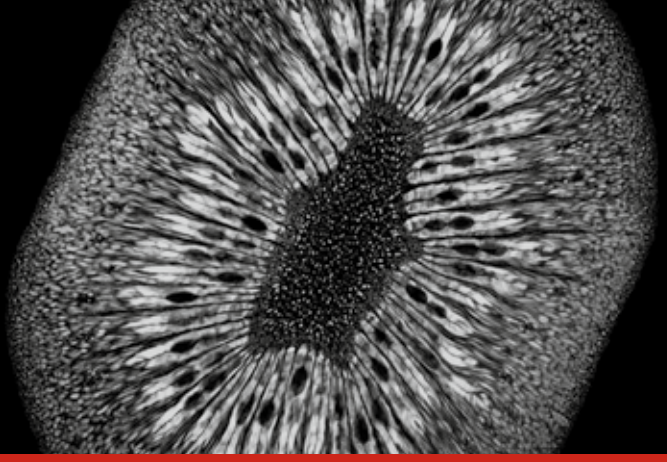
viscover



Left ventricular volume estimation

Left ventricular volume estimation using contrast-enhanced low-dose cone-beam micro-CT

Stefan Sawall[1], Sören Schüller[1], Jan Kuntz[3], Michael Knaup[1], Andreas Hess[2] and Marc Kachelrieß[1,3]
[1] Institute of Medical Physics, Friedrich-Alexander-University of Erlangen-Nürnberg, Erlangen, Germany
[2] Institute of Experimental and Clinical Pharmacology and Toxicology, Friedrich-Alexander-University of Erlangen-Nürnberg, Erlangen, Germany
[3] Medical Physics in Radiology, German Cancer Research Center (DKFZ), Heidelberg, Germany

Introduction

Pre-clinical cardiac micro-CT of small rodents such as rats or mice is used for phenotyping, drug studies, and to design and study animal models of heart disease. The extraction of morphological or functional cardiac parameters requires CT volumes with high spatial and temporal resolution.
For longitudinal animal studies one needs to keep radiation dose at its absolute minimum and in general one cannot intubate the rodents. Hence the scans are carried out under free breathing conditions and the scans or the reconstructions need to be respiratory and cardiac gated[1,2].
A conventional phase-correlated (PC) reconstruction of a given cardiac and respiratory phase utilizes only a small amount of the total data acquired. For example, a respiratory window spanning 10% of the respiratory cycle and a cardiac window of 10% width imply that only 1% of the projections are used for a PC reconstruction.
The resulting images are very noisy unless acquired with high dose and a fine angular increment. Hence functional parameters estimated from these data, e.g. the end-diastolic left ventricular volume (EDV), are error-prone. We propose a low-dose phase-correlated (LDPC) image reconstruction algorithm that combines iterative reconstruction with 5D (three spatial dimensions, two temporal dimensions: respiratory and cardiac) edge-preserving anisotropic filtering.
We demonstrate that phase-correlated reconstruction at an order of magnitude less dose compared to the gold standard PC reconstruction can be performed. This allows to estimate cardiac parameters with less dose and hence less metabolic inference to the animal under examination as will be exemplarily shown by estimating the EDV.

Materials and Methods

Cone-beam micro-CT scans of four mice were used to perform retrospectively correlated image reconstruction. Each mouse was scanned three times, repositioned after each scan and the scans are supposed to be statistically independent thus our population is of size twelve (n=12). Each scan mode comprises 7200 projections during 10 contiguous rotations within 5 minutes. The mice showed an average respiratory rate of about 150 rpm and a heart rate of about 350 bpm.
ExiTron™ nano 12000 (Viscover™, *nanoPET Pharma* GmbH, Germany) was used to deliver sufficient contrast between blood and myocardium of about 400 HU (150 µL/mouse). To correlate our reconstruction with the motion phases of the animal heart and lung we detect corresponding synchronization information directly from the raw data. This intrinsic gating technique, which is also called wireless gating or kymogram-based gating, was first developed for clinical cone-beam spiral CT scanners and has then been adopted for micro-CT applications[3]. Intrinsic gating in case of clinical CT is very difficult due to the fact that the scanner rotates up to three times during one motion cycle. In our case of slowly rotating micro-CT scanners, and most other flat detector CT scanners in general, a motion period is much shorter than the time needed for a half or full rotation.
The extraction of the synchronization signal may therefore neglect the gantry rotation and rather simple methods may be used to detect the periodic motion.
Our standard PC 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 comprise a low signal-to-noise ratio and fine morphological details vanish within the noise.
The standard McKinnon-Bates (MKB) algorithm[4] can be adapted to address these issues. First a prior image based on all acquired projections is reconstructed. This image is blurry in regions where motion takes place and of high quality in all other regions. Afterwards the prior image is forward projected and the result is subtracted from the measured raw data. These subtracted data are then used for a phase-correlated reconstruction which is added to the prior image. Since the respiratory motion dominates the cardiac motion we extend the standard MKB method to a

