Heart and Respiratory Gating of Cardiac microPET®/CT Studies in Mice

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Abstract-- Despite recent developments in high resolution small animal PET, cardiac studies in mice are still of limited quality due to the small size of the imaged organ and motion within the cardiac and respiratory cycle. By gating for one or both motions an improvement of the quantitative PET-data and images can be expected.

We used a data acquisition and analysis system with multiple analog channel recording capability, consisting of a general purpose transducer amplifier for respiration and an ECG amplifier. A small plastic pressure pad connected to a pressure transducer served as respiratory sensor. To avoid artifacts in CT and attenuation corrected PET we used carbon electrodes and lead wires for ECG. Two digital trigger units received analog signals from both amplifiers and generated negative trigger impulses. The signal was fed into our microPET® and integrated into the listmode mode file. For reconstruction microPET® Manager (Concorde Microsystems) was used. The nongated CT was used for attenuation correction and anatomical orientation.

With the system described we were able to generate reliable trigger pulses for both cardiac and respiratory motions. By eliminating inspiratory motion and reducing the influence of systolic spillover better quantitative blood pool values were achieved. A significant visual improvement in image quality was observed in diastole. The reconstruction process was computationally intensive due to the large number of sinograms generated in the histogramming process.

I. INTRODUCTION

Considerable progress has been made in the field of high resolution small animal PET [1]-[3], but cardiac studies in mice are still of limited quality due to the small size of the heart. Cardiac and respiratory motions also play a significant role [5]. By synchronizing the PET data collection to one or both motions, an improvement in image quality can be expected. In addition, cardiac gating can also yield valuable information on abnormal wall motion and ejection fraction in murine models of cardiac disease [6].

II. METHODS

A. Data acquisition & analysis

Data acquisition and analysis was performed using a MP150 system from Biopac Systems Inc. (Santa Barbara, CA, USA), which allows recording of multiple analog data channels. The configuration of our MP150 system consisted of a differential amplifier module (DA100C, Biopac Systems Inc.) for respiration sensing and an electrocardiogram (ECG) amplifier (ECG100C, Biopac Systems Inc.) for monitoring the ECG signal.

B. Respiratory Sensing

A small, foam rubber filled, plastic pressure pad (Part number 0108-0007 infant respiration sensor, Graseby Medical Limited, Watford, UK) was placed under the upper abdomen of a prone mouse. The pad was connected to a disposable pressure transducer with a sensitivity of 50μV/mmHg when excited by 10 volts. The transducer was then attached to the differential amplifier module.

C. Cardiac Sensing

Self adhesive carbon neonatal monitoring electrodes with pre-attached carbon lead wires (part number 2269T, 3M Health Care, St. Paul, MN, USA) were used to sense the ECG signal. In order to establish contact of the electrodes to the skin, the fur was shaved at both shoulders and on the lower left back. Two electrode configurations were used depending on which one provided the highest amplitude signal: One configuration was to use both shoulder electrodes as signal positive and negative and the lower left back as ground. Another lead arrangement connected the two signal inputs to the right shoulder and left lower back with the ground not used. The leads were attached to the electrocardiogram amplifier module.

D. Hardware Triggering

Trigger pulses were generated by two digital trigger units (DTU100, Biopac Systems Inc.), which received input analog signals from the ECG amplifier and the transducer amplifier. A negative trigger pulse was generated when the analog input signal crossed a preset voltage threshold. The two trigger units were

connected to the two gate input channels of the small animal PET (microPET® FOCUS 220, CTI Concorde Microsystems LLC, Knoxville TN, USA).

E. Signal display and trigger control

The MP150 system was connected to an Apple ibook computer (Apple Computer Inc.). For display purposes we used the software package AcqKnowledge 3.7.3 for MAC (Biopac Systems Inc.). By feeding the trigger signals back into two input channels of the acquisition unit, we were able to monitor the gating signals on the same display as the two analog data channels.

