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4D micro-CT for cardiac and perfusion applications with view under sampling

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Abstract

Purpose—Micro-CT is currently used to provide anatomical information in preclinical studies. There is however significant interest in obtaining functional measurements on the same systems. We report here novel strategies for 4D Micro-CT with a focus on two applications: i) cardiac imaging based on retrospective gating and ii) pulmonary perfusion using multiple contrast injections/rotations paradigm.

Methods—A dual source micro-CT system is used for image acquisition with pulsed x-rays exposures (80 kVp, 70mA, 10 ms) and a sampling rate of 20 projections/sec. The cardiac micro-CT protocol involves the use of a liposomal blood pool contrast agent containing 123 mg I/ml delivered via a tail vein catheter in a dose of 0.01 ml/g body weight. Fast scanning of free breathing mice is achieved using retrospective gating. The ECG and respiratory signals are used to sort projections into 10 cardiac phases. The pulmonary perfusion protocol uses a conventional contrast agent (Iovue 370). The total volume of contrast agent is limited to 0.4 ml and is delivered by a micro-injector in 4 injections separated by 2 minute intervals to allow for clearance. Each injection is synchronized with the rotation of the animal, and each of the 4 rotations is started with an angular offset of 22.5° from the starting angle of the previous rotation. Both cardiac and perfusion protocols result in an irregular angular distribution of projections that causes significant streaking artifacts in reconstructions when using traditional filtered back projection algorithms. To alleviate these artifacts, we construct the point spread function (PSF) of our micro-CT system and analyze the distribution of the reconstructed data in the Fourier domain. This enables us to correct for irregular angular inconsistencies via deconvolution and also identify regions where data is missing. These regions are filled in with data from a high quality but temporally averaged image reconstructed with all available projections.

We implemented parts of this algorithm on a graphics processing unit (GPU) to reduce run time. The proposed method was validated with numerical simulations and experimental micro-CT data.

Results—The simulations indicate that deconvolution successfully removes the streaking artifacts while preserving temporal information. 4D cardiac micro-CT in a mouse was performed with adequate image quality at isotropic voxel size of 88 microns and 10 ms temporal resolution. 4D pulmonary perfusion images were obtained in a mouse at 176 microns and 687 msec temporal resolution. Compared with FBP reconstruction, the streak reduction ratio is 70% and the contrast to noise ratio is 2.5 times greater in the deconvolved images. The radiation dose associated with the proposed methods is in the range of a typical micro-CT dose (0.17 Gy for the cardiac study and 0.21 Gy for the perfusion study).

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Conclusions—The low dose 4D micro-CT imaging protocols presented here can be applied in high throughput longitudinal studies in a wide range of applications, including drug safety and cardiopulmonary phenotyping.

Keywords

Micro-CT; contrast imaging; lung; perfusion; cardiac

Introduction

The relatively recent development of functional clinical CT has highlighted the value the fourth dimension (time) in characterizing cardiac function and blood flow. Translation of the technology to preclinical studies has enormous potential to help understand critical pathways in genetic models and to highlight potential concerns in drug safety evaluation. But there are considerable challenges in scaling these modalities to the temporal and spatial resolution required for the mouse and rat since a mouse heart is only about 5 mm in diameter and can beat up to 600 times/minute. We present here novel strategies for low dose 4D Micro-CT with a focus on two applications: i) high throughput cardiac imaging based on retrospective gating and ii) pulmonary perfusion.