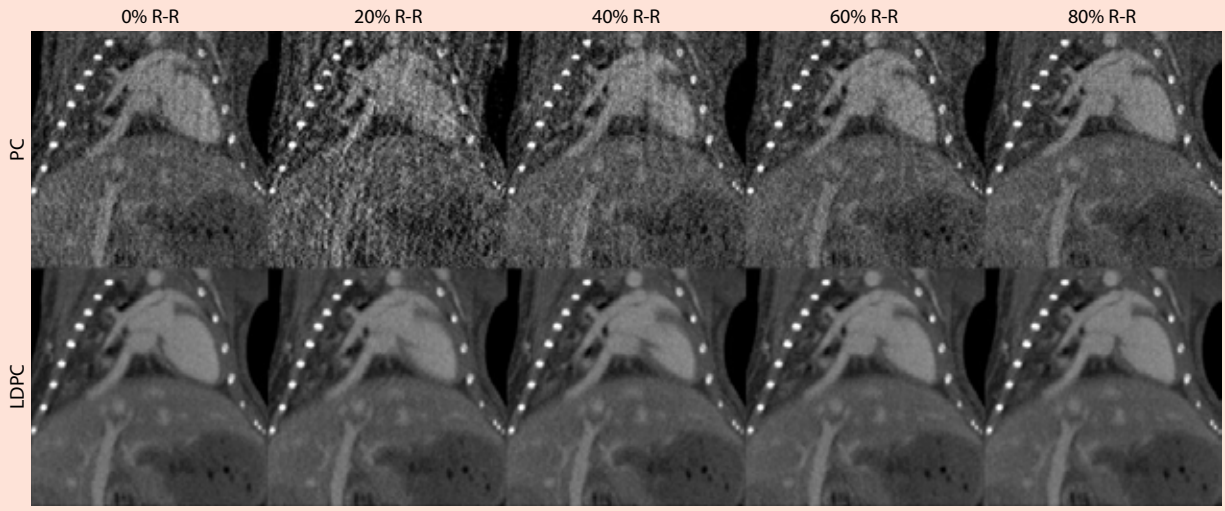


Figure 1: Coronal slices spaced equidistantly within one heart cycle starting in diastole during inhale acquired at a dose of 250 mGy. Standard PC (top) and LDPC reconstruction (bottom). The enhancement of the left ventricle to the myocardium due to the contrast agent is clearly visible. Note the varying noise structure in the PC images caused by the different numbers of projection contributing to each reconstruction. (C/W=300/700 HU)

two-step algorithm. In a first step, we apply MKB only to the respiratory signal and in the second step, we use the respiratory gated MKB-image as prior for the cardiac gating. We then apply an edge-preserving, anisotropic denoising filter in up to five dimensions. This is a filtering in three spatial dimensions as well as in the temporal respiratory and temporal cardiac direction. The final volumes obtained by MKB-reconstruction and filtering are the LDPC volumes (refer to figure 1)[5]. As a consequence of the extension of the MKB algorithm and the filtering our new LDPC method is computationally five times as demanding as standard PC reconstruction.

To estimate the EDV a multi-level Otsu method[6] is applied to the data resulting in a classification of the present tissue into three types (refer to figure 2): contrast agent/blood (red), muscle (green) and intermediate tissue (blue).

The 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 and Discussion

In our cases LDPC typically reduces image noise by a factor of six (e.g. from 170 HU to 30 HU) while our dose values lie in the range from 200 mGy to 500 mGy (refer to figure 1). Compared to other publications[1], that apply up to 1840 mGy dose for the same task (similar spatial resolution and image noise), our LDPC approach achieves a more than ten-fold dose usage improvement[5]. Image noise was measured in the difference image of adjacent slices in z-direction to provide a fair comparison. LDPC boosts image quality compared to PC and enables high fidelity low-dose double-gated imaging of free breathing rodents without compromise in image quality and thus the proposed method allows for longitudinal micro-CT studies with reduced metabolic inference. The evaluation of the EDV for all mice using the PC reconstructions results in a mean EDV of 41±16 µL whereas the estimation based on the LDPC volumes results in a mean end-diastolic volume of 48 µL with a standard deviation of 6 µL (refer to table 1). The reference EDV was estimated as 48±5 µL and corresponds well to recently published work[7]. The large deviations of the EDV estimated from the PC volumes originate from errors in the segmentation of the contrast agent/blood due to high noise and artifacts as can be easily seen in figure 2. This proofs that the proposed LDPC method allows for an accurate quantification of functional cardiac parameters with high fidelity compared to the standard PC reconstructions at reduced radiation dose.

