authors	MR sequence	MR acquisition time / min	Voxel size / mm ³	Number of gates	Motion estimation
Würslin et al. 2013	2D multi-slice	3.0	2.0×2.0×10.0	4	3D
Petibon et al. 2014	2D multi-slice	3.0	2.0×2.0×8.0	7	3D
Dutta et al. 2015	2D radial	5.5 to 7.0	2.0/2.3×2.0/2.3×5.0/8.0	6	3D
Fayad et al. 2015a	2D multi-slice	1.5	2.0×2.0×10.0	4	3D
Fayad et al. 2015b	2D multi-slice	3.0	2.0×2.0×10.0	4	3D
Fürst et al. 2015	radial stack-of-stars	10.0	1.7×1.7×5.0	5	3D
Grimm et al. 2015	radial stack-of-stars	3.0 to 10.0	1.7×1.7×5.0	5	3D
Manber et al. 2015	2D multi-slice	1.0 and 2.7	1.8×1.8×10.0 ^a	10 ^b	2D
proposed	radial stack-of-stars	1.0 and 5.0	1.6×1.6×4.5	20^{b,c}	3D

^a 25 mm gap between slice centers

^b discrimination between inhalation and exhalation

^c motion phases have an overlap of 50%

4D PET/MR Motion Compensation

Generation of Highly Undersampled MR Data Set

- Retrospective generation of a sparse MR rawdata set reproducing an interlaced MR acquisition

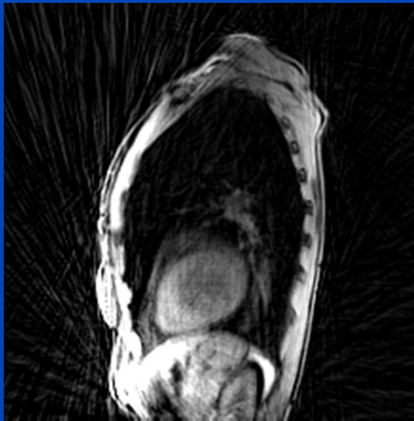


- Intrinsic gating: motion amplitudes were estimated from measured MR data
- MR and PET data were sorted retrospectively into 20 overlapping motion phase bins (10% width)

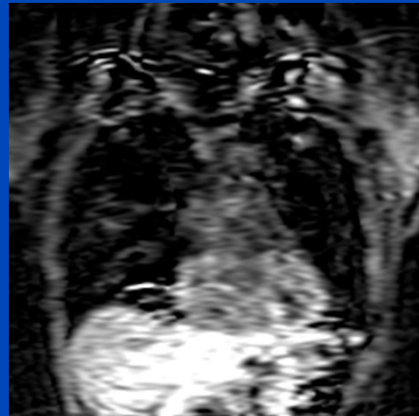
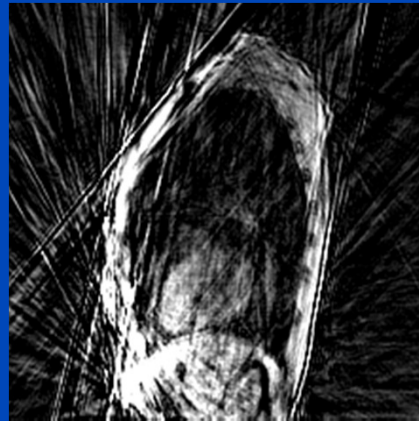
Results of MR Reconstruction

4D gated gridding

5 min / bed

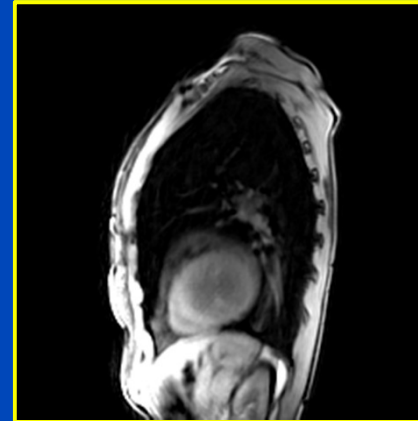


1 min / bed

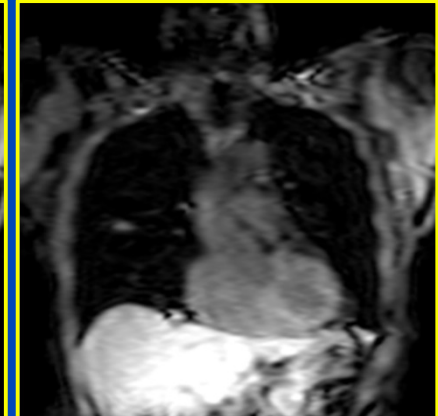
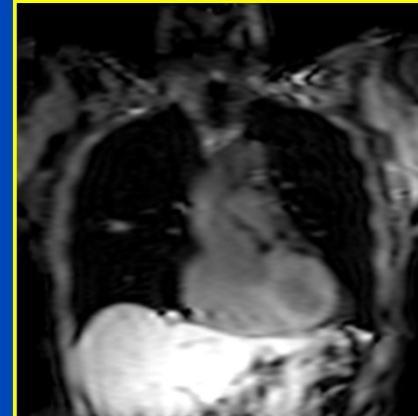
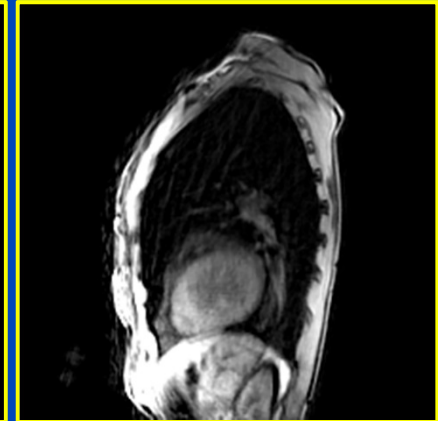


4D MoCo¹

5 min / bed



1 min / bed

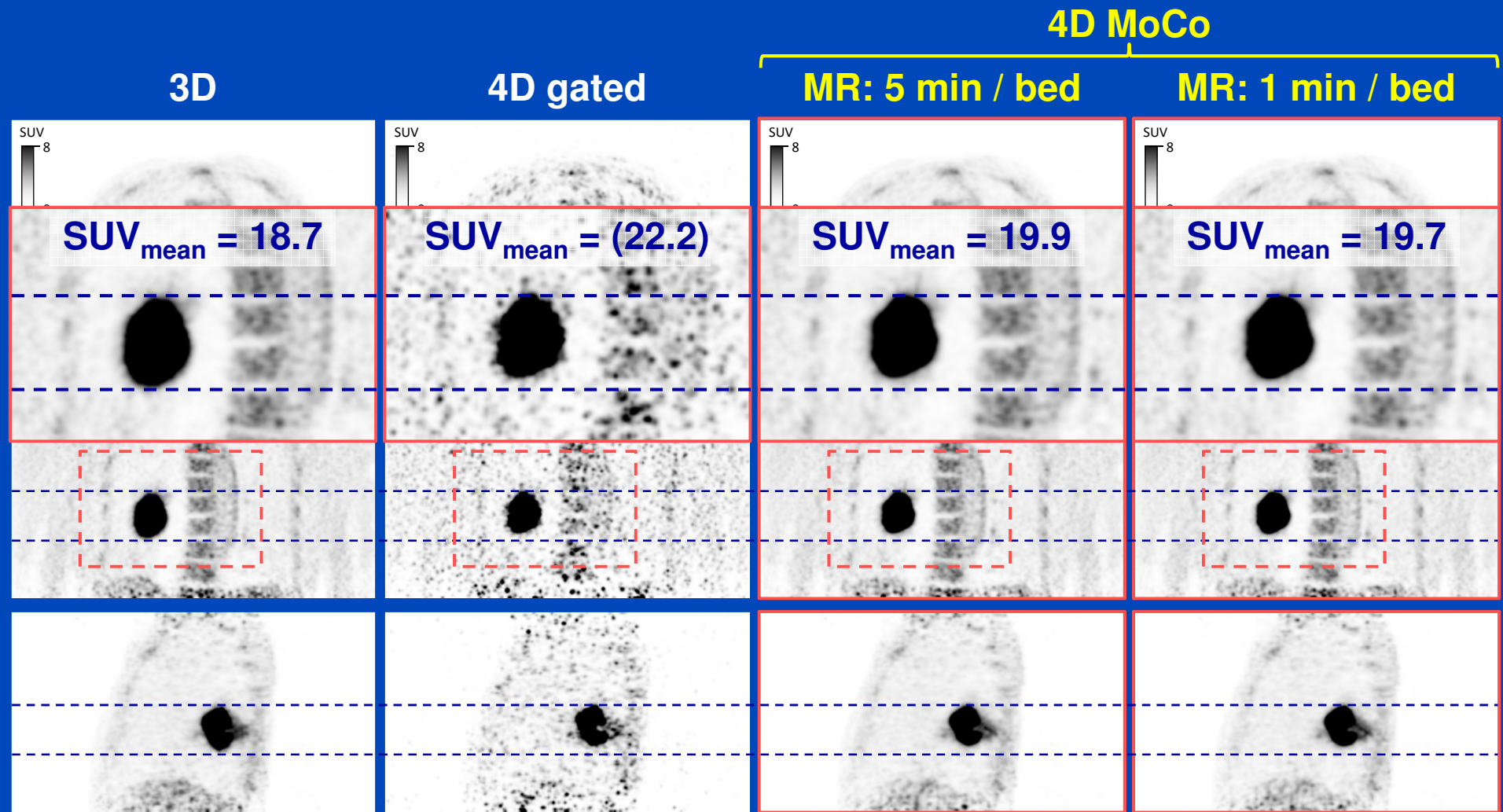


MVFs

MVFs

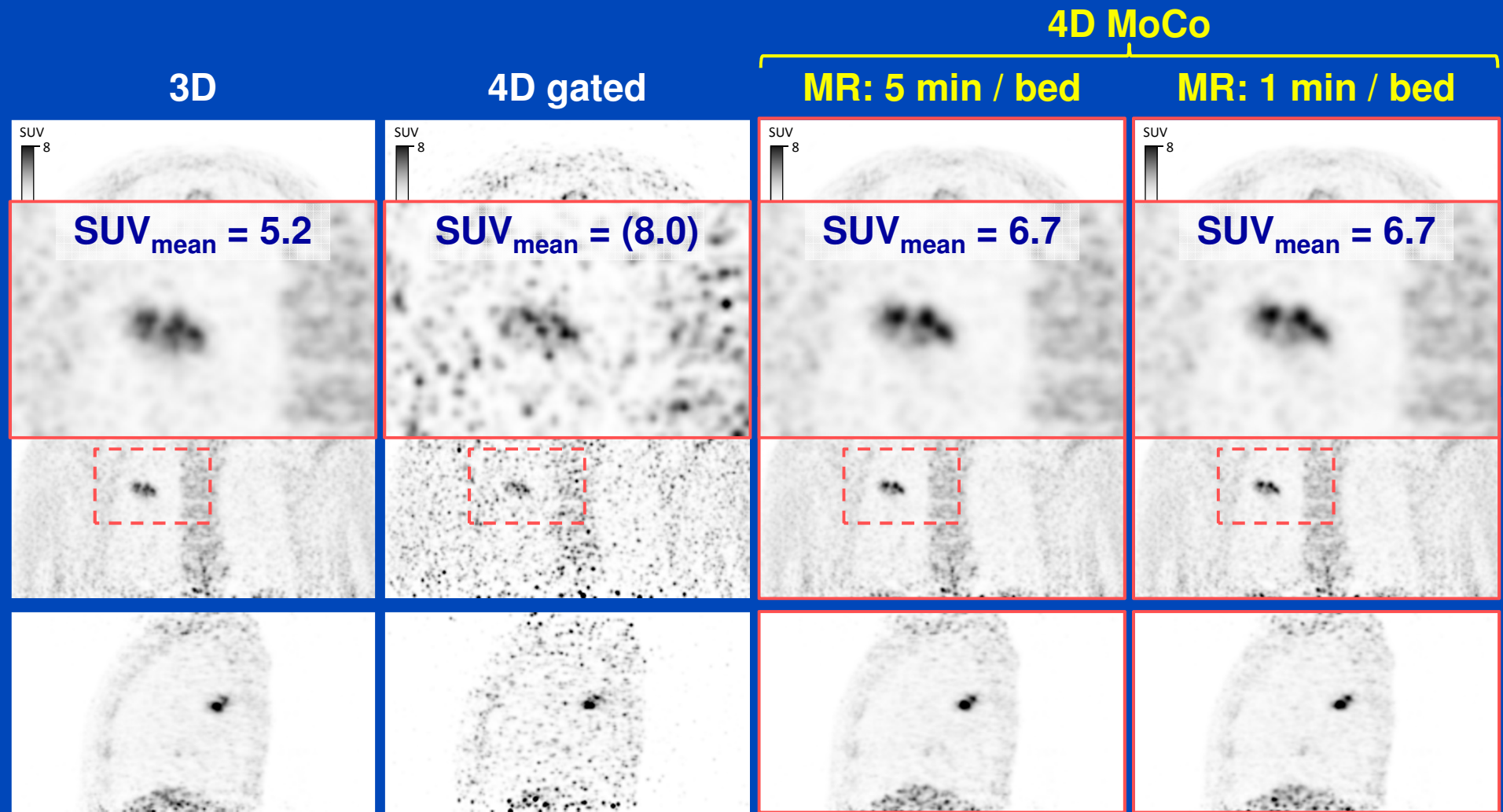
[1] Rank, Heußner, Buzan, Wetscherek, Freitag, Dinkel, Kachelrieß. 4D respiratory motion-compensated image reconstruction of free-breathing radial MR data with very high undersampling. *Magn Reson Med*, accepted for publication.

Results of PET Reconstruction (I)



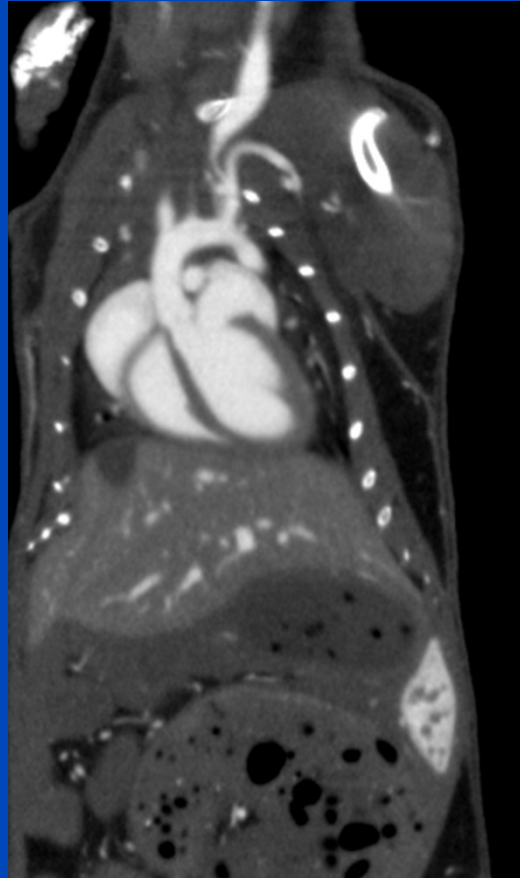
due to the high noise level of 4D gated PET,
 SUV_{mean} was systematically overestimated

Results of PET Reconstruction (II)



due to the high noise level of 4D gated PET,
SUV_{mean} was systematically overestimated

Is There More?