Our first target application is 4D cardiac micro-CT. To date, the most frequently employed imaging modalities in murine models of cardiovascular disease are echocardiography² and magnetic resonance imaging (MRI)²⁻⁶. Although cardiac CT is quite common in the clinical arena, cardiac micro-CT in the mouse is not widely used. We previously introduced cine cardiac micro-CT based on prospective gating⁷. Prospective cardio-respiratory gating ensures regular angular distribution of projection but may involve long acquisition time since the images are triggered by the coincidence of two events i.e. the end-expiration in the breath cycle and the imaging time point (e.g. systole, diastole) in the cardiac cycle. Other groups have performed cardiac micro-CT studies in mice using slip-ring flat panel based CT and retrospective gating^{8, 9}. In retrospective gating, the projections are sampled much faster, with an equiangular step but at random time points in the cardiac and breathing cycle. Both ECG and a respiration signal are recorded during acquisition and used in post-processing to cluster the projections in sets corresponding to the cardiac and respiratory phases to be reconstructed. For each of the cardiac phases, the corresponding projections have an irregular angular distribution since many views may be missing. The number of projections in each set may be limited by dosage, scan time, and the number of separate cardiac phases to be reconstructed.

The second 4D imaging application that we target is pulmonary perfusion. Recently, we have proposed an approach to measuring lung perfusion in rats using micro-CT with a temporal sampling equivalent to one heart beat¹⁰. We have based our approach on the paradigm that multiple carefully controlled injections of contrast agent create reproducible time attenuation curves¹¹. The method involved the use of a conventional radiographic contrast agent such as Isovue 370, (Bracco Diagnostics, Princeton, NJ) delivered via a jugular vein catheter. Unfortunately, this approach limits one's ability to perform longitudinal studies.

This work addresses limitations associated with our previous dynamic micro-CT imaging. More specifically, we base our cardiac micro-CT sampling on retrospective gating to allow faster acquisition speed and we use a novel sampling protocol with multiple injections (delivered via tail vein) and rotations for pulmonary perfusion imaging. Both cardiac micro-CT and perfusion micro-CT can produce sets of projection data with angular distributions that are sparse and irregular. When an analytical reconstruction algorithm is applied to data

with these properties, the resulting volumes suffer from prominent streaking artifacts and noise. Galigekere *et al* has proposed intermediate view reprojection method to reduce these artifacts in 3D CT with limited number of views¹². In the context of cardiac micro-CT we have previously introduced a sparseness prior-based iterative image reconstruction solution using total variation¹³. Recently, another total variation-based algorithm has emerged that uses a prior image and constrained compressed sensing (PICCS)¹⁴ and was applied in perfusion micro-CT^{1, 15}. Other solutions to the same problem were proposed for 4D cone beam CT using on-board x-ray imaging devices integrated into radiation therapy systems^{16, 17}. To alleviate these artifacts, we construct the point spread function (PSF) of our micro-CT system and analyze the distribution of the reconstructed data in the Fourier domain. This enables us to correct for irregular angular inconsistencies via deconvolution and identify regions where data is missing. These regions are filled in with data from a high quality but temporally averaged image reconstructed with all available projections. Similar deconvolution approaches has been previously used with CT to solve limited angle problems^{18–21}. In spite of the theoretical elegance of this approach, deconvolution involves the division of two volumes in Fourier domain and results in noise due to singularities associated with the division. We propose to avoid the singularities problem by borrowing data from a prior image.

Materials and Methods

The challenges of dynamic micro-CT acquisition were addressed by using a dual source micro-CT system with two different scanning protocols: one designed for cardiac imaging with 10 ms temporal resolution and a second designed for perfusion with 687 msec temporal resolution. Both protocols use our novel reconstruction strategy incorporating deconvolution combined with Fourier data from a fully sampled prior image to reduce streaking artifacts.

1. Dual Source Micro-CT System

Imaging data was acquired on a dual source micro-CT system developed explicitly for these dynamic applications that has been described in detail previously²². The x-ray tubes and the detectors are arranged orthogonally. The system involves:

- 2 G-297 x-ray tubes (Varian Medical Systems, Palo Alto, CA) with 0.3/0.8 mm focal spot size.
- 2 Epsilon High Frequency X-ray generators produced by EMD Technologies (Quebec, Canada).
- 2 CCD based detectors with a Gd2O2S phosphor (XDI-VHR 2 Photonic Science, East Sussex, UK) with pixels of 22 microns which are typically binned to 88 microns.

