Functional Phase–Correlated Micro–CT Imaging of Small Rodents with Low Dose

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ABSTRACT

Functional imaging of an animals thoracic region requires cardiac and respiratory gating. The information on respiratory motion and ECG required for double-gating are extracted from the rawdata and used to select the projections appropriate for a given motion phase. A conventional phase-correlated reconstruction (PC) therefore uses only a small amount of the total projections acquired. Thus the resulting images comprise a high noise level unless acquired with very high dose, and streak artifacts may occur due to the sparse angular sampling. Here, we are aiming at getting high fidelity images even for relatively low dose values. To overcome these issues we implemented an iterative reconstruction method encompassing a five-dimensional (spatial, cardiac-temporal, respiratory-temporal) edge-preserving filter. This new phase-correlated low-dose (LDPC) reconstruction method is evaluated using retrospectively-gated, contrast-enhanced micro CT data of mice. The scans performed comprise 7200 projections within 10 rotations over 5 minutes. A tube voltage of 65 kV was used resulting in an administered dose of about 500 mGy. 20 respiratory phases and 10 cardiac phases are reconstructed. Using LDPC reconstruction the image noise is typically reduced by a factor of about six and artifacts are almost removed. Reducing the number of projections available for reconstruction shows that we can get comparable image quality with only 200 mGy. LDPC enables high fidelity low-dose double-gated imaging of free breathing rodents without compromises in image quality. Compared to PC image noise is significantly reduced with LDPC and the administered dose can be reduced accordingly.

1. INTRODUCTION

Double-gated in–vivo small animal cone–beam micro–CT scans provide five–dimensional information about the object: the three volume dimensions plus the temporal dimensions of the respiratory motion and the heart motion, respectively. Double gating is typically performed to separate respiratory from cardiac motion when imaging the animal’s lung or heart. When ignoring the fact that cardiac motion also induces motion in the lung itself imaging the lung can be done using respiratory gating only.\textsuperscript{1} However, to image the heart of small animals one cannot neglect the translations and deformations of the heart induced by the respiratory motion. Hence cardiac imaging requires double gating.\textsuperscript{2–6} To obtain functional information of the heart or lung it may be important to cover the complete motion cycles and thereby to reconstruct four– or five–dimensional representations of the object. While this paper focusses on the five–dimensional reconstructions the low–dose phase–correlated image reconstruction method we propose can also be applied to four–dimensional data. It is our aim to significantly improve the image quality achievable in low–dose single– or double–gated micro–CT scans of small specimen. On the one hand we want to reduce streak artifacts that result from sparse angular sampling and on the other hand we want to reduce image noise resulting from the small amount of photons available in a given combination of respiratory and cardiac phase.

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2. METHOD

2.1 Scan Mode

For our scans we chose a scan mode that acquires 7200 projections during 10 contiguous rotations. In case of unexpected incidences, such as object motion, we may use only the subset of data that is not corrupted. In addition this scan mode allows us to study the dose reduction potential by doing reconstructions from only a subset of the data, e.g. by using only the first five rotations for image reconstruction.

2.2 Intrinsic Gating

To correlate our reconstruction with the motion phases of the animal heart and lung we detect corresponding synchronization information directly from the rawdata by evaluating the center of mass within certain ROIs in the projection images.\textsuperscript{6–9} In the case of slowly rotating micro–CT scanners a motion period is much shorter than the time needed for a half or a full rotation as in contrast to fast rotating clinical CT scanners. The extraction of the synchronization signal may therefore neglect the gantry rotation and such rather simple methods are sufficient to detect the periodic motion.

2.3 Image Reconstruction

Let $f$ denote the object, $X$ the x–ray transform operator, and $p$ be the projection data, such that $p = Xf$. Our standard image reconstruction is the Feldkamp algorithm which we denote with $X^{-1}_{\text{std}}$ and which results in the standard image $f_{\text{std}} = X^{-1}_{\text{std}}p$.\textsuperscript{10} The standard Feldkamp algorithm is not phase–correlated. We make us of it below to define the McKinnon–Bates algorithm. To perform respiratory and cardiac–correlated image reconstruction we use a phase–correlated Feldkamp algorithm $X^{-1}_{\text{PC}}$ that filters and backprojects only those projections that lie in the desired temporal window. The temporal window itself is defined by specifying the respiratory phase $r$ and the cardiac phase $c$, both are values between 0 and 1 and count relative to one motion period, and by specifying the widths $\Delta r$ and $\Delta c$ of these temporal windows. The respiratory and cardiac phase–correlated image is denoted as $f_{\text{PC}} = X^{-1}_{\text{PC}}p$. Since only few projections fall into the desired temporal window, streak artifacts may occur unless a very large number of projections at very fine angular increments is acquired. The McKinnon–Bates (MKB) algorithm can be used to address this issue.\textsuperscript{11,12} It works as follows. First, a standard reconstruction is performed to obtain a prior image. This prior image is blurry in those regions where motion is present, and it is of high image quality elsewhere. Then, a forward projection of the prior image is performed and subtracted from the measured rawdata. These subtracted data are then used for a phase–correlated reconstruction which is added to the prior image. Mathematically:

$$f_{\text{MKB}} = f_{\text{std}} + X^{-1}_{\text{PC}}(p - Xf_{\text{std}}).$$
Since the respiratory motion dominates the cardiac motion we extend the MKB approach to a two step algorithm. In a first step we apply MKB only to respiratory gating and in the second step we use the respiratory–gated MKB image as a prior for the additional cardiac gating. This procedure ensures the best possible prior for cardiac gating.

