Dose Limitations for the Estimation of Functional Cardiac Parameters in Rodents

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Purpose

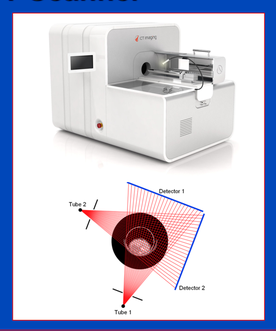
The examination of small rodents using cone–beam micro–CT with focus on functional cardiac parameters is a routine task in most small animal imaging labs. The evaluation of these parameters requires the reconstruction of phase-correlated (PC) volumes using appropriate reconstruction methods. The phase-correlated volumes suffer from high noise and streak artifacts unless not acquired with high dose. It was shown that these high dose values cause metabolic interferences and e.g. influence tumor growth. Recently, several algorithms in the context of the compressed sensing framework have been proposed that address this issue. These algorithms allow for a reduction in dose while image quality and hence the accuracy of estimated parameters is maintained. We therefore conducted a study that exemplarily illustrates for three algorithms what reduction in dose can be achieved without sacrificing image quality or accuracy if these sophisticated algorithms are used by estimating the end-diastolic left ventricular volume (EDV).

Materials and Methods

Cone-beam micro-CT scans of four mice were used to perform retrospectively phase-correlated image reconstruction. Each mouse was scanned four times, repositioned after each scan and the scans are supposed to be statistically independent. Each scan mode comprises 14400 projections during 20 contiguous rotations. The dose per scan was estimated as 1 Gy. This high number of projections allows us to simulate low-dose scans by using only a reduced number of projections per reconstruction. ExiTron nano 12000 (Miltenyi Biotec, Bergisch Gladbach, Germany) was used for blood pool enhancement. To correlate our reconstruction with the motion phases of the heart and lung we intrinsically estimate the ECG and respiratory signal and synchronized them with the rawdata. Our standard reconstruction is based on a Feldkamp-like algorithm that processes only those projections that lie in the desired motion phase. As only a few of the total projections acquired contribute to the reconstruction, the resulting volumes show very high noise and fine morphological details vanish. We further used the low-dose phase-correlated (LDPC) algorithm for image reconstruction [1]. This algorithm is a modification of the McKinnon-Bates method combined with edge-preserving bilateral filtering. Additionally a high-dimensional total variation (HDTV) method was used as another example for the methods provided in the compressed sensing framework [2]. As we perform phase-correlated reconstructions we divide the respiratory cycle in ten phases and the cardiac cycle in four phases.

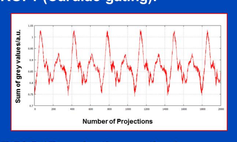
Dedicated In-Vivo Small Animal Micro-CT Scanner

- TomoScope Synergy Twin scanner (CT Imaging GmbH)
- X-ray source:
  - RTW MCBM
  - Focal spot size: 50 µm x 50 µm
  - Tube voltage range: 40 kV – 60 kV
  - Tube current range: 0.3 mA – 0.8 mA
- Detector:
  - Hamamatsu flat panel detector
  - 1024x1024 pixel, 2x2 binning
  - 100 µm pixel size
  - 40 ms integration time
- Protocol:
  - Scan time: 5 min
  - Number of projections: 7200
  - Number of rotations: 10
  - Spatial sampling: 80 µm
  - Estimated dose: 500 mGy

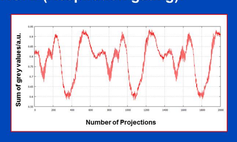


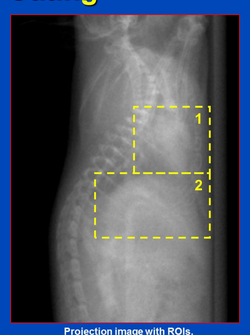
Intrinsic Gating

- ROI 1 (Cardiac-gating):



- ROI 2 (Respiration-gating):





Projection image with ROIs.