The sampling is controlled by a sequencing application written in LabVIEW (National Instruments). We use pulsed x-rays (80 kVp, 70mA, 10 ms per exposure). The dual tube/detector configuration acquires images with a sampling rate of 20 projections/sec and projections from the two imaging chains can be combined in a single reconstructed volume based on a geometric calibration demonstrated previously²³.

2. 4D Cardiac Micro-CT using Retrospective Gating

4D Cardiac micro-CT requires the use of contrast agents, a gating strategy and appropriate post processing and image reconstruction. To provide the necessary blood/tissue contrast differences we use a liposomal blood pool contrast agent containing 123 mg I/ml and delivered via a tail vein catheter in a dose of 0.01 ml/g body weight. This blood pool

contrast has a long residence time and due to high Iodine concentration provides at least 500 HU opacification without causing hypervolemia²⁴.

To provide cardiac images, a gating strategy incorporating information on respiration and heart motion is required. For high throughput 4D imaging, we selected retrospective gating. The respiratory and ECG signals are recorded together with the exposure time and projection angles and used post-sampling in a retrospective gating strategy (see Fig. 1). A mixture of air and isoflurane is delivered through a nose cone to freely breathing animals. Thus, we avoid the intubation/ventilation approach used previously⁷ ensuring easier, faster set-up and higher throughput. This facilitates longitudinal studies, where repeated endotracheal intubation may be traumatic to the animals. Respiration information is obtained by a pneumatic pillow coupled to a pressure transducer that detects chest motion. ECG pads placed on the paws of the animals are used to detect heart motion. The signals are processed using a Coulbourn Instruments (Allentown, PA) LabVIEW (National Instruments, Austin TX) system. We collect up to 2250 projections acquired over 5 rotations with a rotation time of 22 sec. The minimum time required for this acquisition is 110 secs. Due to limited storage capacity of the sampling computers, we currently require ~ 5 minutes to acquire a complete study. Post-sampling, the recorded ECG signal is used to assign projection images to their respective phase in the cardiac cycle. The clustering process is implemented in MATLAB (The MathWorks, Natick, MA) and starts by detecting the R peaks in the ECG signal. Next, each projection is registered with the ECG signal by finding the closest two R peaks to the projection sampling time. Each R-R interval in the ECG cycle is divided by the number of temporal intervals (each equal to 10%). The respiration signal is used to eliminate those projections associated with large respiratory motion. Alternatively, the respiratory motion images can be used with a decreased weighting factor in the reconstruction as we previously explored²⁵.

3. Pulmonary Perfusion

The sampling strategy for the pulmonary perfusion protocol is illustrated in Fig. 2. A single 360° rotation is achieved in 22 secs and permits the acquisition of 440 projections. This projection data allows the reconstruction of 4 time points by using a different quadrant of projections from each tube/detector. This results in a temporal resolution of $22/4=5.5$ secs which may be inadequate for accurate perfusion estimation in the mouse where heart rate is 10 times faster than in humans. But the number of time points (and therefore the temporal resolution) during first pass perfusion can be increased by using a biological pulse sequence with multiple injections and rotations¹⁰. In the proposed protocol we use ($m=4$) different injections and full rotations. Sampling time is approximately 8 mins. The total volume of contrast agent is limited to 0.4 ml and is delivered using a LabVIEW-controlled micro-injector²⁶ as 4 injections (each 0.1 ml) separated by 2 minutes intervals to allow for clearance. Each rotation is started with an angular offset of $90^\circ/m$ i.e. 22.5° for 4 injections and rotations. As indicated in Fig. 2B, if the complete arcs are used for reconstruction, the temporal resolution is increased m times i.e. to 1.38 secs. Post sampling, data can be selected from the complete set of $440 \times 4 = 1760$ projections and used for reconstruction using Feldkamp's algorithm since there is no undersampling or irregular angular distribution of projections. Note however, that the temporal resolution can be further increased if subsets of projections are used. Unfortunately in such situations we again encounter a case of limited and irregular angular distribution of projections. For example, by selecting only half of the number of projections (see Fig. 2C) we double the temporal resolution and reconstruct 32 time points every 687 miliseconds.