To reduce noise we apply edge preserving denoising bilateral filters\textsuperscript{13} in up to five dimensions. To define the bilateral filter let us restrict to one dimension, for convenience. Bilateral filtering of a function $f(x)$ is then defined as

$$Bf(x) = \frac{\int dt \, D(x, t)R(x, t)f(t)}{\int dt \, D(x, t)R(x, t)}$$

with $B$ denoting the bilateral filtering operator and

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

and

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

being the domain and the range filter, respectively. The parameters $\sigma_x$ and $\sigma_f$ are the widths of the Gaussian domain and range filters, respectively. Since respiratory and cardiac gating yields five–dimensional volumes $f(x, y, z, r, c)$, with $r$ denoting the respiratory and $c$ denoting the cardiac phase, we can apply bilateral filtering in up to five dimensions. The corresponding domain filter parameters are denoted as $\sigma_x$, $\sigma_y$, $\sigma_z$, $\sigma_r$ and $\sigma_c$, respectively.

The final volume, obtained by bilateral filtering the MKB volume, is the low–dose phase–correlated volume $f_{\text{LDPC}} = Bf_{\text{MKB}}$ which we want to compare against the conventional (and more simple) phase–correlated volume $f_{\text{PC}}$ in the following.

### 3. MEASUREMENTS

We currently have several data sets available for double gating that were measured in-house. Two of them shall be presented here. The data of both mice were acquired with a dedicated in–vivo cone–beam micro–CT scanner (TomoScope Synergy Twin, CT Imaging GmbH, Erlangen, Germany) in single source mode installed at the Institute of Medical Physics, Erlangen, Germany. The system consists of a micro focus x–ray source mounted at a distance of 170 mm to the isocenter and a 1024 × 1024 flat panel detector mounted at a distance of 39 mm to the isocenter. The size of the quadratic detector pixels was 50 µm. To increase the detector's readout rate to 25 frames per second a two–by–two binning of the detector pixels was performed. The scans were conducted at 65 kV tube voltage with a tube current of 0.3 mA. 7200 projections were acquired per scan in a circular trajectory over an angular range of 3600°. The scan time for these ten rotations was 288 s. The tube current time product was 87 mAs, the absorbed dose was measured as 500 mGy in each case.

Both mice were anesthesized with a combination of ketamine and rompun. A bloodpool contrast agent (Fenestra VC, Advanced Research Technologies, Saint Laurent for mouse 1 and Binition, Binitio Biomedical Inc., Ottawa for mouse 2) was used for contrast enhancement. The mean respiratory rate of mouse 1 was 150 rpm (respirations per minute) and the mean heart rate was 300 bpm (beats per minute) whereas mouse 2 showed a mean respiratory rate of 120 rpm and a mean heart rate of 260 bpm. With 40 ms exposure time per projection, about 11 projections were acquired during one respiration cycle and about 6 projections were acquired during one cardiac cycle of each mouse. This, in turn, implies that the respiratory temporal resolution is limited to about 10% of the respiratory cycle and that the cardiac temporal resolution is limited to about 20% of the cardiac cycle. To avoid a further decrease in temporal resolution the RC–correlated image reconstructions were carried out with a respiratory window width of $\Delta r = 10\%$ and a cardiac window width of $\Delta c = 20\%$. The size of each reconstructed volume was set to $512 \times 512 \times 512$ voxels with a voxel size of 40 µm. Volumes were...
generated with a step size of 5% in the respiratory cycle and a step size of 10% in the cardiac cycle. Therefore, each 5D dataset consisted of a total of 200 volumes resulting in a memory requirement of 50 GB. The data were processed on a standard PC equipped with 64 GB of memory using a commercially available software package (RayConStruct-IR, RayConStruct GmbH, Nürnberg, Germany). As the data were collected retrospectively, no vote from the ethical committee was required.