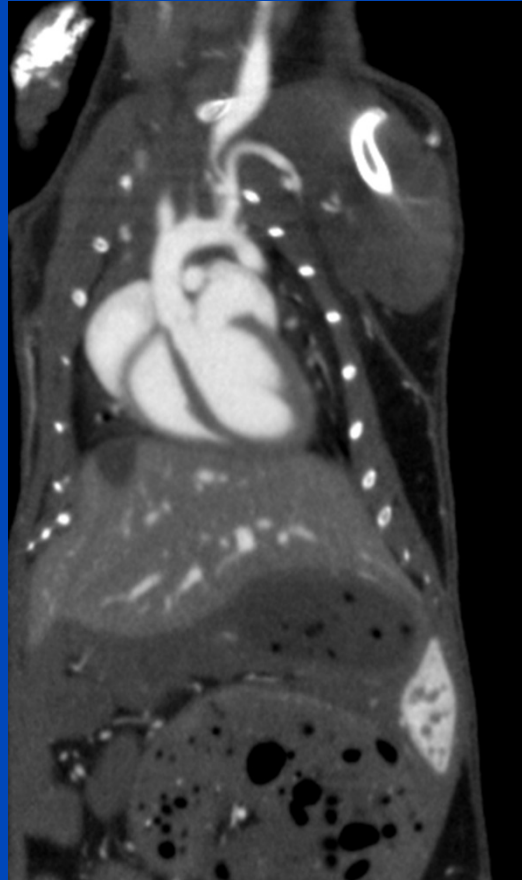


Data displayed as:

Heart: 280 bpm

Lung: 150 rpm

Mouse with 180 rpm and 240 bpm.

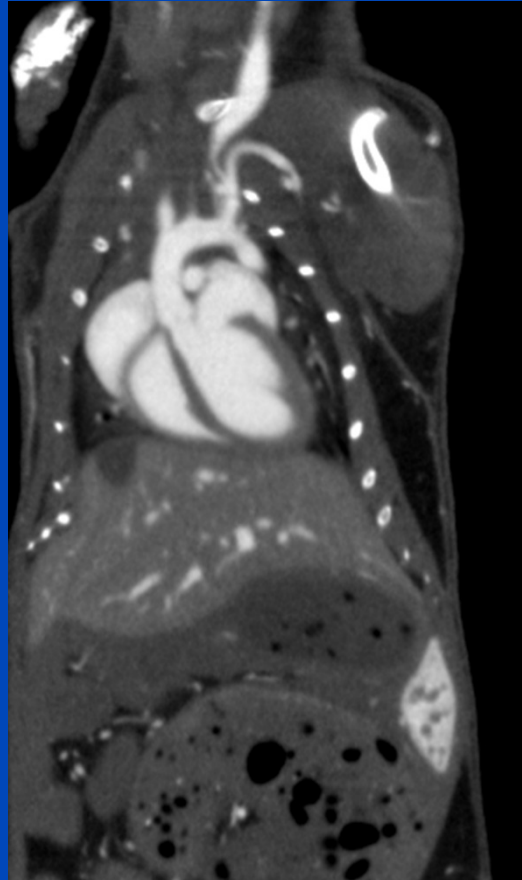


Data displayed as:

Heart: 180 bpm

Lung: 90 rpm

Mouse with 180 rpm and 240 bpm.

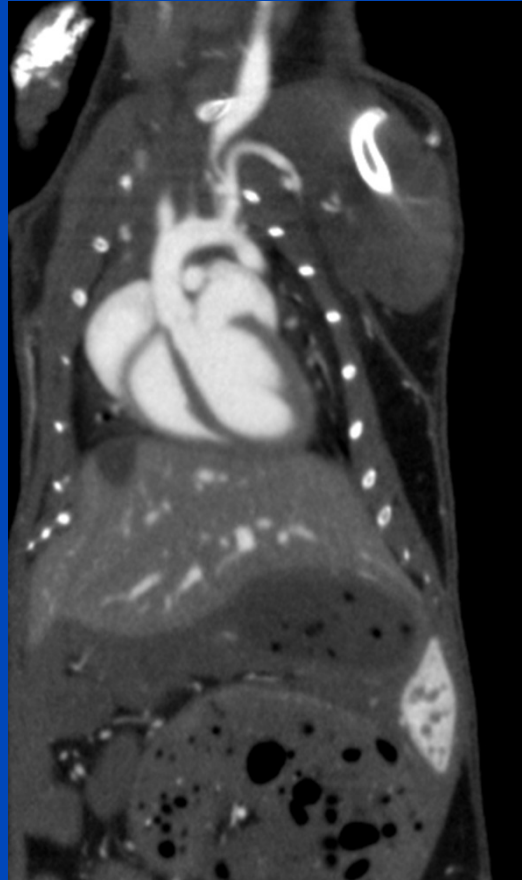


Data displayed as:

Heart: 90 bpm

Lung: 90 rpm

Mouse with 180 rpm and 240 bpm.

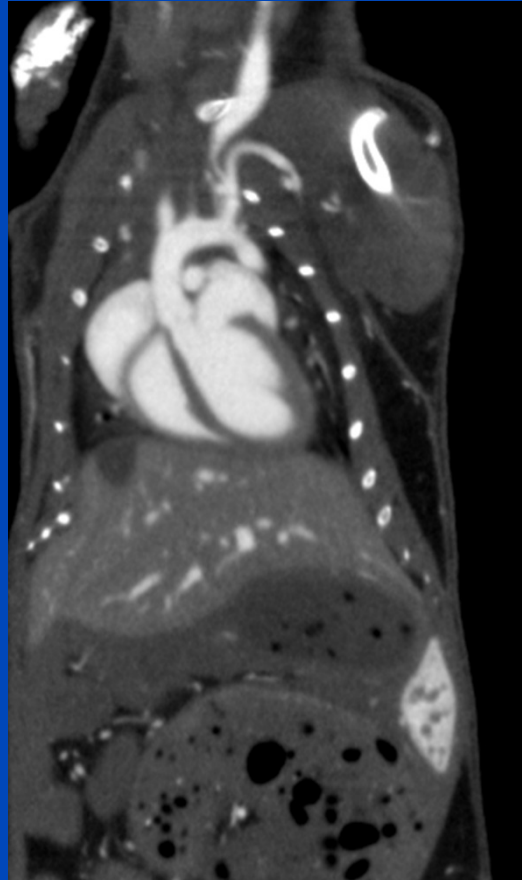


Data displayed as:

Heart: 0 bpm

Lung: 90 rpm

Mouse with 180 rpm and 240 bpm.



Data displayed as:

Heart: 90 bpm

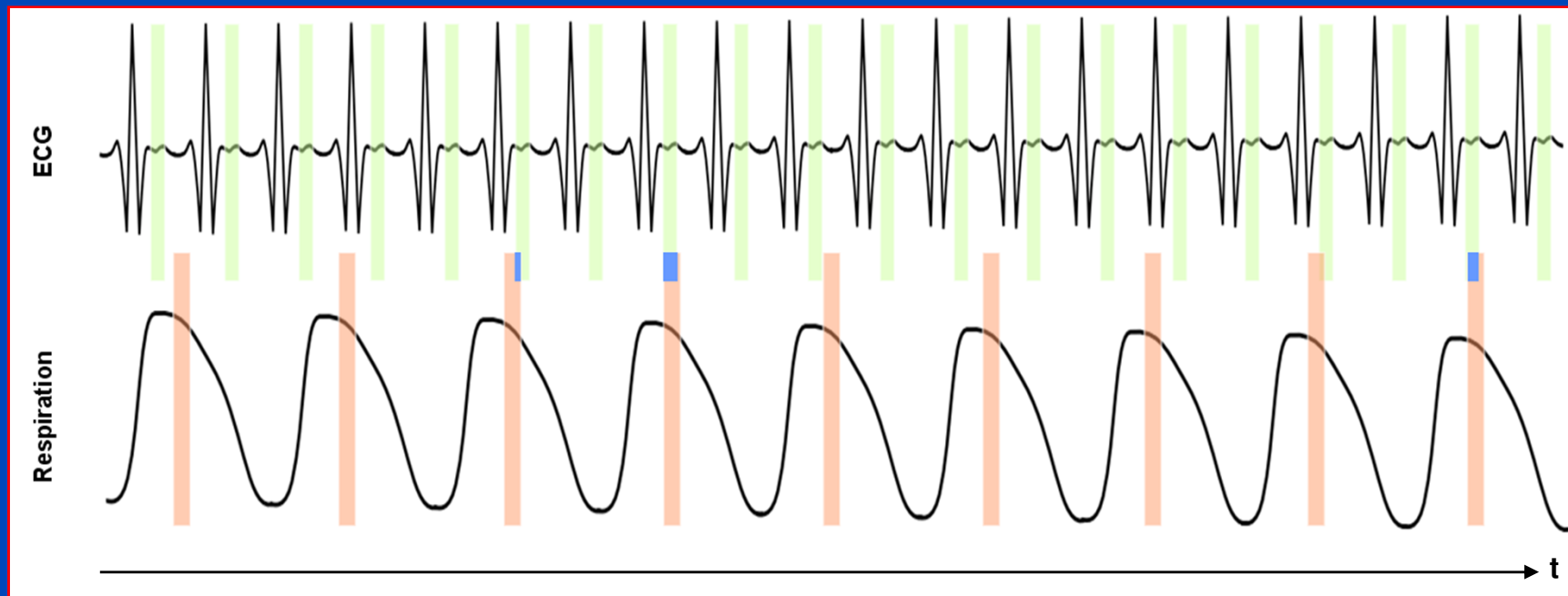
Lung: 0 rpm

Mouse with 180 rpm and 240 bpm.

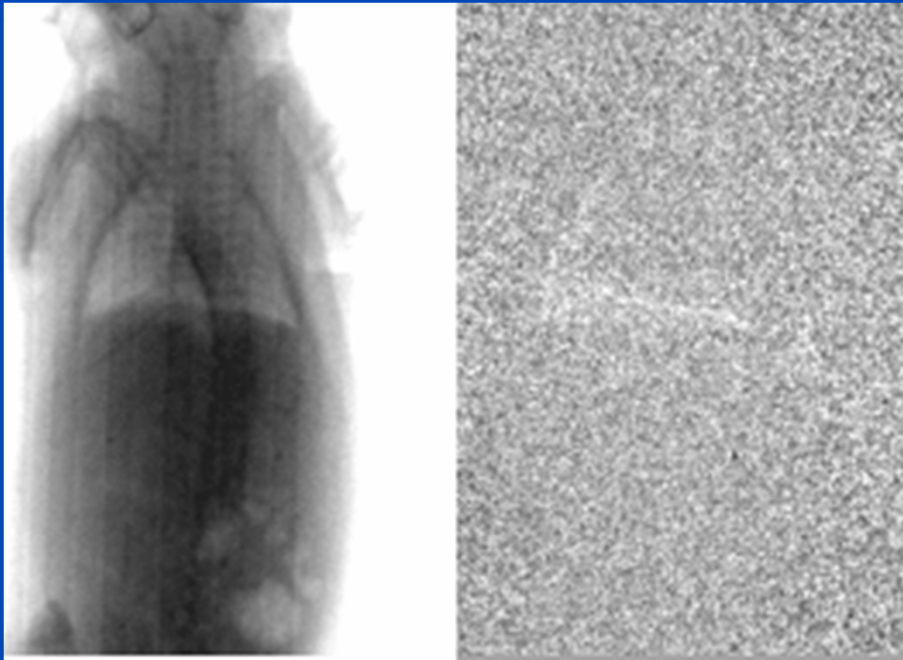
5D with Double Gating?

Double gating example:

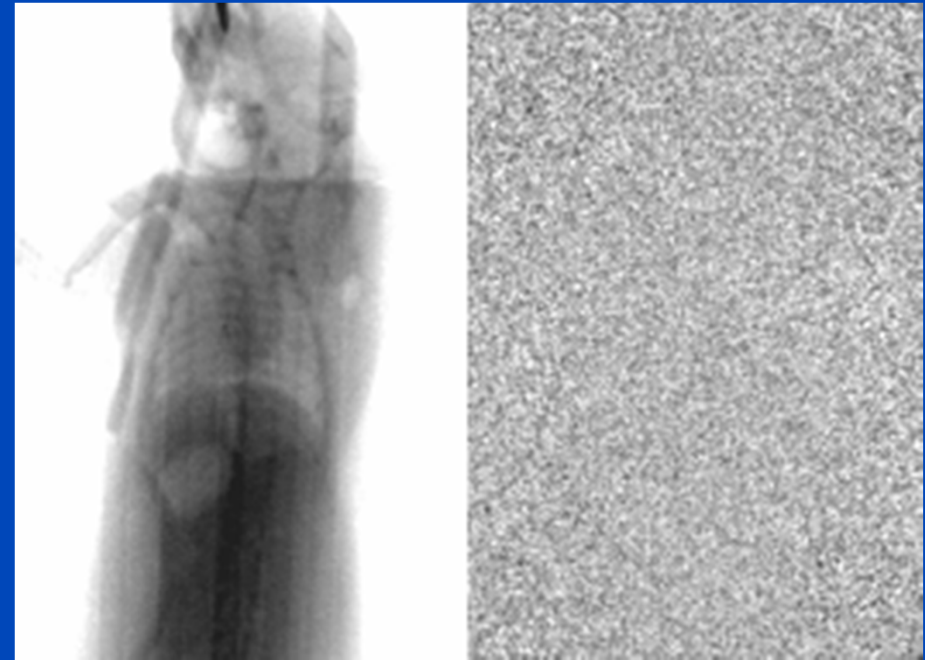
- Cardiac window width: 20%
- Respiratory window width: 10%
- Only 2% of all projections per reconstructed volume