4. Image Reconstruction

The goal of 4D micro-CT imaging is to reconstruct a series of volumes from a set of x-ray projections of an object that rapidly changes over time. Reconstruction is typically performed with an analytical reconstruction algorithm, such as Feldkamp's²⁷, which uses filtered backprojection (FBP). Both cardiac and perfusion micro-CT produce data with angular distributions that are sparse or irregular. When an analytical reconstruction algorithm is applied to these data, the resulting images suffer from prominent streaking artifacts and noise.

To solve this problem, we represent the process of projection P and the FBP operator B of a volume x as a convolution operation:

$$B(p) = x \circ B(P(\delta))$$

Here, $p = P(x)$ represents the projection data of the object acquired during the scan, δ represents a delta function, $B(P(\delta))$ is known as the point spread function (PSF) of the imaging system, and $\circ$ is the convolution operation.

In our implementation, we use a virtual delta function with a value of 1 at the center of the volume and 0 everywhere else, and we project this volume with a virtual cone beam projection function. In theory, we could produce a more physically accurate PSF by scanning and reconstructing a point-like object, but this would increase the complexity of our experimental protocol.

Representing this process as a convolution operation implicitly assumes that the process is linear and shift-invariant. While parallel beam tomography is shift-invariant, cone beam tomography is not. Our micro-CT system has a cone beam geometry, with a magnification of only 1.1 in which the cone angle is typically less than 4° . Consequently our system is close enough to a parallel beam geometry for the convolution model to be a reasonable approximation. For geometries with more divergent beams, we speculate that the volume could be divided into separate regions with different PSFs, so that the convolution model would remain locally valid.

The convolution theorem states that the Fourier transform of a convolution of two functions is equal to the pointwise product of their Fourier transforms:

$$F(x \circ y) = F(x)F(y)$$

This leads to a simple deconvolution algorithm for recovering x from $B(p)$ and $B(P(\delta))$:

$$x = F^{-1} \left(\frac{F(B(p))}{F(B(P(\delta)))} \right)$$

Unfortunately, the Fourier transform of the PSF, known as the Modulation Transfer Function (MTF), is plagued by large gaps corresponding to the geometric information that is missing because of the sparse or irregular distribution of the projection angles. Division by the small values in these gaps produces unrealistically large values in the Fourier domain that result in prominent artifacts in the spatial domain.

To overcome this obstacle, we identify the gaps in the MTF by finding all values that are less than some threshold k . We then fill in these gaps by using the corresponding

information from a prior data set with a dense and regular distribution of projection angles. In the sampling protocols we have described previously, we collect projection data over a broad range of times and selectively reconstruct different time points or phases with different subsets of the data. The individual time points have poorly distributed data, but as a whole the projection data over all times is well distributed. Consequently, we can fill in the gaps in the MTF of each individual time point by taking values from the Fourier transformation of the prior. This leads to a more robust deconvolution algorithm for time point t :

$$x_t = F^{-1} \left(\begin{array}{cc} \frac{F(B_t(p_t))}{F(B_t(P_t(\delta)))} & \text{if } F(B_t(P_t(\delta))) > k \\ F(B(p)) & \text{otherwise} \end{array} \right)$$

A diagram of this algorithm is shown in Fig. 3. Here P_t and B_t represent the projection and filtered backprojection operations performed only at the angles for which projections were acquired during t . The threshold k is chosen empirically, and we have found that values around 10% of the maximum of the MTF work well. The tradeoff between image quality and temporal resolution can be adjusted by varying k .