Phase-Correlated Filtered Backprojection (PC)

Phase-correlated (PC) reconstruction:

- Reconstruct (R_{PC}) only projections (p) in the desired motion phases
- Only a few projections contribute to the volume (f_{PC})
- Streak artifacts may occur
- High noise level

$$f_{PC}=R_{PC}^{-1}p$$

Axial Sagittal Coronal

Low-Dose Phase-Correlated Reconstruction (LDPC)

Filtering in five dimensions (three spatial dimensions, two temporal dimensions):

$$f_{LDPC}=Bf_{MKB}=\frac{\int d^5t\ D(\vec{x},\vec{t})R(\vec{x},\vec{t})f(\vec{t})}{\int d^5t\ D(\vec{x},\vec{t})R(\vec{x},\vec{t})}$$

Range filter:

$$R(x,t)=e^{-(\frac{f(x)-f(t)}{\sigma_f})^2}$$

Domain filter:

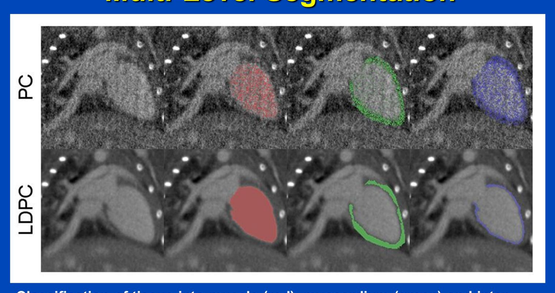
$$D(x,t)=e^{-(\frac{x-t}{\sigma_x})^2}$$

High Dimensional Total Variation Reconstruction (HDTV)

- Now the L_1 norm of the high-dimensional gradient is minimized under the constraint of a small raw data error.
- The optimization is performed using the iTV method [2].

$$\min\|\nabla_{\boldsymbol{r},t}f(\boldsymbol{r},t)\|_1 \text{ subject to } \sum_t \|\mathrm{R}_t f(\boldsymbol{r},t)-p_t\|_2^2<\epsilon.$$

Multi-Level Segmentation



Classification of tissue into muscle (red), myocardium (green) and intermediate tissue (blue) using a multi-level Otsu segmentation. This is exemplarily shown for the the LDPC reconstructions.

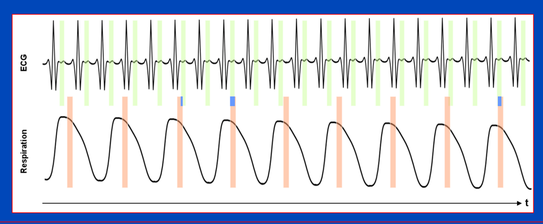
Reconstruction From Sparsely Sampled Data: Prior Art

- **Phase-correlated FBP**
  K. Lackner, and P. Thurn, *"Computed tomography of the heart: ECG gated and continuous scans,"* Radiology, vol. 140, pp. 413–420, 1981.
- **McKinnon-Bates algorithm**
  G. C. McKinnon, and R. Bates, *"Towards imaging the beating heart usefully with a conventional CT scanner", IEEE Transactions on Biomedical Engineering, vol. 28, pp. 123–127, 1981.*
- **Low dose phase-correlated reconstruction (LDPC)**
  S. Sawall, F. Bergner, M. Karolczak, A. Hess, R. Lapp, M. Mronz, and M. Kachelrieß, *"Low-dose cardio-respiratory phase-correlated cone-beam micro-CT of small animals"*, Med. Phys., vol. 38, pp. 1416-1424, 2011.
- **Constrained total variation (TV) minimization**
  E. Y. Sidky, and X. Pan, *"Image reconstruction in circular cone-beam computed tomography by total variation minimization" , Phys. Med. Biol., vol. 53, pp. 4777–807, 2008.*
- **High-dimensional total variation (HDTV) minimization**
  L. Ritschl, S. Sawall, M. Knaup, A. Hess, and M. Kachelrieß, "Iterative 4D cardiac micro-CT image reconstruction using an adaptive spatio-temporal sparsity prior", Phys. Med. Biol., vol. 57, pp. 1517-1525, February 2012.

Phase-Correlated Binning

Double gating example:

- Cardiac window width: 25%
- Respiratory window width: 10%
- Only 2.5% of all projections (≈360 of 14400) per reconstructed volume

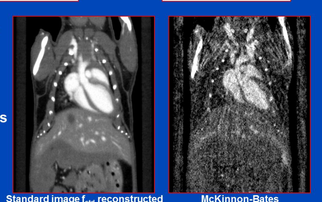


Low-Dose Phase-Correlated Reconstruction (LDPC)

For each signal

$$f_{std}=X^{-1}p \rightarrow p_{diff}=p-Xf_{std} \rightarrow f_{MKB}=f_{std}+X^{-1}p_{PC}p_{diff}$$

- Use image based on all projections as prior (standard image)
- Apply McKinnon Bates to respiratory phases only
- Apply MKB to cardiac phases using desired respiratory phase as prior



Standard image f_{std} reconstructed from all projections.