Injection Techniques*



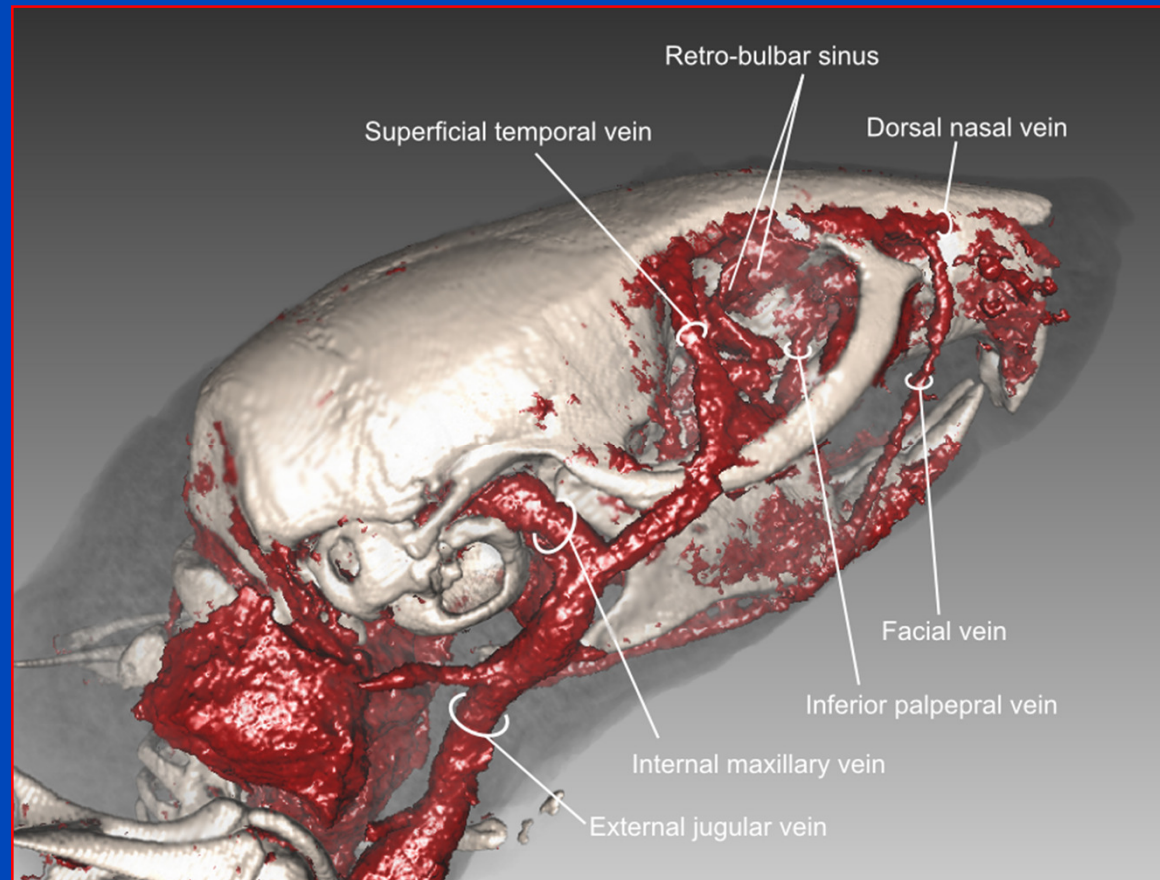
Tail Vein Injection



Retro Bulbar Injection

*M. Socher, J. Kuntz, S. Sawall, S. bartling, and M. Kachelrieß. The retrobulbar sinus is superior to the lateral tail vein for the injection of contrast media in small animal cardiac imaging. Lab. Anim. 48(2), pp. 105-113, February 2014.

Contrast Injection



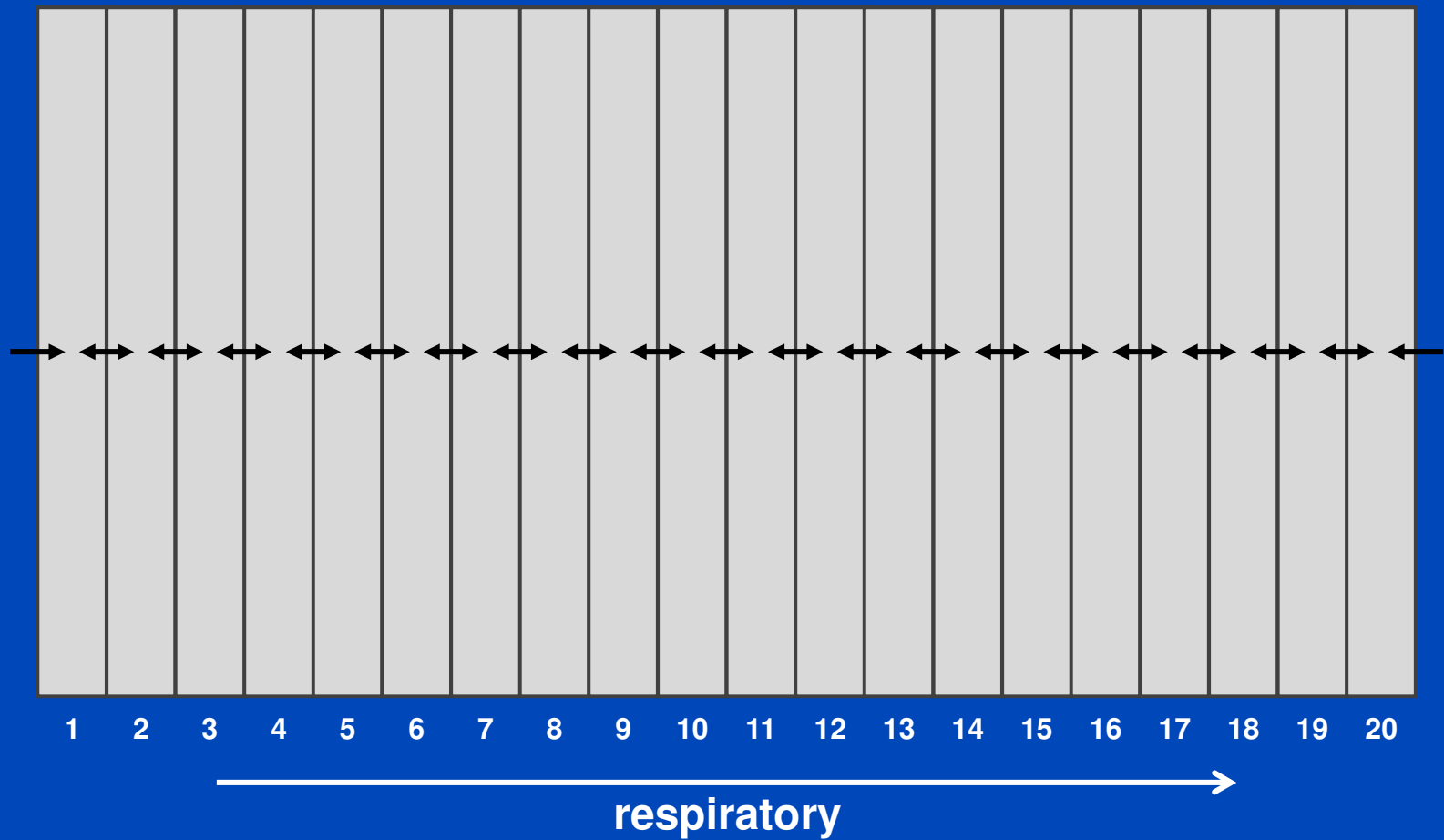
**Volume rendering of a high resolution micro-CT scan
with a spatial resolution of about 40 μm .**

***M. Socher, J. Kuntz, S. Sawall, S. Bartling, and M. Kachelrieß. The retrobulbar sinus is superior to the lateral tail vein for the injection of contrast media in small animal cardiac imaging. Lab. Anim. 48(2), pp. 105-113, February 2014.**

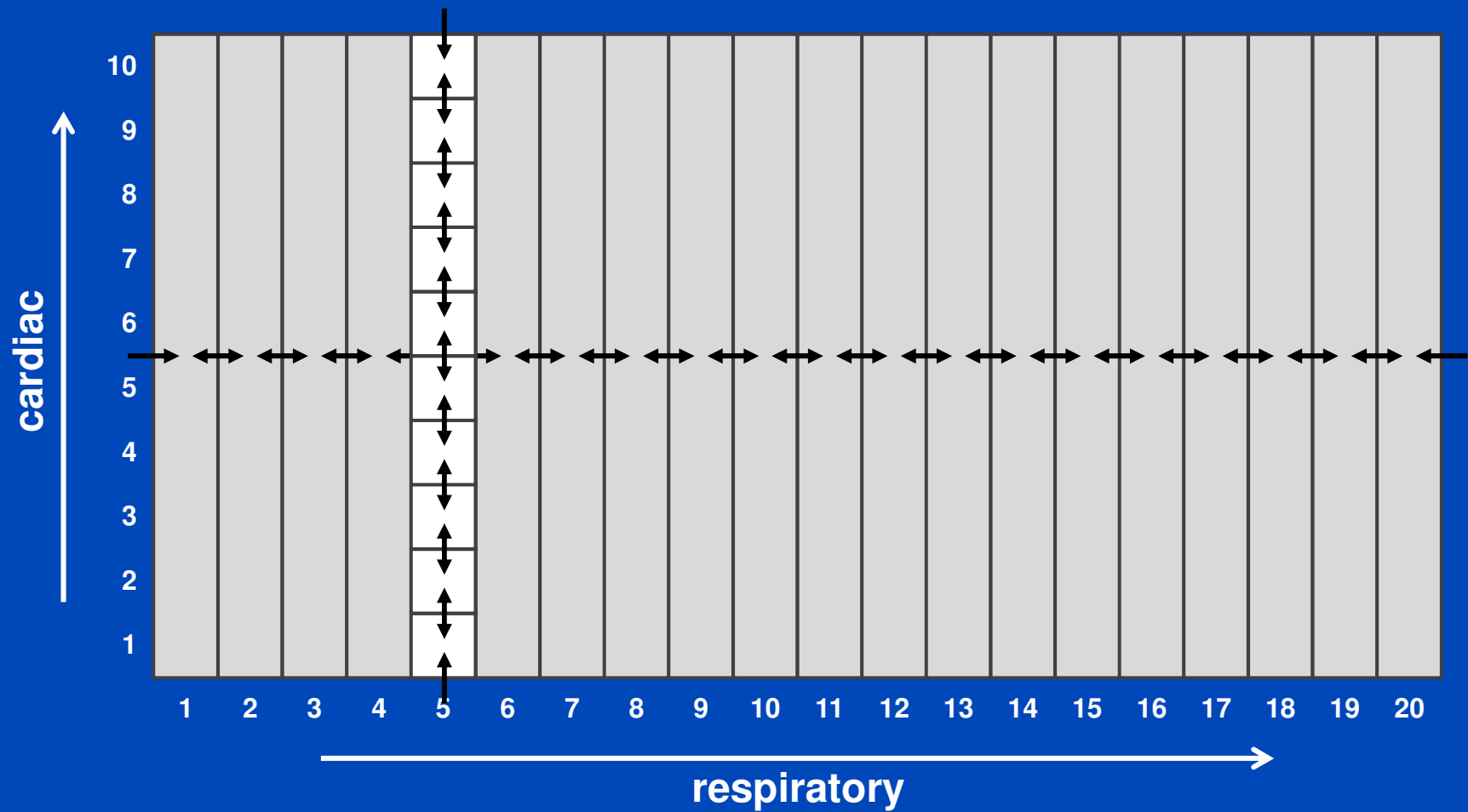
5D Motion Compensation

- **First, perform acMoCo wrt the respiratory motion.**
 - Now the data are free of respiratory motion.
 - 100% of the data are used.
 - Any desired motion phase can be displayed.
 - The MVFs can be used for other purposes (e.g. prediction).
- **Then perform acMoCo wrt the cardiac motion.**
 - Now the data are free of any motion.
 - 100% of the data are used.
 - Any desired motion phase can be displayed.
 - The MVFs can be used for other purposes (e.g. prediction).