To perform the operations in the Fourier domain, some additional modifications must be made to the data. The volumes are constructed on grids with dimensions that are powers of 2, and this increased volume size can necessitate the reconstruction of multiple overlapping sub volumes when large volumes are desired. A 3D cosine window is used to smooth the values at the edges of the volumes to 0, and division by this window after the final inverse Fourier transform can cause additional numerical difficulties. We rescale the values in the volumes before entering and after exiting the Fourier domain to ensure that the reconstructed attenuation values are consistent.

5. Implementation

Reconstruction is computationally demanding. We address this problem by using a graphics processing unit (GPU), which consists of hundreds of processors capable of performing the same function in parallel. This architecture is ideal for performing back projection, projection, and Fourier transforms, in which the same memory and arithmetic operations must be performed over every voxel in the volume or every pixel in the projection images.

To exploit this acceleration while minimizing transfers between disk and memory and remaining flexible in our choice of algorithms, we have built a client-server reconstruction framework²⁸. The server runs constantly in the background, maintains large arrays containing the projection and reconstruction data, and performs computationally demanding tasks on the GPU, as well as other arithmetic and utility functions on the CPU. The server receives instructions from clients via sockets, and the clients can be created dynamically from MATLAB, allowing us to implement our reconstruction algorithms as MATLAB scripts. The server is written in C/C++ and the GPU is programmed with the Compute Unified Device Architecture (CUDA). The GPU used in this study is a GeForce GTX 285 (NVIDIA, Santa Clara, CA).

This architecture imposes several constraints on our implementation. The volumes to be reconstructed must fit in the memory available on the graphics card, and after accounting for the memory required by other variables and other processes active on the computer, this typically limits us to 512 MB. Spatial resolution and the size requirements of the Fast Fourier Transform (FFT) may compel us to reconstruct volumes with slices of size 1024×1024 voxels with single precision floating point values, limiting us to reconstructing 128

slices at a time. Depending on the size of the object we intend to reconstruct, this size may be too small, necessitating the reconstruction of multiple overlapping subvolumes.

Furthermore, development on the GPU requires frequent recompilations and restarts of the server, a process less amenable to rapid algorithm development. For this reason, for the results that we present in this paper, the steps of the deconvolution algorithm that take place inside the Fourier domain were performed in MATLAB and not on the GPU, and this presents a substantial performance bottleneck. Consequently, further work is needed to optimize the performance of our algorithm. The volumes we present in this paper required around 5 minutes for each time point when no subdivision of the volume was necessary, compared to less than a minute for the equivalent Feldkamp reconstruction. For volumes with larger numbers of slices, reconstruction required approximately 10 minutes.

6. Simulations

We have tested the deconvolution approach via simulations based on two modified 3D Shepp and Logan (S&L) phantoms²⁹. In the first S&L phantom, one of the ellipsoids expands and contracts over the course of sampling. This motion simulates a change in the size of the heart over 10 different phases. We generated 1000 projections at randomly selected phases to simulate a cardiac CT scan with retrospective gating. The projections were then sorted into sets corresponding to each phase. The irregular angular distribution and limited number of projections causes streaking artifacts in an FBP reconstruction.

The second S&L phantom simulated a perfusion experiment. This time the same ellipsoid was kept at constant size but allowed to change in attenuation value according to a gamma variate function mimicking the time attenuation curve of the passage of a bolus of contrast agent. We considered 4 injections, with one complete 360° rotation over 22 secs for each injection. Projection images were acquired with a sampling rate of 0.1 secs. We generated 200 projections per rotation for each imaging chain for a total of 1600 projections. The number of time points and therefore the temporal resolution can be decided at the reconstruction stage, but high temporal resolution is associated with gaps in the angular distribution of projections. We reconstructed 32 time points to investigate if we could recover the true values of the phantom at each of these time points.

We added Poisson noise to the x-ray projections to match the noise levels that are typically found in reconstructed volumes produced by our micro-CT system. Specifically, the noise level given by the standard deviation in a uniform region in a volume reconstructed with Feldkamp's algorithm²⁷ was 80 HU.