F. Trigger handling and image reconstruction

The ^{18}F-deoxyglucose (FDG) studies were recorded in listmode together with one or two gate signals. For histogramming as well as for reconstruction the program microPET® Manager 2.1.5.0 version 3/22/04 (CTI Concorde Microsystems LLC, Knoxville TN, USA) was used. The listmode data are histogrammed into multiple sinograms by using dynamic framing, only gating (with one or two gates and up to 32 bins per cycle) or both dynamic and gated. The user also has the option between a moving average of the gates and a user defined range of gates that allows elimination of false trigger impulses. Small animal CT (microCAT™, ImTek Inc. Knoxville, TN, USA) imaging was performed after the PET studies for anatomic orientation and CT-based attenuation correction [7]. All CT studies were non-gated. For image display and analysis we used ASIPro® VM (CTI Concorde Microsystems LLC, Knoxville TN, USA) and AMIDE (by Andy Loening, Stanford, CA, USA).

III. RESULT

A. Sensor sensitivity and triggering

By setting the threshold of the hardware trigger to the inspiratory pressure peak, stable trigger impulses for respiration could be generated (Fig. 1). The derived ECG across the chest yielded a high amplitude QRS complex (Fig. 1). In some mice the ECG signal from right shoulder to lower left back was more suitable for triggering. Respiratory artifacts in the ECG usually could be eliminated by changing the electrode placement.
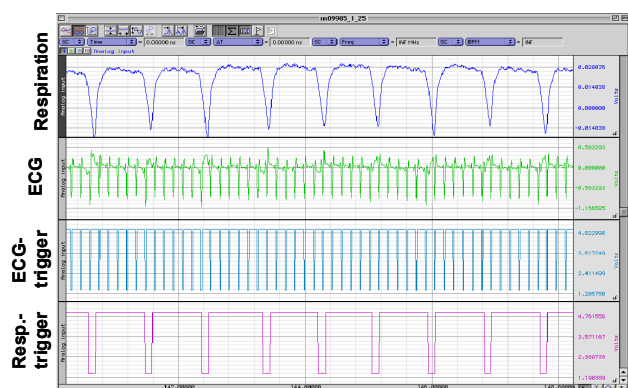

Fig. 1. Signal display in AcqKnowledge 3.7.3. From top to bottom: respiration, ECG, ECG-trigger signal, respiration trigger signal. The horizontal axis is time (2s/interval) and the vertical axes are in volts.

B. Data handling

The software generated for each dynamic frame a number of sinograms which corresponded to the number of bins per cycle, i.e. 12 sinograms for a study with one dynamic frame and 12 bins per cardiac cycle. When using dual gating, several sinograms (number of bins on gate two) are generated. The total number of sinograms equals the number of dynamic frames times the bins/cycle on gate one times the bins/cycle on gate two. Because it is not possible to exclude certain frames or bins from histogramming, large amounts of data arise, especially for dual gating. This limited us to mostly reconstruct data either cardiac or respiratory gated.

C. Images

1) Respiratory gating

Fig. 2 shows the respiratory gated images and the nongated image of a mouse heart in a transverse view with a line profile drawn at the same location. In keeping with the respiratory signal there is a small but significant displacement of the heart seen in the gated images. Due to that displacement, spillover of activity from myocardium to the blood pool of the left ventricle is greater in the nongated images. In contrast, the profile in the expiration image displays less spillover.
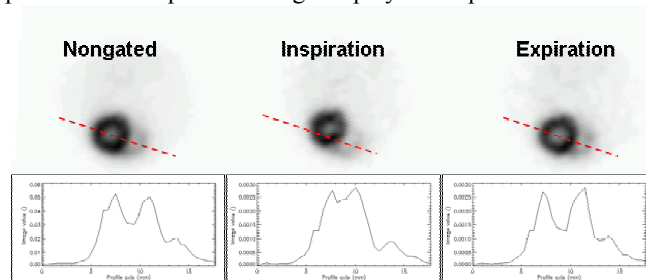

Fig. 2. Comparison of a transverse nongated image and profile with those of respiratory gated images of a mouse heart (respiratory gated with 12 bins/cycle). OSEM reconstruction without attenuation correction, 90-100 min. p.i. 64 MBq FDG.