5D Motion Compensation



5D Motion Compensation



5D Motion Compensation

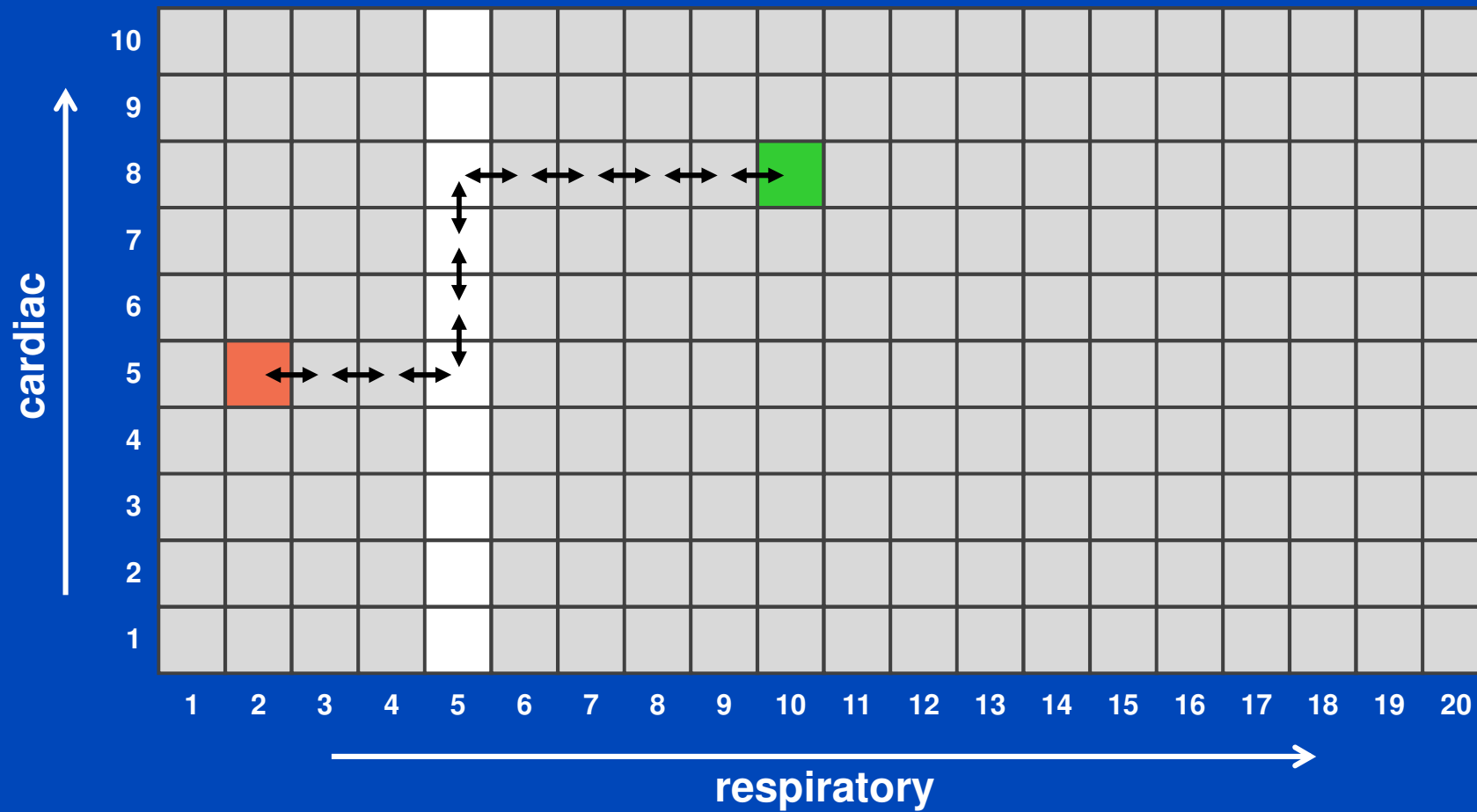
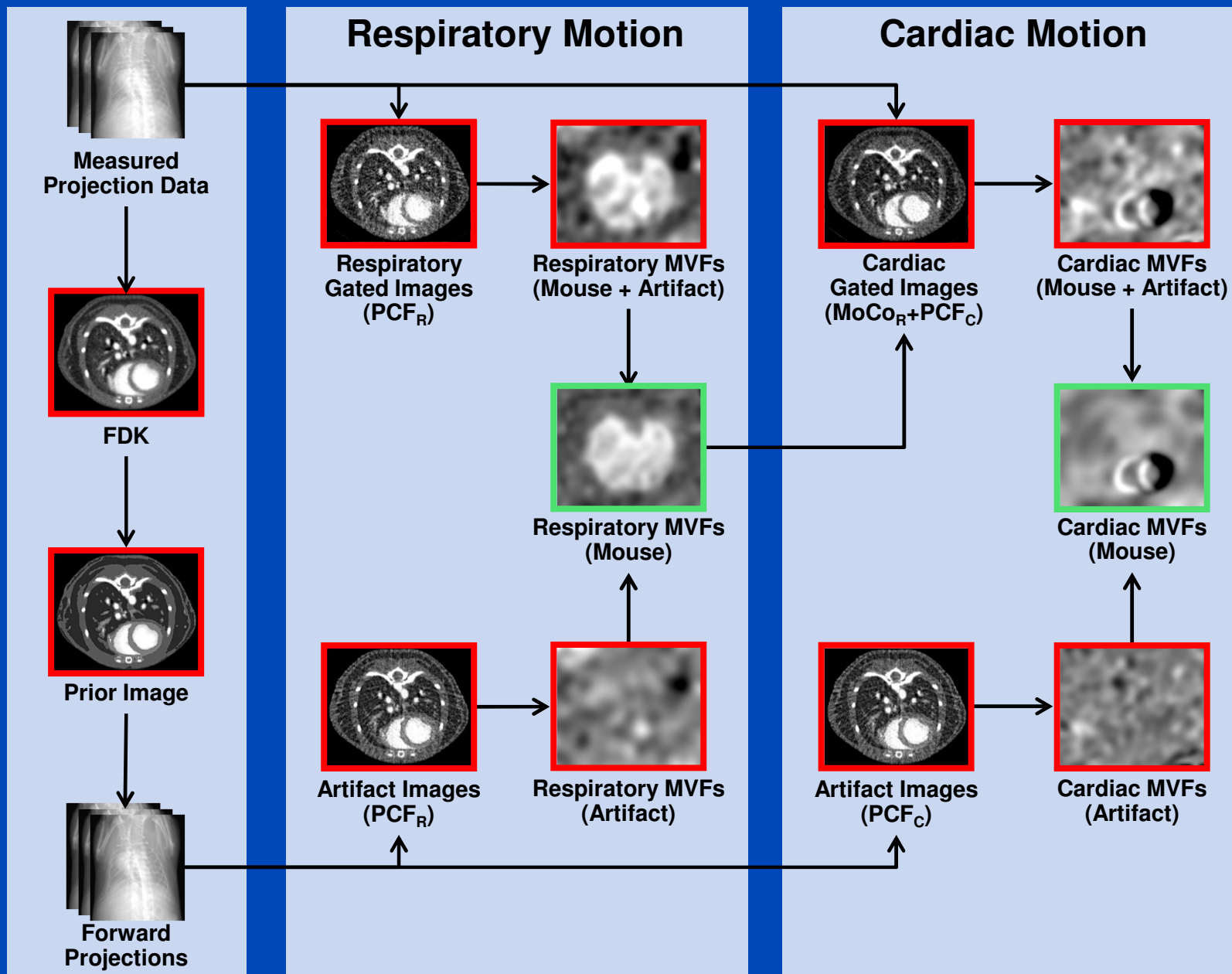
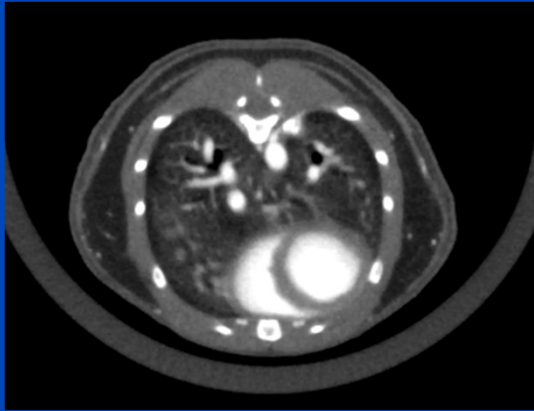


Illustration of Workflow

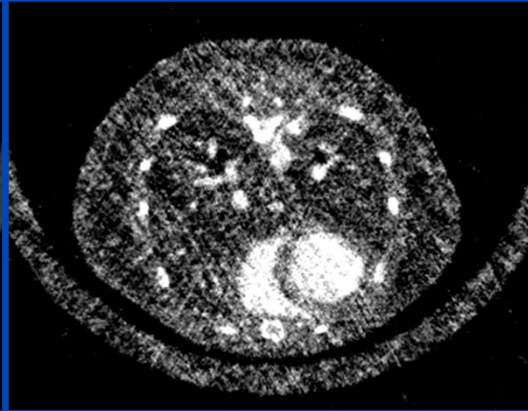


$$\Delta r = 10\%, \Delta c = 20\%$$

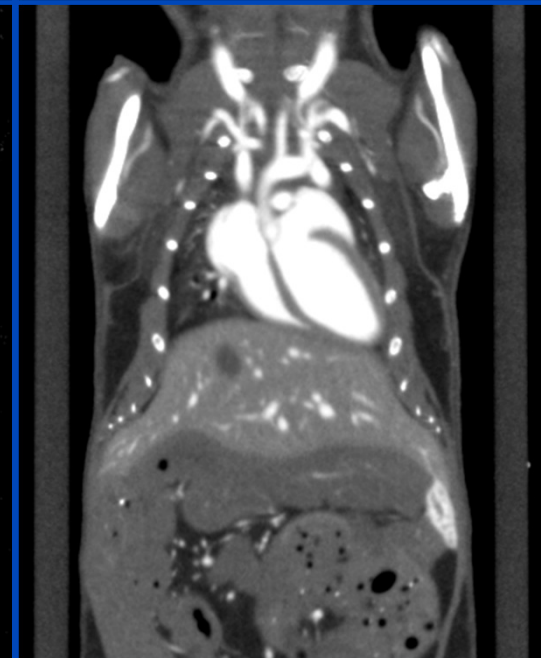
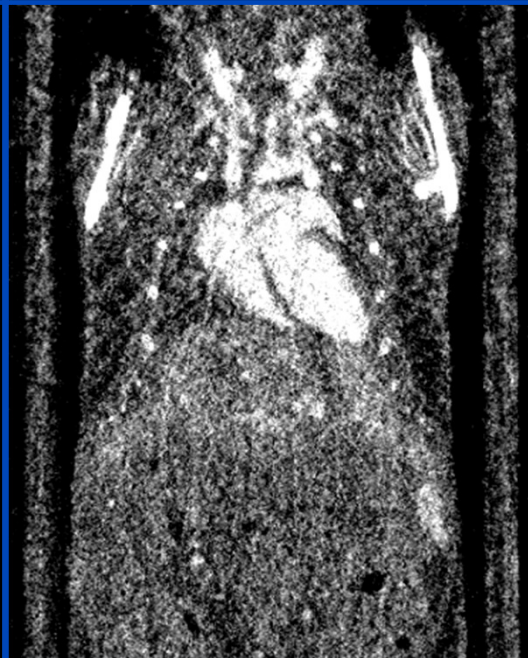
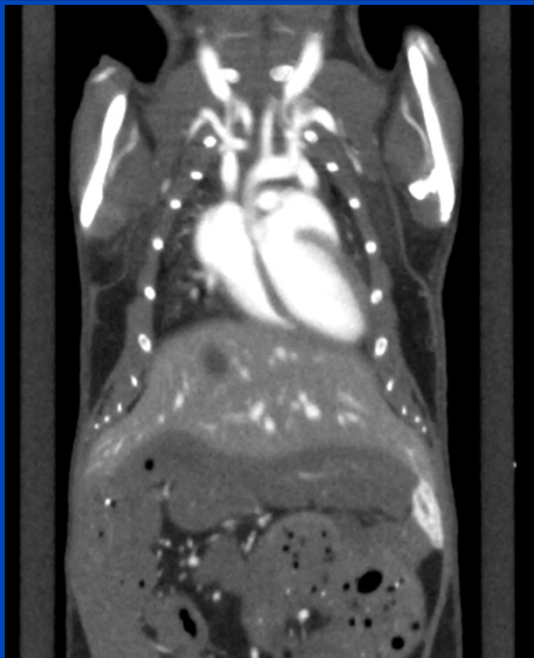
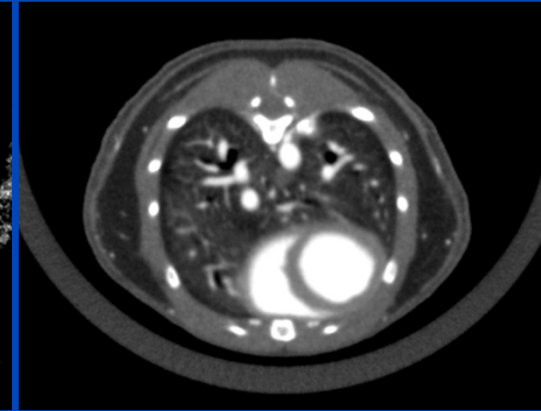
3D CBCT



Double-Gated 5D CBCT



Sequential acMoCo



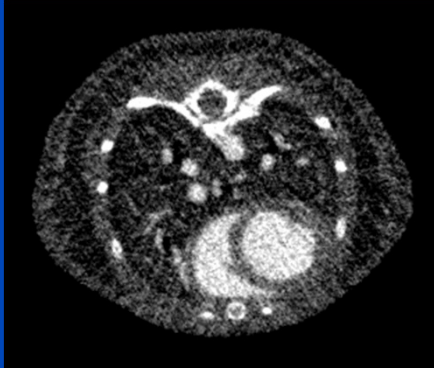
The cardiac motion is shown at a fixed respiratory phase.

7200 Projections

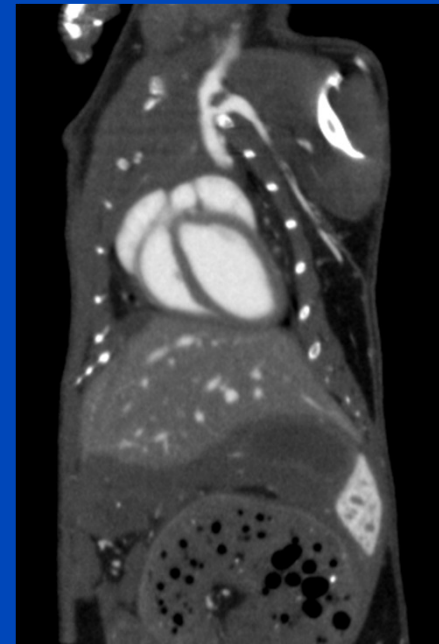
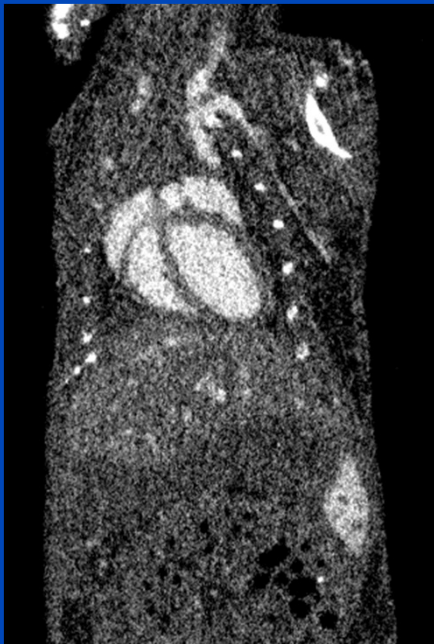
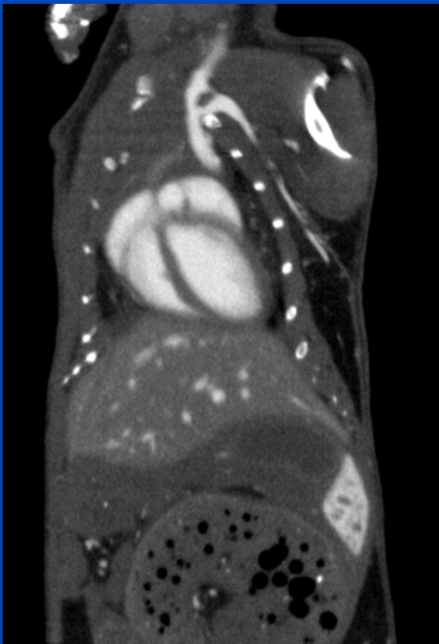
3D CBCT



Double-Gated 5D CBCT



5D Motion Compensation



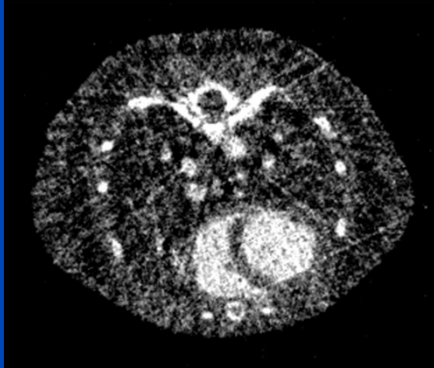
The images show a fixed respiratory and cardiac phase.

