Low–Dose Phase–Correlated Cone–Beam Micro–CT of Small Animals

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I. 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 [1], [2], [3], [4], [5].

We are aiming at significantly improving 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.

II. METHOD

A. 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 (kymogram). In our case of a slowly rotating micro-CT scanner approaches that evaluate the center of mass of certain ROIs within each two–dimensional projection image have been quite successful to detect the respiratory and cardiac motion [6], [7].

B. 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 $f_{\text{Std}} = X_{\text{Std}}^{-1} p$ [8]. The standard Feldkamp algorithm is not phase–correlated. We make use 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 $f_{\text{PC}} = X_{\text{PC}}^{-1} p$.

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 [9], [10]. 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:

$$f_{\text{MKB}} = f_{\text{Std}} + X_{\text{PC}}^{-1} (p - Xf_{\text{Std}}).$$

To compensate for the loss in spatial resolution due to the additional forward and backprojection steps and to correctly compensate for the longitudinal truncation effects we rather
domain filters may be used as well. In this study, however, we restricted ourselves to considering Gaussian–shaped filters.

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. We also apply the edge–preserving filtration to the first prior volume (in \( x, y, z \), and \( r \)) using the same filter parameters as for the final five–dimensional filtering.

The final volume, obtained by bilateral filtering the MKB volume and the intermediate prior volumes, is the low–dose phase–correlated volume \( f_{LDPC} = Bf_{MKB} \) (6) which we want to compare against the conventional (and more simple) phase–correlated volume \( f_{PC} \) in the following.

### III. Measurements

We currently have several different data sets available for double gating that were measured in–house. Three of them shall be presented here. The first and second mouse was scanned with a dual source micro–CT scanner in single source mode while the third mouse was scanned in a dual source micro–CT scanner. Additionally data of recent publications were made available to us [4].

#### A. Mouse 1 and 2

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 \( \times \) 1024 flat panel detector mounted at a distance of 39 mm to the isocenter. The size of the quadratic detector pixels was 50 \( \mu \)m. 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 360°. 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.

The mice was anesthesized using a combination of Ketamine and Xylazine. The contrast agents used were Binitio (Binitio Biomedical Inc., Canada) and Fenestra VC (ART Advanced Research Technologies, Canada), both injected via a tail vein.

#### B. Mouse 3

The data were acquired with a dedicated in–vivo dual source cone–beam micro–CT scanner (TomoScope Synergy Twin, CT Imaging GmbH, Erlangen, Germany) installed at the Weizmann Institute, Rehovot, Israel. Each source–detector...
thread 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 62 mm to the isocenter.
Both detectors were laterally shifted to increase the field of
measurement [12]. Both threads were mounted under an angle of approximately 90°.

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 scan was conducted at 40 kV tube voltage with a tube current of 1.0 mA per tube. 7200 projections were acquired in a circular scan over an angular range of 3600°. The scan time for these ten rotations was 288 s resulting in an overall tube current time product of 576 mAs and an absorbed dose of 1077 mGy.

The mouse was anesthetized using a combination of Ketamine and Xylazine. The contrast agent used was Omnipaque Iohexol.

IV. RESULTS

Figure 1 compares the results of our new LDPC approach with a conventional PC approach of mouse 1. The PC reconstruction suffers from significantly increased image noise and from streak artifacts due to sparse view sampling. With the new 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).

Furthermore we want to compare our results to those published in the literature. We have therefore prepared table I 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 [13]

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

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% 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.
Fig. 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. Values for image noise are shown in the axial slices. (400 HU / 800 HU)

Fig. 4. Phase–correlated reconstructions of the reference [4] mouse 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 63 mGy to 250 mGy were obtained by using only fractions of the data available. Values for image noise are shown in the sagittal slices. (300 HU / 700 HU)
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. To further illustrate the dose reduction capabilities of the LDPC method a corresponding study has been performed based on the data of reference [4] that were made available to us and its results are shown in figure 4. A decrease in dose from 250 mGy to 63 mGy yields significant streak artifacts in the phase–correlated images which are not visible in the low–dose phase–correlated images.

V. 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. Using LDPC appears to allow for longitudinal in–vivo examinations of the rodent heart and enables long term studies with reduced metabolic inference.

REFERENCES