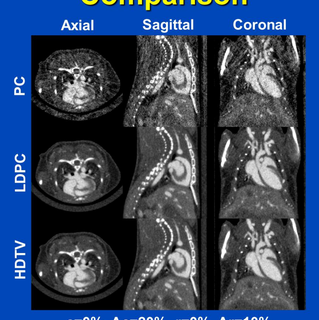
McKinnon-Bates reconstruction f_{MKB}.

High Dimensional Total Variation Reconstruction (HDTV)

- Use a gradient in spatial and temporal direction .
- The main idea is, that there is a high correlation between neighboring motion phases, which lead to a low gradient in temporal direction.
- α is a parameter which controls the weight between temporal and spatial gradient.

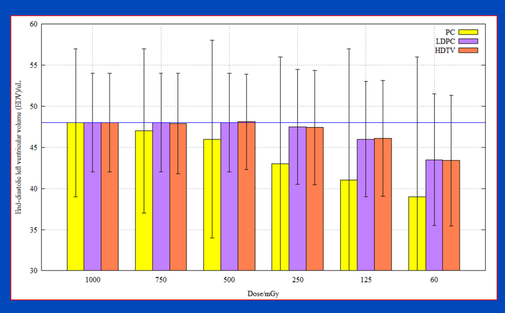
$$\nabla_{\boldsymbol{r},t}f(\boldsymbol{r},t)=\begin{pmatrix}\alpha\cdot\frac{1}{\Delta x}(f_{x,y,z,t}-f_{x-1,y,z,t})\\ \alpha\cdot\frac{1}{\Delta y}(f_{x,y,z,t}-f_{x,y-1,z,t})\\ \alpha\cdot\frac{1}{\Delta z}(f_{x,y,z,t}-f_{x,y,z-1,t})\\ (1-\alpha)\cdot\frac{1}{\Delta t}(f_{x,y,z,t}-f_{x,y,z,t-1})\end{pmatrix}$$

Comparison



c=0%, Δc=20%, r=0%, Δr=10%
C/W=400 HU/1000 HU

EDV Estimation



This results in the usage of only about 360 projections per volume. To estimate the EDV a multi-level Otsu method [3] is applied to the data resulting in a classification of the present tissue into three types: contrast agent/blood, muscle and intermediate tissue. EDV is estimated by summing the volumes of all voxels classified as contrast agent/blood in all volume slices. To provide a ground truth to the estimated ventricular volumes a high dose scan (1 Gy) was carried out for each mouse and the resulting images were analyzed to estimate a reference EDV.

Results

In our cases LDPC and HDTV typically reduce image noise by a factor of about six (e.g. from 170 HU to 30 HU) and thus allow for an accurate segmentation of different tissue types. The reconstruction of data obtained using 1 Gy results in an artifact-free image and we consider the obtained EDV the ground truth of 48 µL. The standard deviation in case of PC is ±9 µL and ±6 µL in case of LDPC and HDTV. In case of an administered dose of 250 mGy the EDV can be estimated as 43±13 µL for PC, 47.5±7 µL for LDPC, and 47.5±8 µL for HDTV . The EDV estimated with only 60 mGy using PC is 39±17 µL, 43±8 µL using LDPC and 43±7 µL using HDTV. In general the EDV is underestimated if only a limited number of projections is used. The LDPC and HDTV algorithms are less sensitive to such a reduction than the PC reconstruction.

Conclusion

The evaluation of the EDV using different dose levels and reconstruction algorithms proved that a reduction in dose by a factor of four (1000 mGy to 250 mGy) is possible when sophisticated reconstruction algorithms are used. This does not only result in a reduced metabolic interference to the animal under examination but also in a reduction of scan time by a factor of four. The usage of more sophisticated segmentation algorithms will allow for an even higher reduction in dose.

References

[1] 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(3), pp. 1416-1424, 2011.

[2] L. Ritschl, S. Sawall, M. Knaup, A. Hess, and M. Kachelrieß. Iterative 4D cardiac micro-CT image reconstruction using an adaptive spatio-temporal sparsity prior. Physics in Medicine and Biology, vol. 57(6), pp. 1517-1525, February 2012.

[3] N. Otsu. A threshold selection method from gray-level histograms. IEEE Transactions on Systems, Man and Cybernetics, vol. 9, no. 1, pp. 62–66, 1979.

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