3600 Projections

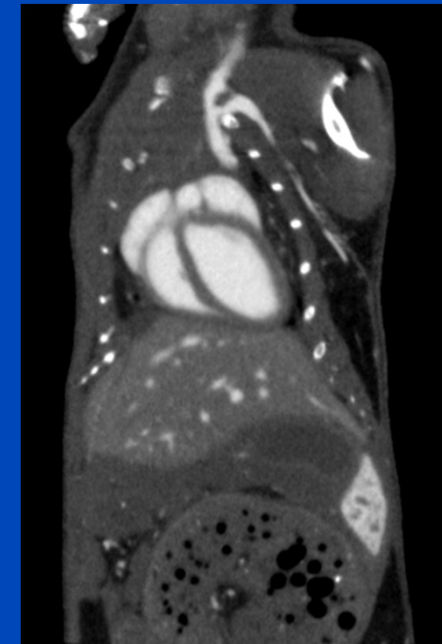
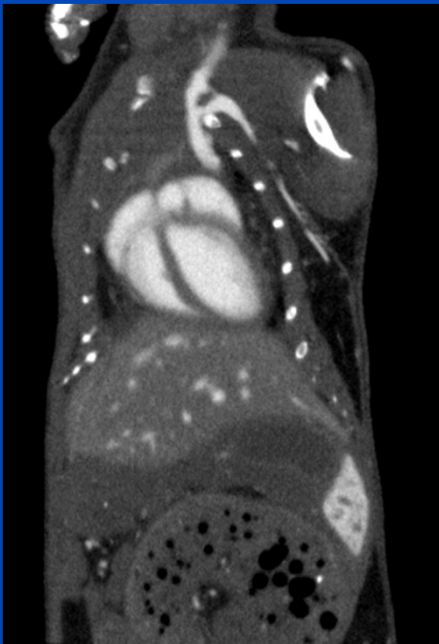
3D CBCT



Double-Gated 5D CBCT



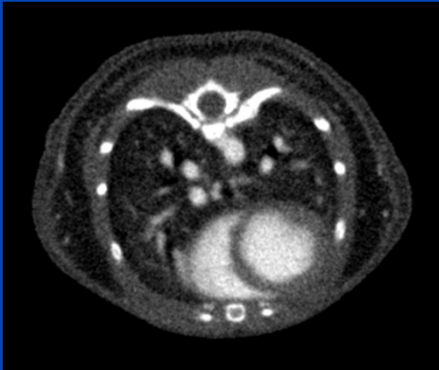
5D Motion Compensation



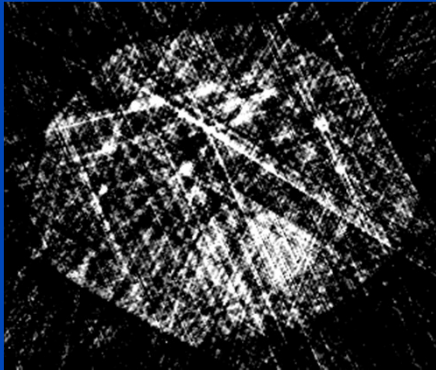
The images show a fixed respiratory and cardiac phase.

720 Projections

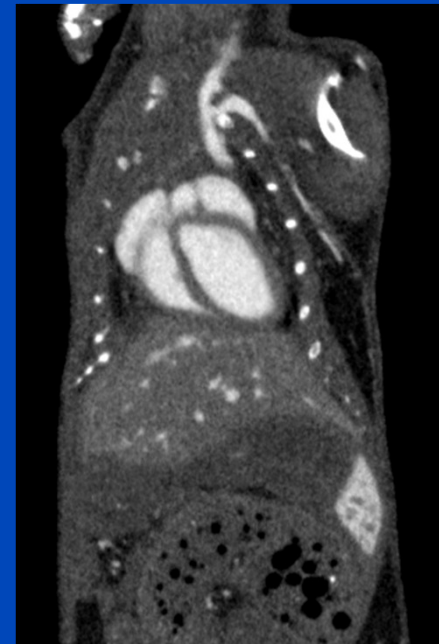
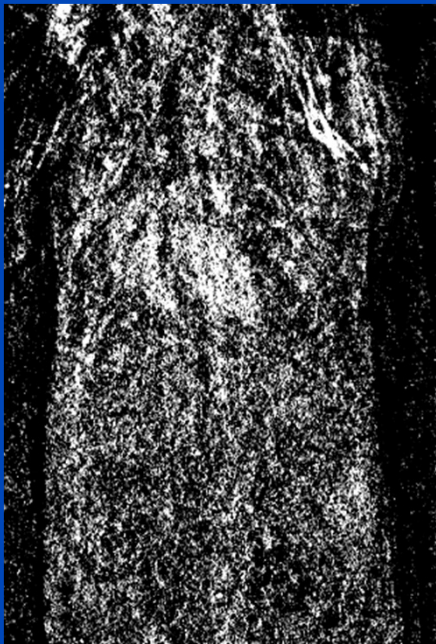
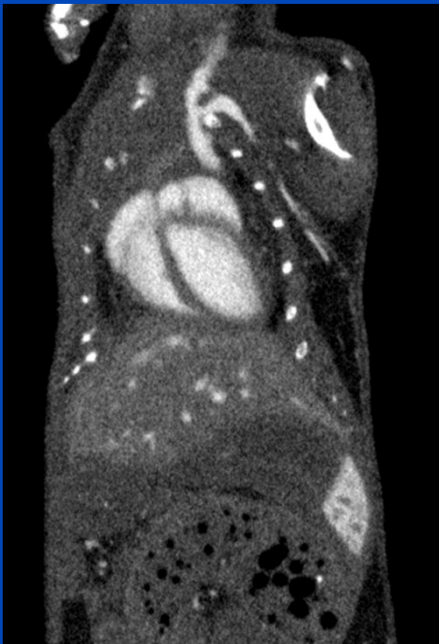
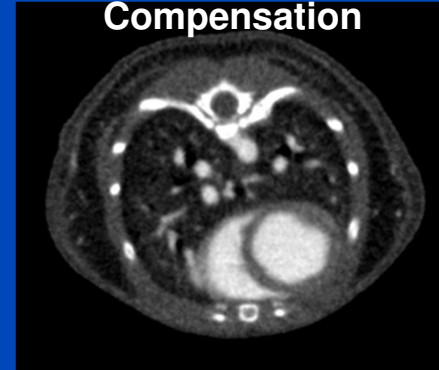
3D CBCT



Double-Gated 5D CBCT



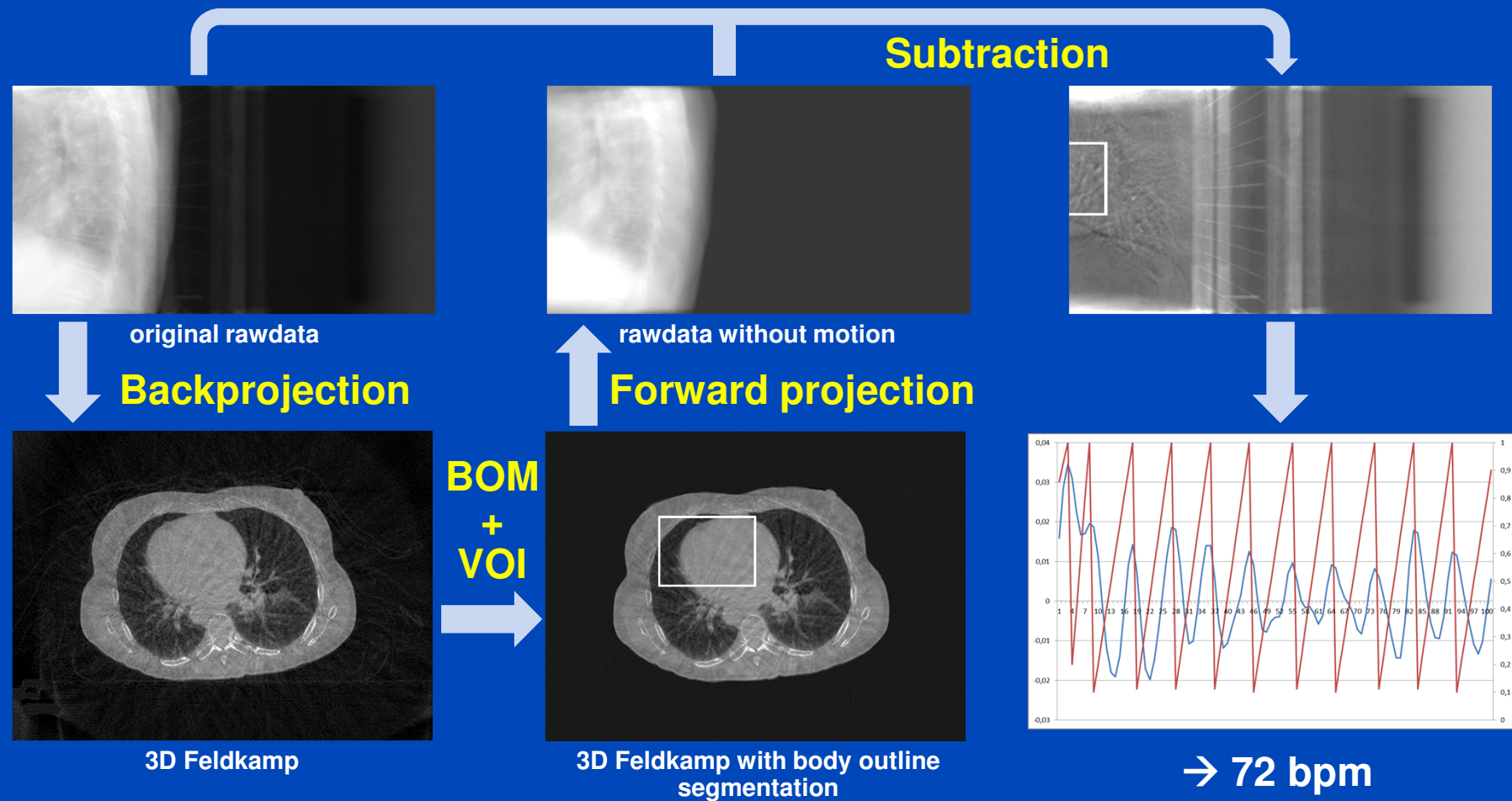
5D Motion Compensation



The images show a fixed respiratory and cardiac phase.

Intrinsic Gating

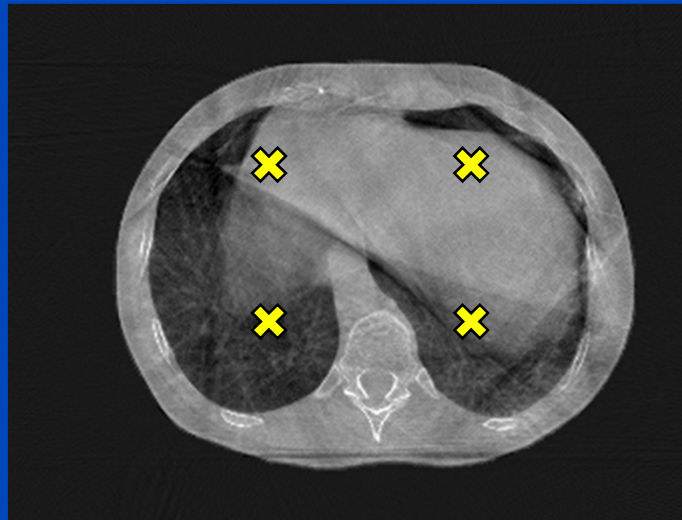
Cardiac Gating



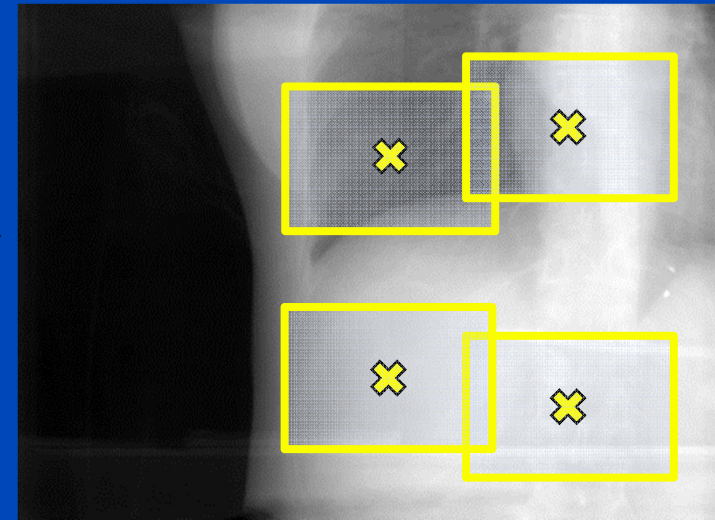
Images: $C=0$ HU; $W=2500$ HU

Optimal ROI Identification

1. Define ($N_x \times N_y \times N_z$) grid points in volume. Here: $2 \times 2 \times 2$
2. Each grid point can be traced in the rawdata after forward projection.
3. Create rectangular ROI around grid point in projections. ROIs for the respiratory signal have to be larger since the respiratory motion is stronger than the cardiac motion.