2) Cardiac gating

Fig. 3 shows the cardiac gated and nongated images of the same mouse. Reconstruction was OSEM (6 iterations) with attenuation correction, 12 bins/**cardiac** cycle. The cavity of the left ventricle can not be differentiated in systole due to a clearly smaller diameter and thickened myocardium. The profile accordingly only shows a slight drop in count rate in the left ventricular blood pool. In contrast, in diastole the walls of the ventricle are further apart, resulting in a smaller effect of myocardial spillover on the left ventricular blood pool counts. This increased left ventricular size also accounts for the better image quality.
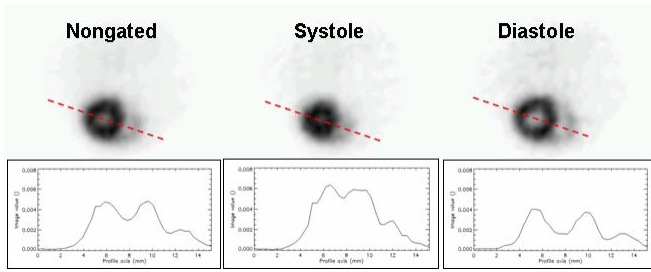
Fig. 3. Comparison of nongated image and profile with those of cardiac gated images of a mouse heart (12 bins/cycle). OSEM reconstruction with attenuation correction, 75-90 min. p.i. 64 MBq FDG.

3) Dual gating.

Fig. 4 shows the cardiac gated, respiratory and dual gated images of the same mouse. Reconstruction was performed using filtered back projection with attenuation correction, 8 bins/cycle. It was noted that cardiac gating clearly improves the image quality and activity profile more than respiratory. The dual gated image has more noise; the profile is very similar to that of the cardiac gated.
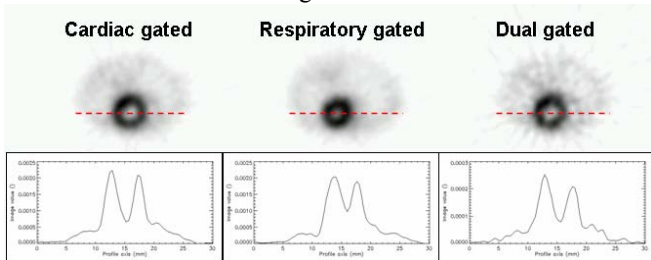

Fig. 4. Comparison of cardiac, respiratory and dual gated images and profiles of a mouse heart (8 bins/cycle). The cardiac gated image shows the heart in diastole, the respiratory gated the heart in expiration. For the dual gated image diastole as well as expiration was selected. FBP reconstruction with attenuation correction, 60-90 min. p.i. 32 MBq FDG.

D. Computer tomography

Fig. 5 is a volume rendered 3D CT image of a mouse with sensors (gray scaled in a bone window). The low attenuation material did not cause any artifacts in the PET-images when CT-based attenuation correction was used.
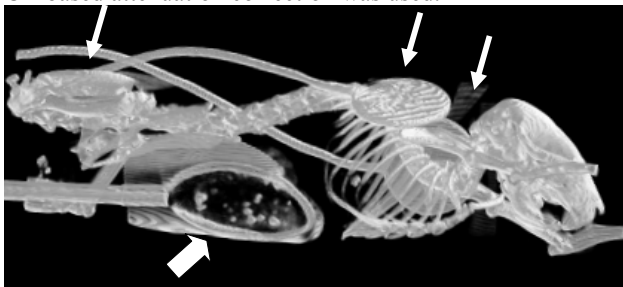

Fig. 5. 3D CT image of a mouse with gating sensors. The respiratory sensor pad was placed under the upper abdomen (thick arrow). Three carbon electrodes (thin arrows) are attached to the skin over both shoulders and on the lower left back.

IV. CONCLUSIONS

We demonstrate the feasibility of respiratory and cardiac gating of cardiac PET/CT studies in mice. Elimination of cardiac and respiratory motion produced cardiac images of greater anatomic detail and resulted in a diminished effect of spillover from the myocardium to the left ventricular blood pool. This will be useful to evaluate cardiac function and radiotracer kinetics. An evaluation of regional myocardial wall motion and the determination of ejection fraction appear to be possible with cardiac gated images. Currently the enormous amount of data poses a problem for data archiving and computation. Software allowing the elimination of certain frames or bins in the histogramming process should solve this problem.

V. ACKNOWLEDGMENT

VI. REFERENCES

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