4. RESULTS

Although the contrast enhancement in the heart between blood and myocardium of mouse 1 is only about 110 HU our reconstruction and postprocessing approach yields images of surprisingly high quality. Figure 2 compares the results of our new RC–gated approach (LDPC) with a conventional RC–gated approach (PC) that simply feeds only those projections corresponding to the desired motion phases into a modified Feldkamp reconstruction algorithm. With our gating parameters of using a respiratory window of 10% width and a cardiac window of 20% width only 2% of the projections fall into desired motion phases. Hence the conventional simple gating approach suffers from significantly increased image noise and from streak artifacts due to sparse view sampling. With the new and improved algorithm we can reduce image noise from 175 HU to 30 HU and we can remove all streak artifacts while maintaining the full temporal resolution (as far as one can tell from the difference images). It should be noted that image noise was measured in a homogeneous volume of interest (VOI) in the liver region. The same VOI was used for all reconstructions and it is not necessarily intersecting those slices that are shown in the images. Mouse 2 shows an enhancement between blood and myocardium of about 450 HU. Figure 3 contains a comparison of the PC reconstruction method against the proposed LDPC method at different dose levels. A decrease in dose was simulated by limiting the number of gantry rotations and thus the number of projections available for reconstruction. Compared to the PC reconstruction the usage of LDPC reduces the voxel noise from 125 HU to 26 HU at a dose level of 500 mGy. Furthermore the streak artifacts due to the sparse angular sampling of projections have been reduced significantly. A decrease in dose down to 250 mGy shows an increase of streak artifacts in the images reconstructed with PC which are nearly removed.
Figure 3. Phase–correlated reconstructions of mouse 2 centered at $r = 60\%$ and $c = 0\%$ with window widths $\Delta r = 10\%$ and $\Delta c = 20\%$. The left panel shows the conventional phase–correlated reconstructions while the right panel is the proposed low dose approach. Dose levels ranging from 60 mGy to 500 mGy were obtained by using only fractions of the data available. (400 HU / 800 HU)

within the LDPC reconstruction. The voxel noise is raised to 198 HU in the PC images and 57 HU in the LDPC images respectively. Administering a dose of only 60 mGy reduces image quality more significantly. The images originating from a standard phase–correlated reconstruction suffer from a high noise level of about 345 HU and streak artifacts prevent the anatomical structures of interest, e.g. the heart, from being identified as such. In contrast the LDPC reconstruction is still capable of recovering anatomical details.

4.1 Comparison with other approaches

The experimental data available to us are very limited. Further on, mouse 1 shows only a very low enhancement between blood and myocardium, which is probably due to misadministered contrast agent. Regarding other references, such as references,\(^3\)–\(^5\) for example, it can be seen that a typical enhancement should be in the order of 400 to 500 HU in the mouse heart. Since the said references also state important image quality parameters together with estimates of the dose we want to compare our results to those published in the literature. We have therefore prepared table 1 to see the most important differences at a glance. It should be noted that the data shown in this table only allow for a very rough comparison between the methods, mainly because important details of how certain parameters were measured or calculated are not disclosed in the publications.

The last row of the table further shows a quality parameter $Q$ given as

$$Q \propto \frac{1}{\sigma \sqrt{D \Delta^2}}$$

where $\sigma$ is the image noise observed in unenhanced regions of the mouse tissue, $D$ is the dose reported, and $\Delta$ is the sampling distance of the rays scaled to the isocenter (which would typically be the diameter of the field of measurement divided by the number of detector rows or columns). The definition of the quality parameter reflects the fact that image noise variance is proportional to one over dose and to one over the fourth power of spatial resolution. The constant of proportionality is chosen to obtain a quality value of 100%...
Table 1. Parameters for two different scan and reconstruction approaches in comparison. Note that reference 3 does sample only 50% of the cardiac cycle (six 10 ms wide samples within a 120 ms cardiac cycle). Hence the actual dose reported as 920 mGy is only half of the dose that would be required to sample the complete cycle. Respiratory and heart rates are the averages reported in each reference and correspond to mouse scans. The spatial sampling corresponds to the detector pixel size after binning, if applicable, at the isocenter.

for the LDPC reconstructions of mouse 2. The other quality value stated for our experiment corresponds to the conventional phase–correlated reconstruction and therefore is far lower than 100%. It must be emphasized that the quality parameter is nothing but a rough estimate due to the following reasons. First of all, spatial resolution was assumed to be proportional to the sampling distance and the effect of the reconstruction process, that potentially lowers the spatial resolution, could not be taken into account. In addition the dose values reported are measured using different methods and different phantoms and therefore are not highly accurate. And finally the image noise quoted is neither measured in difference images, and therefore is likely to contain effects such as streak artifacts or non–uniform background, nor was it measured in the same region of the mouse in all cases. Nevertheless, there are two things to be learned regarding the evaluation of the quality parameter: Without advanced image reconstruction and signal processing techniques, our results lie well within the range of what has been published in the literature so far. And switching from standard phase–correlated reconstruction to low–dose phase–correlated reconstruction has the potential to increase the image quality by a factor of about five. A decrease in dose was simulated by limiting the number of rotations and thus the number of projections available for reconstruction. The image acquisition was conducted at a dose of about 250 mGy.

### 5. CONCLUSION AND DISCUSSION

LDPC is a new technique to significantly improve phase–correlated imaging from highly undersampled data. We demonstrate that dose savings of about an order of magnitude are possible compared to standard phase–correlated reconstruction approaches. With sophisticated reconstruction techniques such as the LDPC algorithm it is possible to perform 4D or 5D phase–correlated imaging at about the same dose level as required for conventional 3D studies. Furthermore the method is not limited to a certain type of scanner or geometry as the images shown throughout this paper originate from different imaging systems of different vendors. Using LDPC therefore appears to allow for longitudinal in–vivo studies of the rodent heart as well as for long term studies in preclinical research.

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