Forward
projection



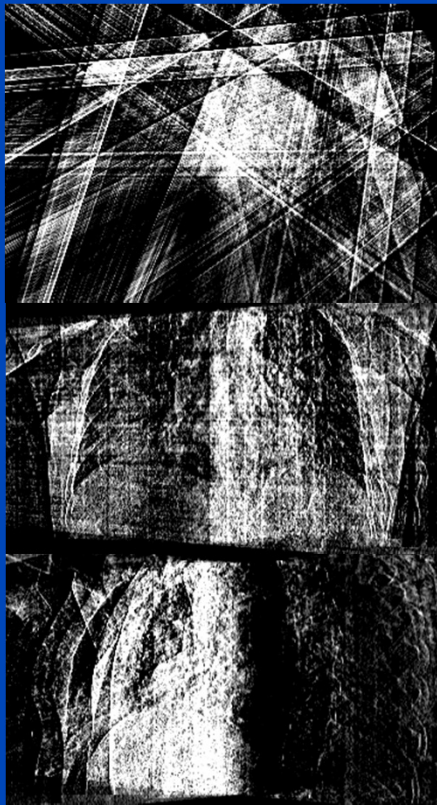
Images: $C=0$ HU; $W=2500$ HU

MoCo 5D Results

20 respiratory phases of 10% width, 10 cardiac phases of 20% width

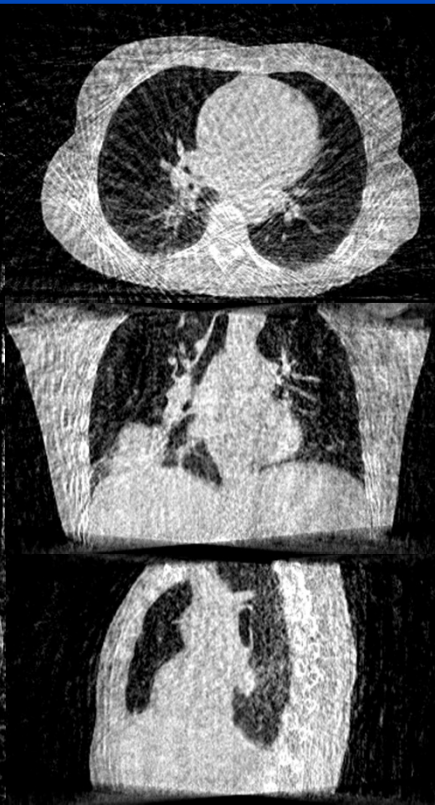
PCF 5D

Respiratory & Cardiac
Gated



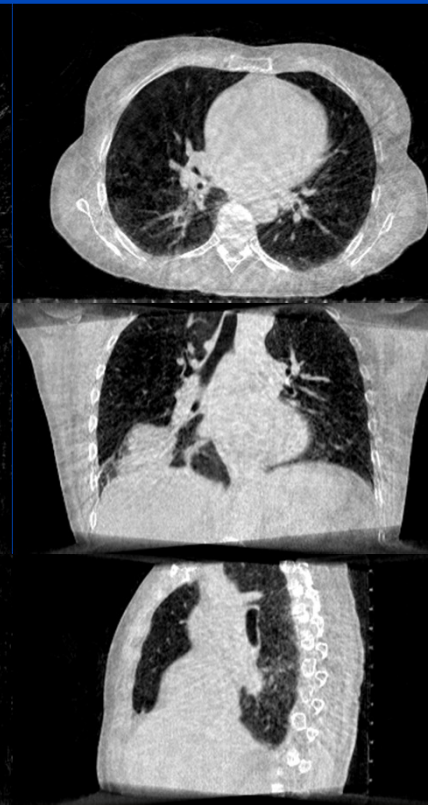
PCF 5D

Respiratory
Compensated &
Cardiac Gated



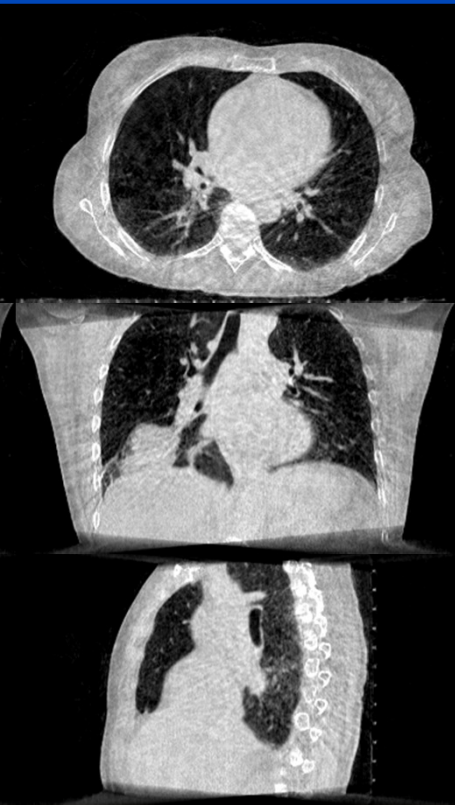
acMoCo 5D

Respiratory & Cardiac
Compensated
 r -loop, $c = 0\%$



acMoCo 5D

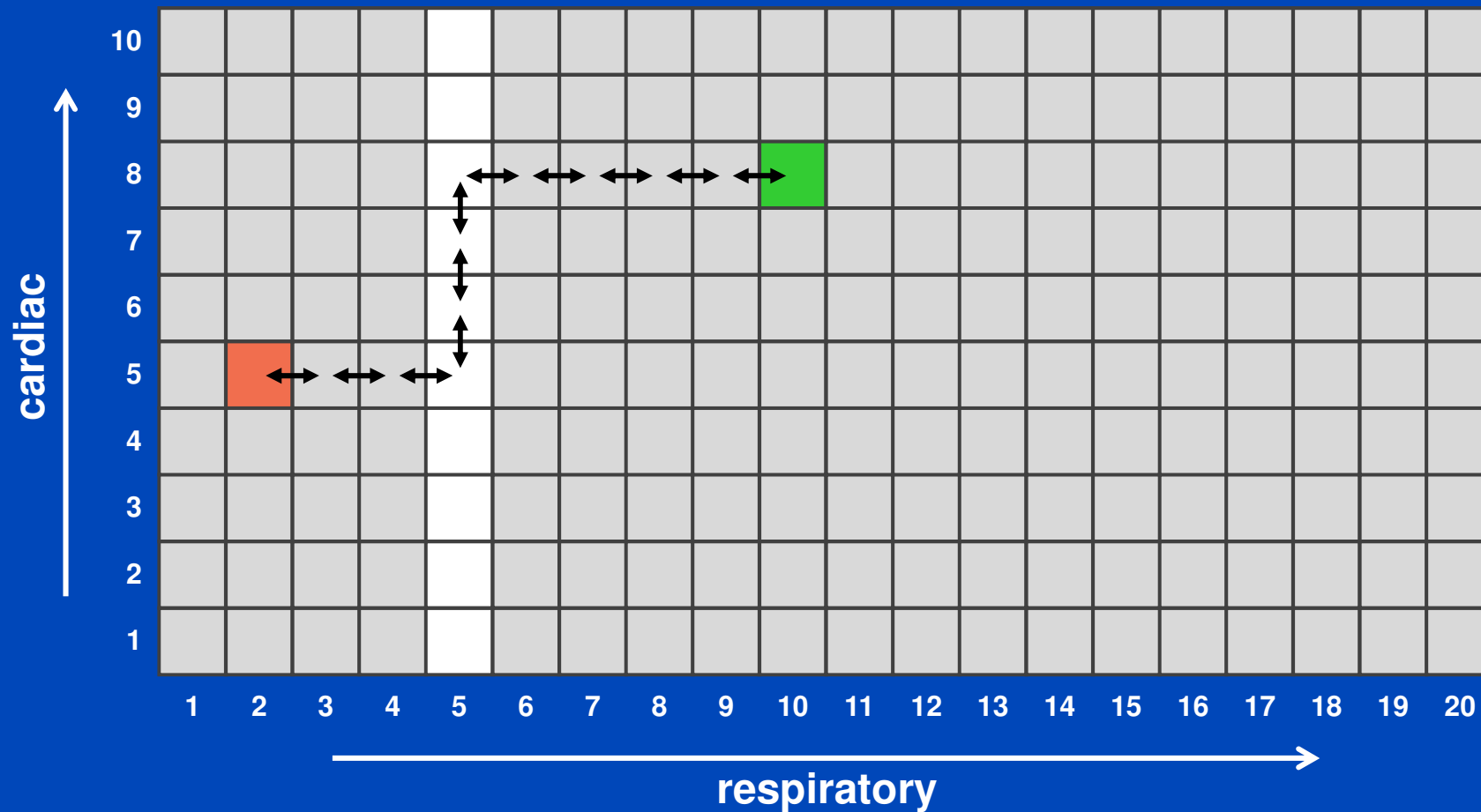
Respiratory & Cardiac
Compensated
 $r = 0\%$, c -loop



$C=-250$ HU, $W=1400$ HU

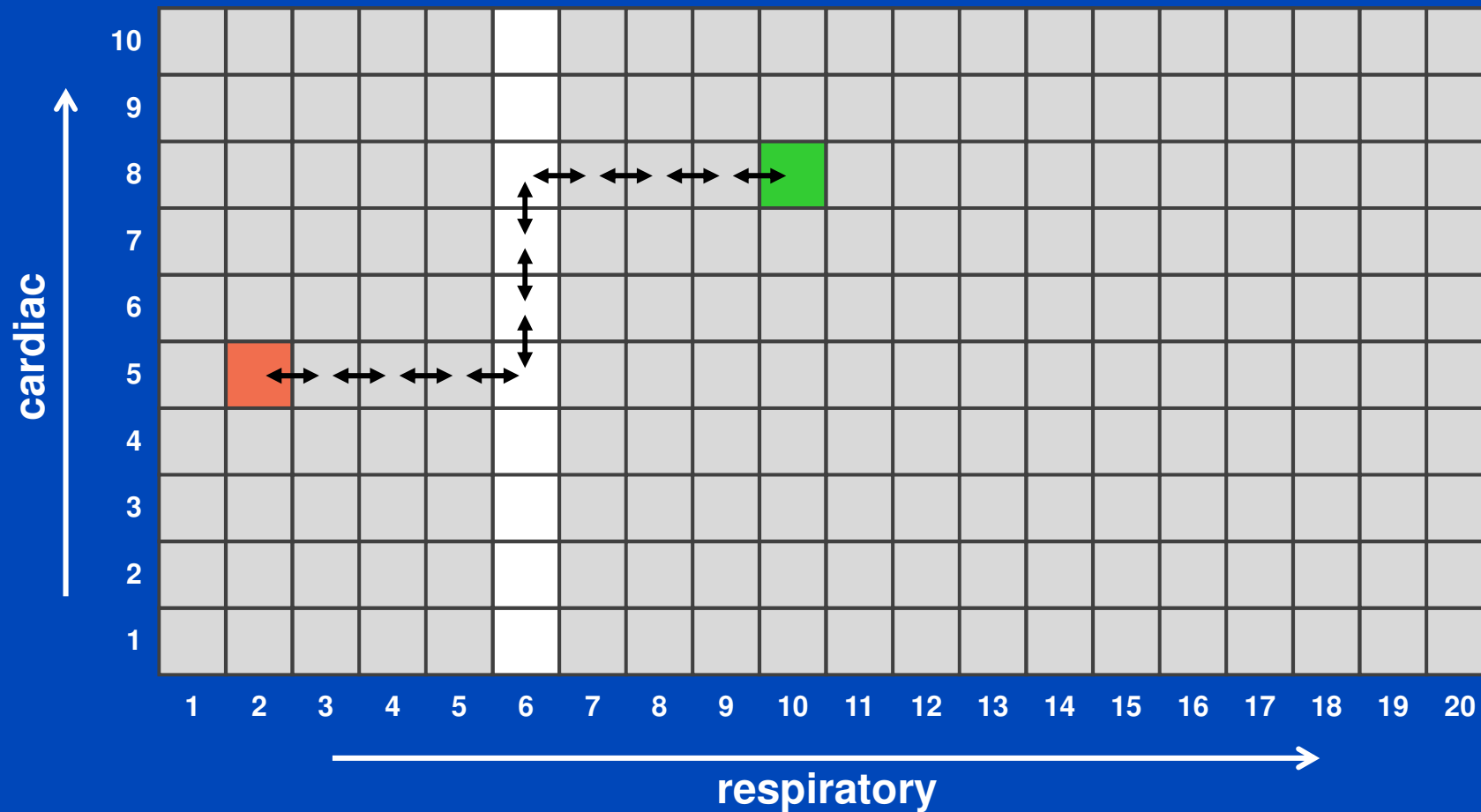
5D Motion Compensation

Does it matter in which respiratory reference phase we estimate and apply cardiac MVFs?



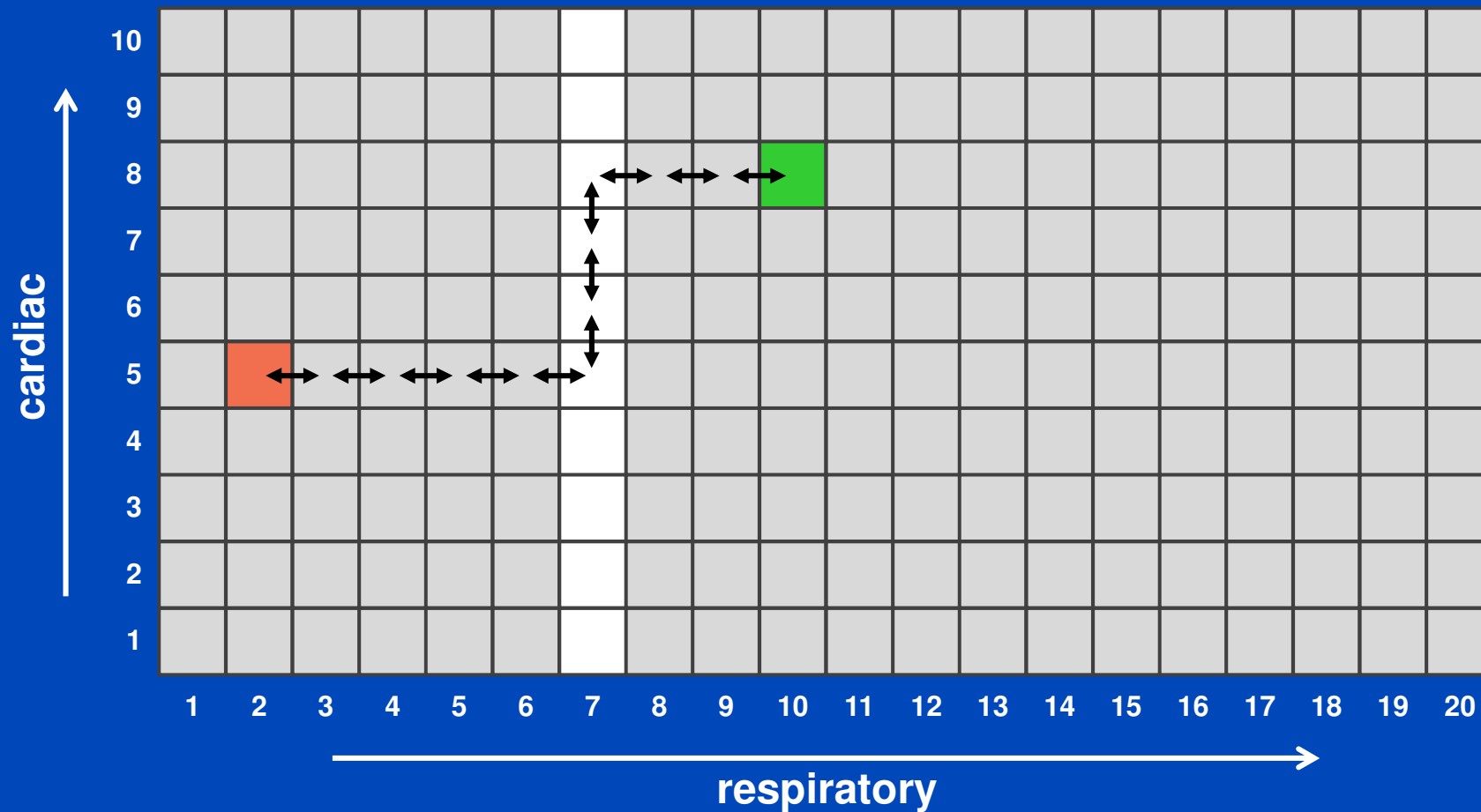
5D Motion Compensation

Does it matter in which respiratory reference phase we estimate and apply cardiac MVFs?