We have used the total variation (TV) of FBP and deconvolved images and obtained the streak reduction ratio (SRR), similar to Leng et al^{16, 17} to quantify the reduction in streaking artifacts:

$$SRR = \frac{TV(x_{FBP}) - TV(x_{deconvolved})}{TV(x_{FBP})}$$

Since the TV is the sum of the magnitude of the spatial first derivative, the SRR quantifies in a relative way the number and magnitude of the edges. It does not explicitly distinguish between edges or streaking artifacts. To show that we preserve the correct edges of the images, line profiles were used. Additionally, we computed the contrast to noise ratio (CNR):

$$CNR = \frac{\mu_A - \mu_B}{(\sigma_A + \sigma_B)/2}$$

where μ refers to mean values and σ to standard deviation computed in two adjacent regions of interest A and B. In perfusion studies, the CNR changes as the bolus of contrast agent moves in and out of a region of interest. Consequently we also report noise reduction as relative changes between standard deviations in regions of interest selected in the deconvolved and FBP reconstructions. These measures are meant to provide information in the improvements in image quality provided by deconvolution.

Results

Our simulations results based on S&L phantom are presented in Fig. 4 and Fig. 5. In Fig. 4, we show the reconstructions of two phases with the ellipsoid at maximum and minimum size, corresponding to diastole and systole in a cardiac cycle. In both situations the projections, represented here as radial lines and color-coded differently for each imaging are both sparse and irregularly distributed (Fig. 4B). We note that the radial representation of projections is only used for visualization reasons. It is based on the Central Slice Theorem²⁹ but is only correct for a 2D parallel beam case. A reconstruction with all projection data has good image quality, but the boundaries of the ellipsoid are blurred (see arrow in Fig. 4A). The two selected phases were reconstructed via FBP (Fig 4. C) and deconvolution (Fig 4. D). Note the reduction in noise and streaking artifacts in the deconvolved images compared to the FBP images. This is also confirmed by the line profile (fig. 4E) which also show that the true levels and size of structure are recovered. The streak-reduction-ratio (SRR) indicated an average reduction of 36% of streaking artifacts in the deconvolved images. The contrast-to-noise ratio (CNR) computed between the values in the variable size ellipsoid and the adjacent structure was increased from 2.6 (FBP) to 5.63 (deconvolved).

In perfusion simulations case (see Fig. 5), we present the reconstruction of two time points from a total of 32 time points reconstructed. The distribution of projections show gaps of information due to missing projections (see Fig. 5B). There are only 64 projections used for each reconstructed time point. For both selected time points, FBP reconstructions contain artifacts (Fig. 5C) but which are successfully removed in the deconvolved images (Fig. 5D). The line profiles through time point 20 (Tp20) images show that the deconvolved image successfully recovers the correct values of the original phantom (Fig. 5E). The global SRR values indicated an average reduction of 35% of streaking artifacts in the deconvolved images. The CNR values for Tp20 were improved from 1.48 (FBP) to 2.55 (deconvolved) while the noise values given by the relative standard deviation was reduced 45% in the deconvolved images relative to FBP reconstruction.

Fig. 6 shows examples of micro-CT images in a C57BL/6 mouse corresponding to diastole and systole with both axial and sagittal cuts and reconstructed using FBP and deconvolution. The voxel size is 88 microns and the temporal resolution is 10 msec. The total number of projections were 116 (diastole) and 92 (systole) acquired over 3 consecutive rotations from a total of 1350 projections. Note the improvements in image quality and reduction of artifacts obtained via PSF deconvolution. The total radiation dose for a study involving 3 rotations is approximately 0.168 Gy. Fig. 7 compares diastole and systole reconstructed images using data acquired with 2,3,4, and 5 rotations. The corresponding number of projections and figures of merit are presented in Table 1. Note that the images reconstructed with FBP using the lowest numbers of projections are especially noisy. The deconvolution technique is more robust in these undersampled conditions, with an SRR of up to 70%. We selected regions of

interest in the myocardium and in the blood in the left ventricle, and found that CNR to be 2.5 times greater in the deconvolved image compared to the FBP image.