	Scan 1	Scan 2	Scan 3
EDV using PC reconstructions			
Mouse 1	51 µL	55 µL	59 µL
Mouse 2	45 µL	37 µL	38 µL
Mouse 3	36 µL	29 µL	34 µL
Mouse 4	63 µL	18 µL	38 µL
EDV using LDPC reconstructions			
Mouse 1	46 µL	49 µL	58 µL
Mouse 2	49 µL	37 µL	45 µL
Mouse 3	54 µL	42 µL	54 µL
Mouse 4	51 µL	49 µL	43 µL

Table 1: EDV estimated using the PC reconstructions and LDPC reconstructions.

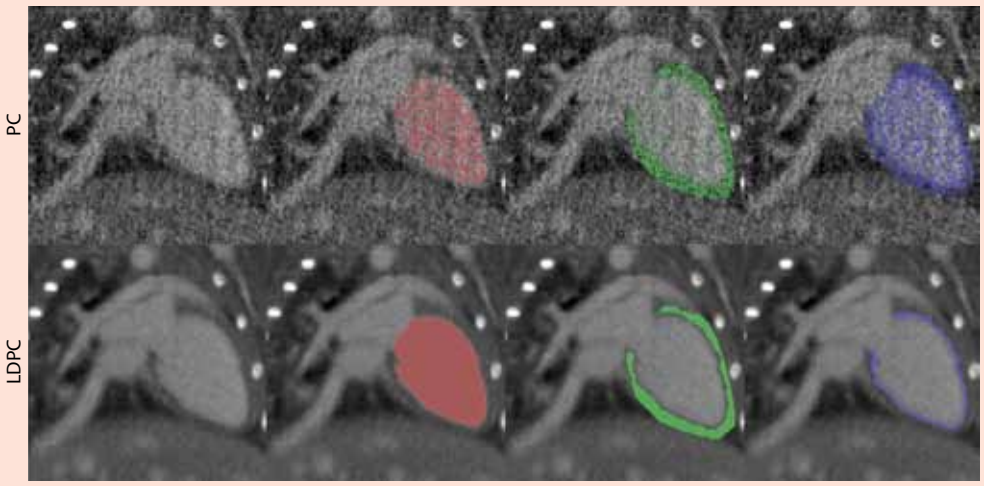


Figure 2: Different tissue types classified in the PC (top) and LDPC (bottom) reconstructions. Contrast agent/blood is shown in red, muscle in green, and intermediate tissue in blue. (C/W=300/700 HU)

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft (DFG) under grant FOR 661. The high-speed image reconstruction software RayConStruct-IR was provided by RayConStruct® GmbH, Nürnberg, Germany. The authors further thank the Intel® Corporation and Fujitsu® Technology Solutions GmbH for providing their latest multicore hardware. The scans of the contrast–enhanced mice were performed by Sandra Strobelt and Johannes Käßer, Institute of Experimental and Clinical Pharmacology and Toxicology, Friedrich-Alexander-University of Erlangen–Nürnberg, Erlangen, Germany.

Viscover™ Product	Order No.
ExiTron nano 6000, 5 injections	130-095-146
ExiTron nano 6000, 25 injections	130-095-147
ExiTron nano 12000, 5 injections	130-095-698
ExiTron nano 12000, 25 injections	130-095-700
ExiTron P, 5 injections	130-095-144
ExiTron P, 25 injections	130-095-145
ExiTron U, 5 injections	130-095-142
ExiTron U, 25 injections	130-095-143
ExiTron V, 5 injections	130-095-283
ExiTron V, 25 injections	130-095-284

References

1. Badea, C.T. *et al.* (2004) Micro-CT with respiratory and cardiac gating. Med. Phys. 31(12): 3324-3329.
2. Badea, C.T. *et al.* (2005) 4D micro-CT of the mouse heart. Mol. Imaging 4(2): 110-116.
3. Kachelrieß, M *et al.* (2002) Kymogram detection and kymogram-correlated image reconstruction from subsecond spiral computed tomography scans of the heart. Med. Phys. 29(7):1489-1503.
4. McKinnon, G. C. and Bates, R.H.T. (1981) Towards imaging the beating heart usefully with a conventional CT scanner. IEEE Trans. Biomed. Eng. BME-28(2):123-127.
5. Sawall, S. *et al.* (2011) Low-dose cardio-respiratory phase-correlated cone-beam micro-CT of small animals. Med. Phys. 38(3):1416-24.
6. Liao, P.-S. *et al.* (2001) A fast algorithm for multilevel thresholding. J. Inf. Sci. Eng. 17:713-727.
7. Chin, B. M. *et al.* (2007) Left ventricular functional assessment in mice: feasibility of high spatial and temporal resolution ECG-gated blood pool SPECT. Radiology 245(2):440-448.

Viscover is powered by

***nanoPET Pharma* GmbH**
Robert-Koch-Platz 4
10115 Berlin, Germany
Phone +49 30 890 49 74-0
Fax +49 30 890 49 74-99
imaging@nanopet-pharma.com

nanoPET Pharma GmbH provides products and services worldwide. Visit **www.viscover.berlin** to find your nearest sales contact.