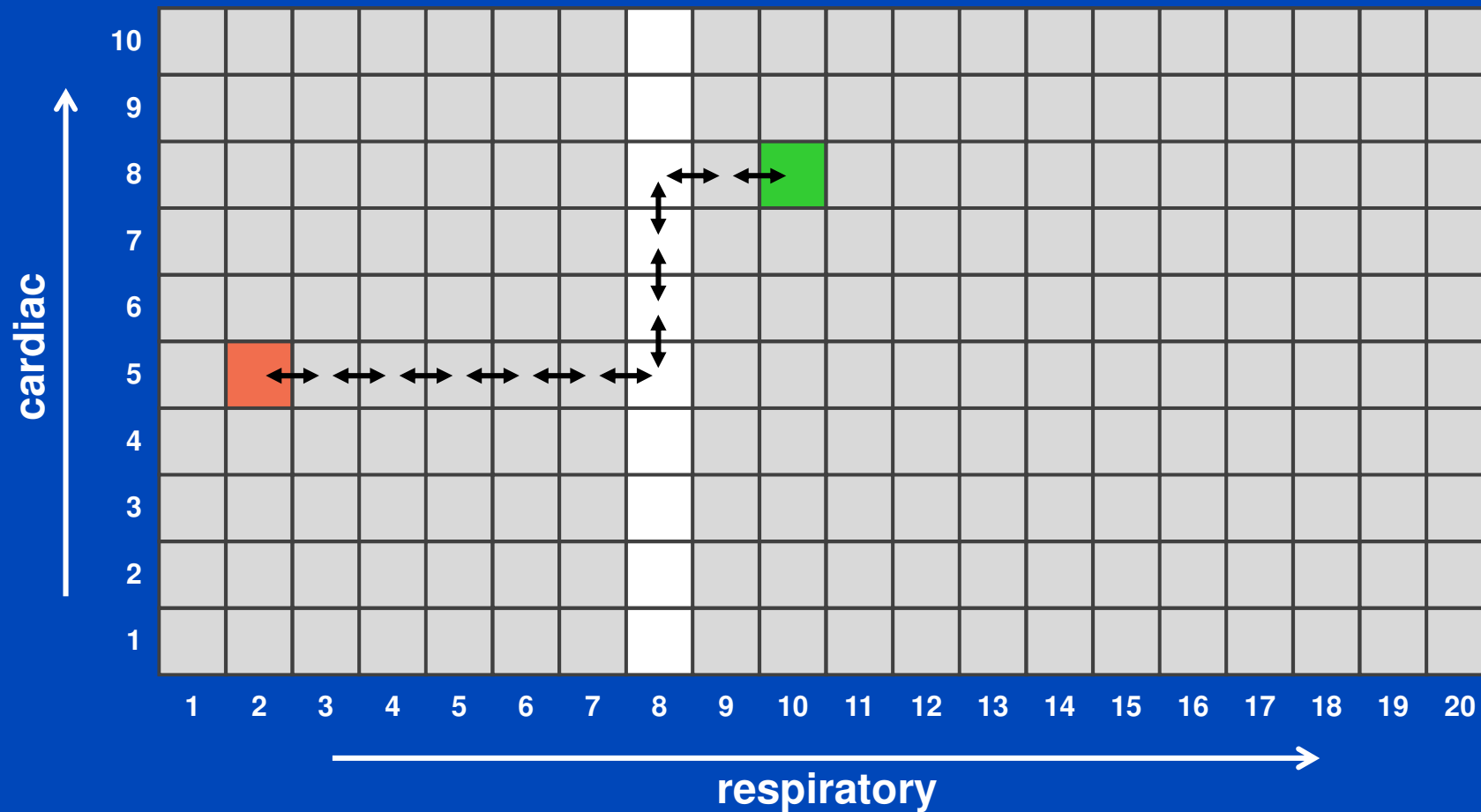
5D Motion Compensation

Does it matter in which respiratory reference phase we estimate and apply cardiac MVFs?



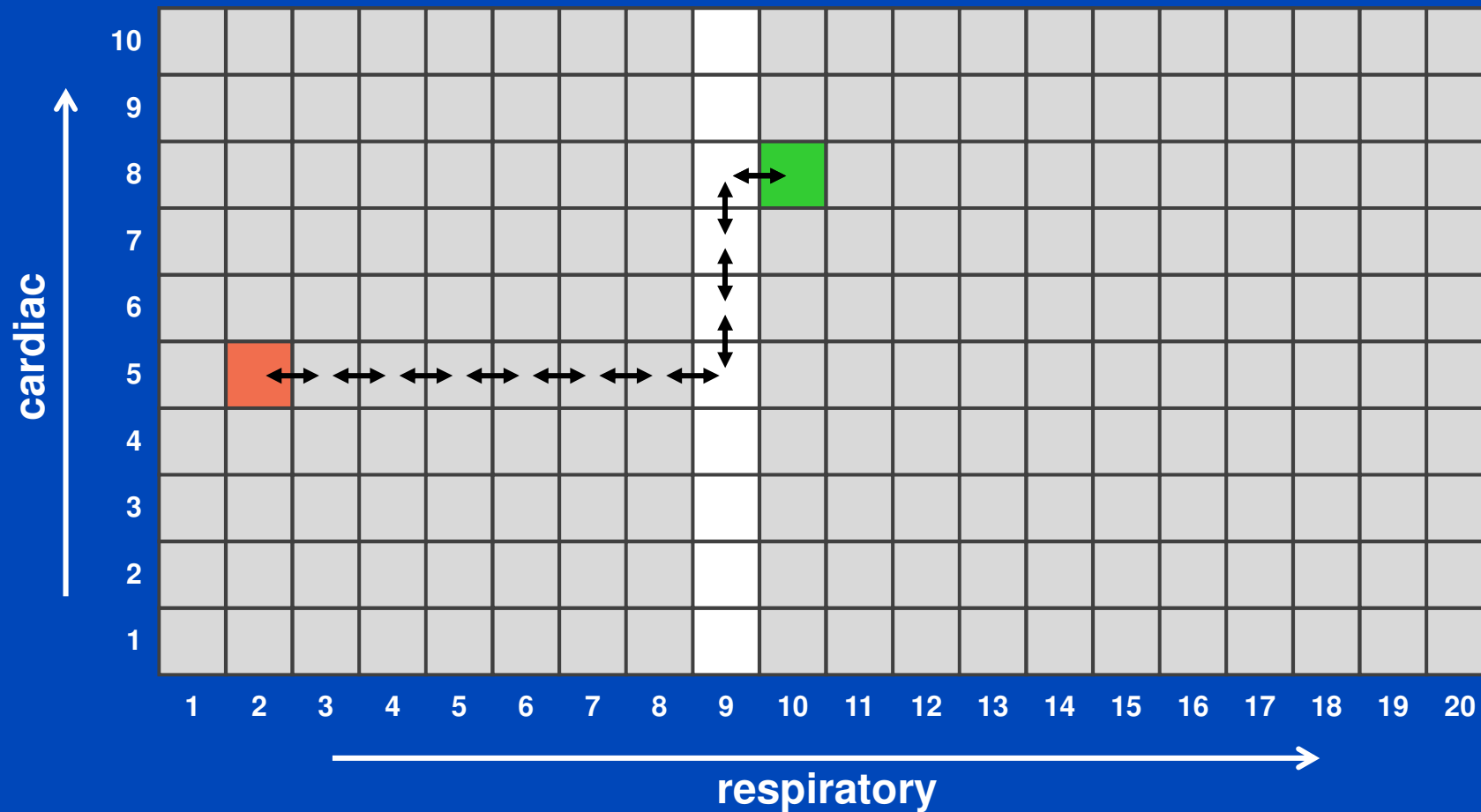
5D Motion Compensation

Does it matter in which respiratory reference phase we estimate and apply cardiac MVFs?



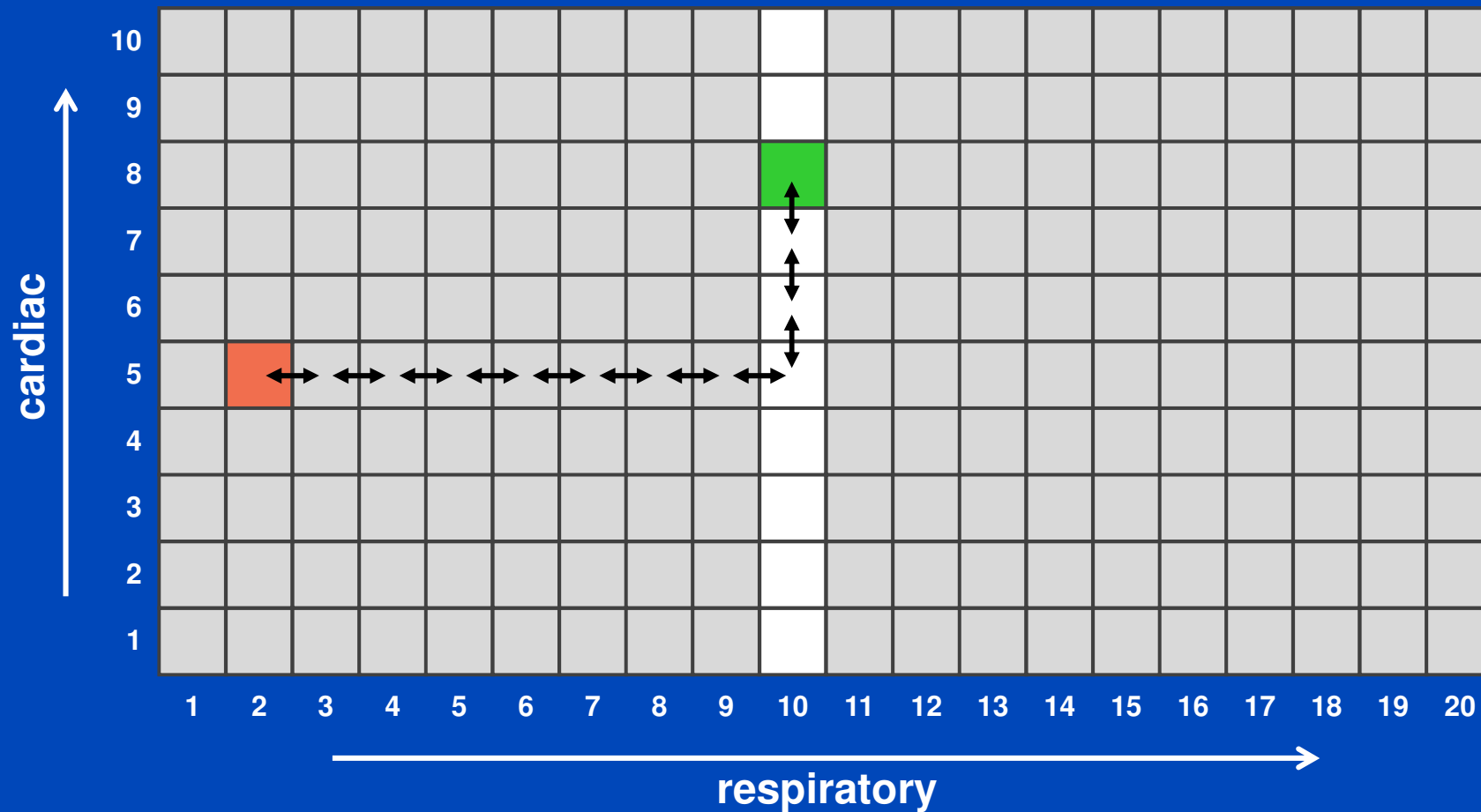
5D Motion Compensation

Does it matter in which respiratory reference phase we estimate and apply cardiac MVFs?



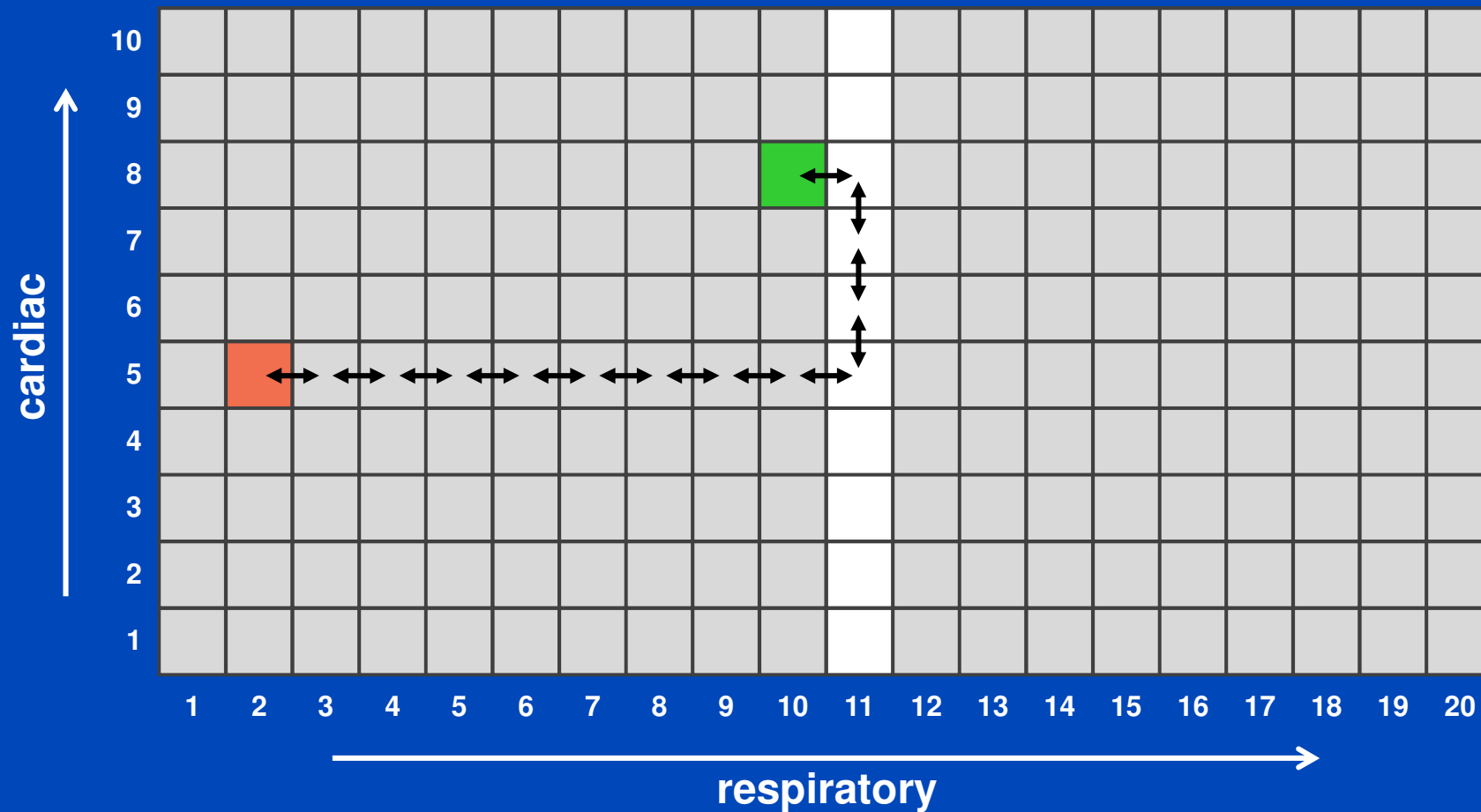
5D Motion Compensation

Does it matter in which respiratory reference phase we estimate and apply cardiac MVFs?



5D Motion Compensation

Does it matter in which respiratory reference phase we estimate and apply cardiac MVFs?