Fig. 8 presents results from a lung perfusion study in a C57BL/6 mouse. Images were reconstructed with Feldkamp's algorithm and via deconvolution at 176 microns voxel size and 687 msec temporal resolution. The time attenuation curves for two selected regions of interest in the lung parenchyma and the pulmonary vessel indicate reduction in noise values (standard deviation) of approximately 69% in deconvolved images (Fig 8C). The global SRR average values were 51%. The total radiation dose for a study is approximately 0.21 Gy.

Discussion and Conclusions

These results demonstrate how micro-CT can be used not only for morphological but also functional imaging that requires 4D data. While our dual source micro-CT system is in many ways unique, the sampling methods and image reconstruction that we describe here can be used with commercial systems based on slip ring technology⁸. Our approach on limiting the streaking artifacts problem is based on deconvolution combined with replacement in the Fourier domain from a high quality but temporally averaged prior image obtained based on all projection data. The use of such a prior in dynamic CT has been also proposed in the PICCS algorithm and applied to perfusion micro-CT^{1, 15} via the total variation and an iterative reconstruction algorithm. In our case, the prior image solves the problem with the division in the Fourier domain. Moreover, there is a transfer of image quality from prior to reconstructions of the individual time points. Note not only the reduction of streaking artifacts but also the improvements in CNR values in the deconvolved images (see Figs. 7,8, and Table 1). The CNR values are higher than 5 therefore satisfying the Rose criterion for human visualization³⁰. In practice, approximately 1200 projections acquired over 3 rotations are able to provide the necessary projection data for cardiac reconstructions. The simulations indicated that we can recover the correct size of the moving heart structures (see Figs. 4,7) and consequently we believe that the prior does not introduce a bias in the reconstruction. The sampling time for such a study can be on the order 2 to 3 minutes. The associated radiation dose (between 0.17 to 0.22 Gy depending on the number of rotations) is in the range of a typical micro-CT exam. With such scanning time and radiation doses, high throughput longitudinal cardiac studies are very convenient. Further work is required to assess the minimum number of projections required by the deconvolution algorithm to guarantee adequate image quality. This image quality should not compromise the analysis of cardiac function, which involves segmentation of the chambers of the heart. We have previously investigated this issue³¹.

Using our novel sampling and reconstruction approach we have achieved an increase in temporal resolution for perfusion micro-CT on the order of 16 times compared to a dynamic micro-CT study based on multiple short scans i.e. ($180^\circ + \text{fan angle}$). This improvement is due to our dual source micro-CT system (a factor of 2 improvement), our novel sampling strategy using 4 injections with synchronized rotations (a factor of 4 improvement) and also due to our deconvolution approach used in reconstruction (a factor of 2 improvement). The novel 4D micro-CT perfusion protocol is based on tail vein catheter injections and therefore unlike our previous approach¹⁰ it facilitates longitudinal studies. Moreover, in our new perfusion protocol we have considerably reduced the number of injections from 32 to only 4 with the penalty of reducing the temporal resolution from 150 ms to 687 ms.

These novel 4D micro-CT acquisition and reconstruction strategies show promise for low dose, high throughput and longitudinal studies with immediate applications in a wide range of preclinical studies such as in cardiopulmonary safety or cancer research.

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Fig. 1.

Fast sampling is achieved via retrospective gating. The sampling sequence involves recording of the respiration, ECG signals, as well as the sampling time and projection angles. Vertical lines display the sampling events. Data is acquired with a combined sampling rate of 20 projections/secs (due to the two imaging chains) during a continuous rotation.

Figure 2.
A diagram of the deconvolution algorithm.

Figure 3.