MoCo 5D Results

Respiratory Reference Phase Comparison

- Does it matter in which respiratory reference phase we estimate and apply cardiac MVFs?
- Video showing cross-sections of a 5D MoCo volume at a fixed respiratory and cardiac phase for all 20 possible reference phases:

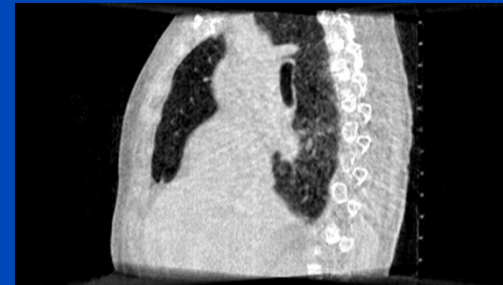
Axial



Coronal



Sagittal



Loop over all reference phases

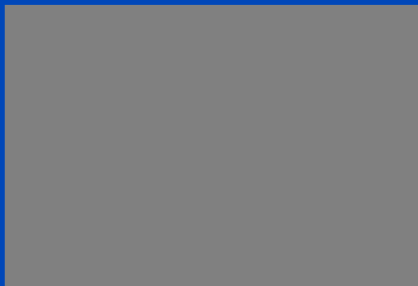
$C = -250 \text{ HU}$, $W = 1400 \text{ HU}$

MoCo 5D Results

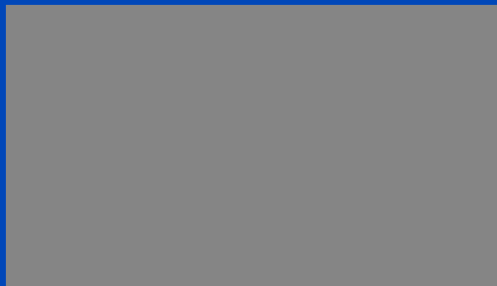
Respiratory Reference Phase Comparison

- Does it matter in which respiratory reference phase we estimate and apply cardiac MVFs?
- Video showing cross-sections of a 5D MoCo volume at a fixed respiratory and cardiac phase for all 20 possible reference phases minus the volume obtained with reference phase $r = 0$:

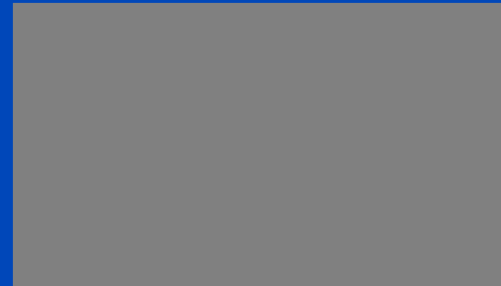
Axial



Coronal



Sagittal



Loop over all reference phases

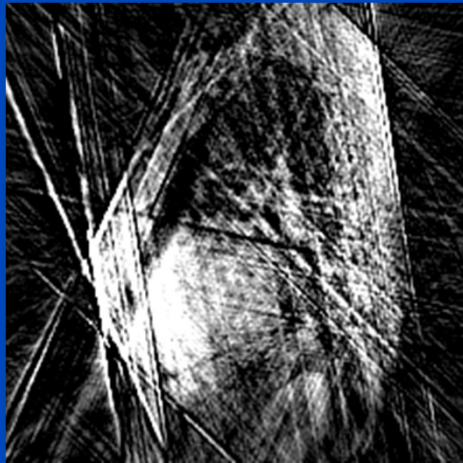
$C = -250$ HU, $W = 1400$ HU

Spin-Off Effects?

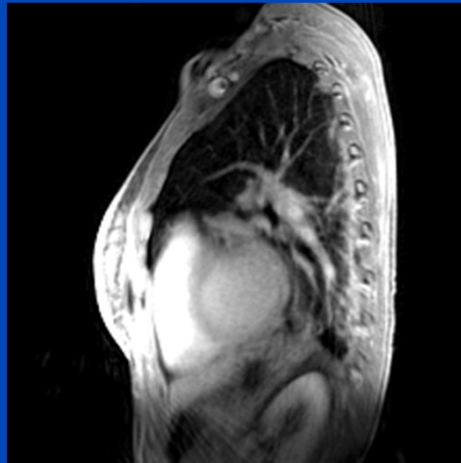
5D MR Motion Compensation

Results Patient c11 (Acquisition Time: 2 min)

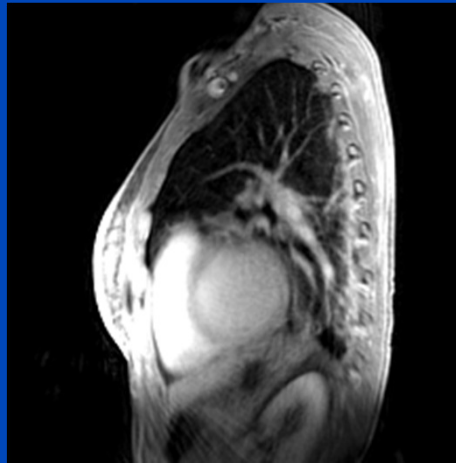
5D double-gated
72 bpm, 18 rpm



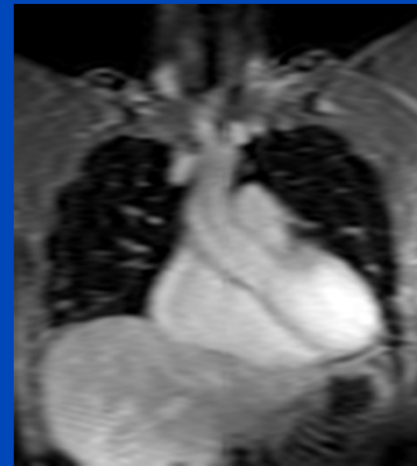
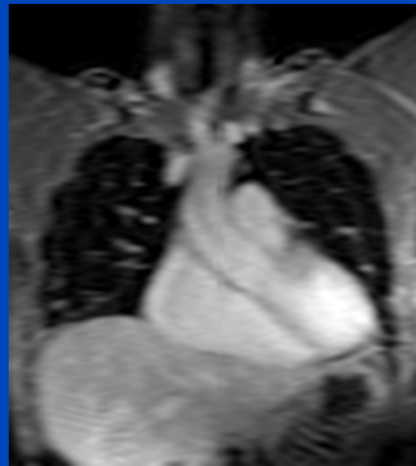
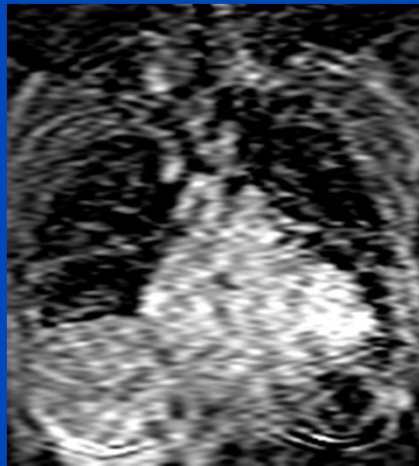
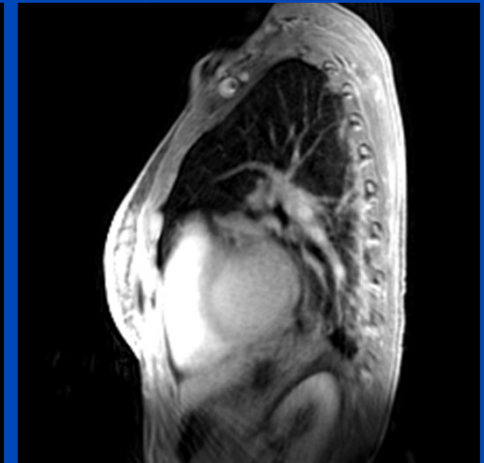
5D MoCo
72 bpm, 18 rpm



5D MoCo
0 bpm, 18 rpm



5D MoCo
72 bpm, 0 rpm

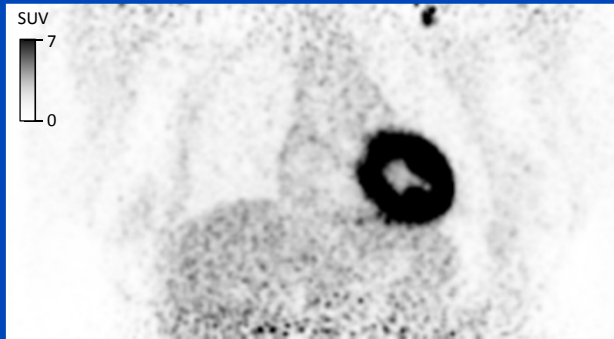


Magnetom Aera at Thoraxklinik, Radial VIBE WIP 528K
 $R = 20$, $\Delta r = 10\%$, $C = 10$, $\Delta c = 20\%$, undersampling = 27.9

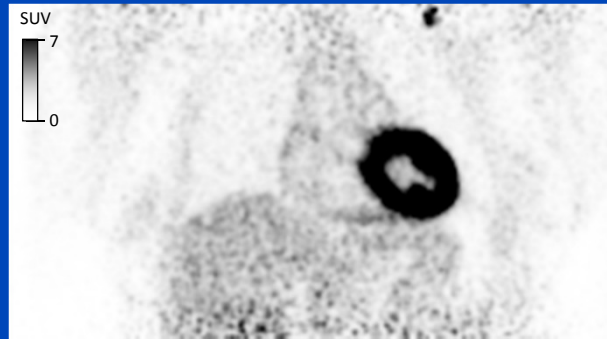
5D PET/MR MoCo: First Results

Patient s08

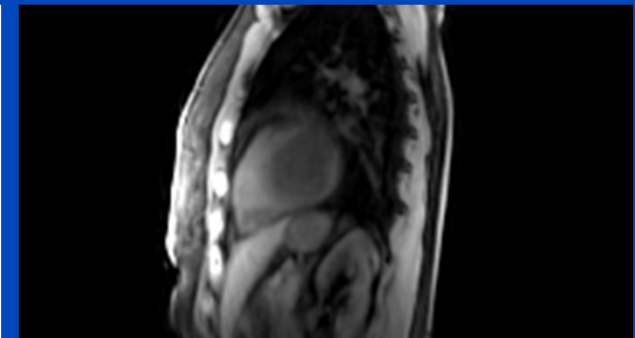
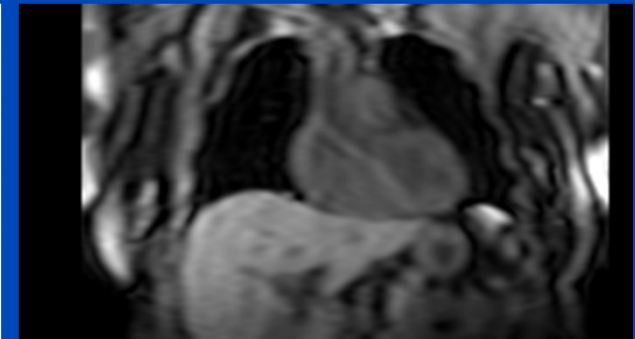
3D PET



5D MoCo PET



5D MoCo MR



$R = 1, \Delta r = 100\%,$
 $C = 1, \Delta c = 100\%$

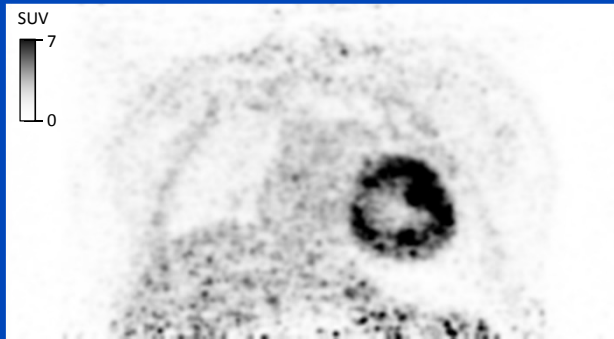
$r = r_{\text{ref}}$
 $R = 20, \Delta r = 10\%,$
 $C = 10, \Delta c = 20\%$

$r = r_{\text{ref}}$
 $R = 20, \Delta r = 10\%,$
 $C = 10, \Delta c = 20\%$

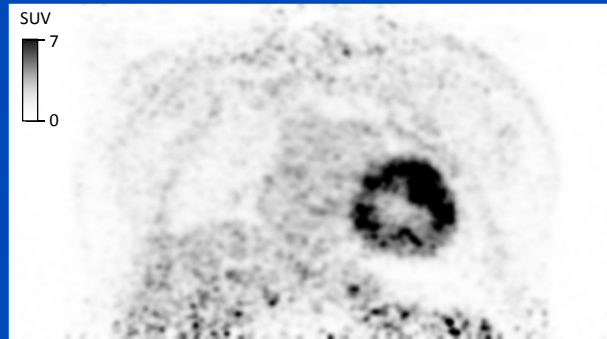
5D PET/MR MoCo: First Results

Patient s10

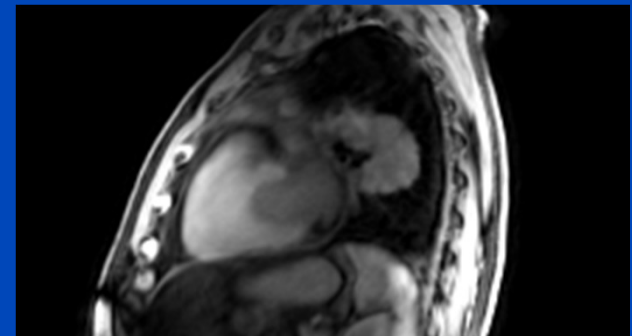
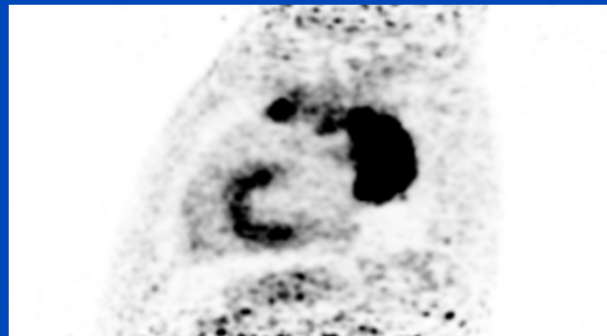
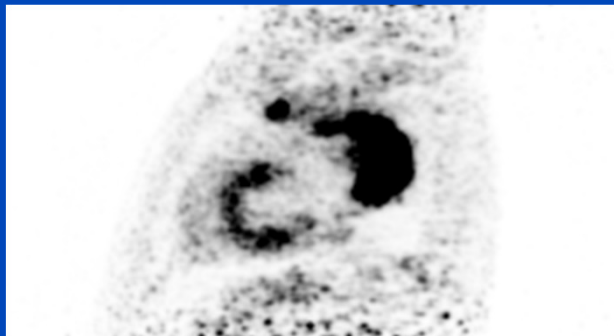
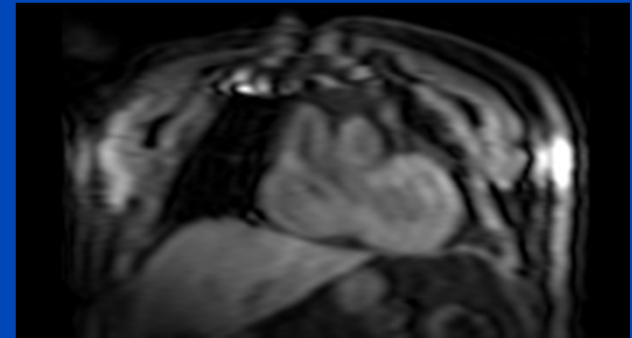
3D PET



5D MoCo PET



5D MoCo MR



$R = 1, \Delta r = 100\%,$
 $C = 1, \Delta c = 100\%$

$r = r_{\text{ref}}$
 $R = 20, \Delta r = 10\%,$
 $C = 10, \Delta c = 20\%$

$r = r_{\text{ref}}$
 $R = 20, \Delta r = 10\%,$
 $C = 10, \Delta c = 20\%$

Thank You!



The 4th International Conference on Image Formation in X-Ray Computed Tomography

July 18 – July 22, 2016, Bamberg, Germany
www.ct-meeting.org



Conference Chair

Marc Kachelrieß, German Cancer Research Center (DKFZ), Heidelberg, Germany

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

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RayConStruct® GmbH, Nürnberg, Germany.**