The PSF of 2D projection and FBP for a small (A,D,G), medium (B,E,F) and a large (C,F,I) fan angle. Two delta functions were constructed, the first at the center (A–C), and the second at the periphery (D–F). Only five irregularly distributed projections were used. A larger fan angle produces a larger space variance (compare (I) with (H) and

Figure 4.

Reconstructed images of the S&L phantom with small, medium and large fan angle. Images reconstructed with FBP are shown in the top row (A–C), together with the prior image in which the moving structure is blurred (D, see arrow). Images reconstructed with deconvolution without a prior are shown in the middle row (E–G), and with a prior in the bottom row (H–J). In the cases without the prior, the values in the MTF below the threshold were set to zero.

Figure 5.

Simulated cardiac scan of the modified 3D S&L phantom with irregular angular distribution of projections (C). Two phases are shown, corresponding to the maximum (left column) and minimum (right column) size of the contracting ellipsoid (arrow) simulating the heart in diastole and systole (A, B). The FBP reconstruction with all projection data appears blurred (F). The two cardiac phases are recovered in FBP reconstructions but contain streak artifacts and the noise (D, E). These flaws are substantially reduced by the deconvolution technique (I, J). We present absolute differences between the original images and FBP (G, H), and the original images and deconvolution (K, L). To assess the temporal resolution we use MTF plots derived from radial profiles through a slice of the contracting ellipsoid (M). The reconstructed images are windowed to $[-.1 \ 1.1]$ and the absolute difference images to $[0 \ 0.4]$.

Figure 6.

Simulated perfusion scan of the modified 3D S&L phantom. One ellipsoid (arrow) changes in attenuation value according to a gamma variate function. There are only 64 projections used for each reconstructed time point. The distribution of projections shows gaps due to undersampling (C). The reconstruction with all projection data has good image quality but averages the ellipsoid over time (F). A total of 32 time points were reconstructed, and two of the time points (4 and 20) are shown here. FBP images suffer from streaking artifacts (D, E), but these are reduced by deconvolution (I, J). The absolute difference images demonstrate the ability of preserving the correct attenuation level of the changing ellipsoid. The reconstructed images are windowed to $[-.1 \ 1.1]$ and the absolute difference images to $[0 \ 0.4]$.

Figure 7.

Examples of cardiac micro-CT images in diastole (A, B) and systole (C, D) using FBP (left column) and deconvolution (right column). Both axial (A, C) and coronal (B, D) slices are shown. The images were reconstructed with data acquired over three rotations. Of the 1350 projections acquired, there were 116 projections available for diastole and 92 for systole. The same windowing has been applied to these images $[-500, 1000]$ HU.

Figure 8.

The same axial slice displaying the heart in diastole (A, B) and systole (C, D) is reconstructed with FBP (A, C) and deconvolution (B, D) using projection data acquired from 2, 3, 4 and 5 rotations. Deconvolution preserves image quality even when the number of projections is drastically reduced. The number of projections and figures of merit for these reconstructions are shown in table 1. The same windowing has been applied to these images $e [-500, 1000]$ HU.

Table 1

A comparison of figures of merit for cardiac micro-CT reconstructions computed for diastole and systole with FBP and deconvolution (see Fig. 7) based on data acquired with 2, 3, 4 and 5 rotations. These measures quantify the reduction in streaking artifacts (SRR) and the reduction in noise (CNR) provided by deconvolution.

Number of Rotations	2	3	4	5
Total Number of Projections	900	1350	1800	2250
Radiation Dose [Gy]	0.11	0.168	0.22	0.28
<i>Diastole</i>				
Number of Projections	78	116	147	198
CNR FBP	1.62	2.21	2.41	2.88
CNR Deconvolution	4.40	5.27	5.76	5.96
SRR [%]	72.12	63.36	62.51	52.01
<i>Systole</i>				
Number of Projections	62	92	132	172
CNR FBP	1.96	1.99	2.46	2.62
CNR Deconvolution	5.04	5.26	5.84	6.04
SRR [%]	71.92	69.20	58.15	51.60