EDITORIAL

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Editorial: Derivation of respiratory gating signals from ECG signals

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With improvements in the spatial resolution of PET, motion blur is becoming an increasingly dominant limiting factor of image spatial resolution, and is therefore receiving increasing attention. The use of cardiac gating is common practice in cardiac imaging as it enables quantification of ventricular blood volumes and ejection fractions, and is useful for visualization of small cardiac structures by capturing the heart mid-stroke. In PET applications involving the lungs, diaphragm, and superior splenic organs, respiratory gating has become common practice to reduce motion blur associated with respiratory motion.[1] Therefore, the technical ability to acquire dual gating signals in conjunction with the PET data has become almost ubiquitous, even if seldom used.

Rejection of respiratory motion artifacts in cardiac PET can improve image spatial resolution, enabling visualization of smaller structures (e.g., the thin walls of the atria, focal plaque lesions), especially when applied in conjunction with cardiac gating. Further benefit may be derived in detection of incidental finding such as lung and liver lesions. Perhaps most importantly for the nuclear cardiology audience, however, motion-related heterogeneity is reduced in tracer uptake (e.g., perfusion and viability) imaging. Images of myocardial walls with uniform tracer concentrations that run orthogonal to the direction of motion can underestimate tracer uptake intensity, while walls that run parallel to the motion do not suffer of this partial volume effect to the same extent; thus creating a typical pattern of symmetric uptake deficit. This effect is demonstrated in Figure 1 for a simplified LV mimicking ring phantom (left), with blur and without motion (center), and with added horizontal sinusoidal motion with peak-to-peak amplitude equal to the wall thickness (right).

While cardiac gating signals are almost exclusively derived from electrocardiograms, various devices have been utilized to derive respiratory gating signals including optical tracking of surface markers, expansion bands, induction coils, impedance measurements, and pressure sensors.[8] Potential down sides to the introduction of additional devices into the imaging suite is increased operational workload and costs associated with acquiring and maintaining the equipment.[2] Thus, systems that are able to perform multiple functions may be advantageous. List-mode-derived gating has also been proposed,[2] but requires vendor-specific implementation and has not been widely utilized to date.

In this issue of JNC, Todica et al evaluate the use of ECG-derived respiratory triggers on small animal cardiac PET scans. The triggers were retrospectively embedded into the list-mode data, enabling dual-gated image reconstruction using the vendor provided reconstruction software. For validation purposes, reference respiratory triggers were also derived using a pressure transducer-based sensor positioned beneath rats or pressure sensing belt in healthy human volunteers.

In their work, respiratory gating was utilized to reject two-thirds of the event data acquired at respiratory phases associated with respiratory motion. Therefore, the reconstructed images consisted of only the end-exhalation phase, having less respiratory motion artifacts, but also lower count statistics. The remaining, accepted data were processed to reconstruct ECG-gated image sequences that were analyzed to quantify left ventricular volumes and ejection fraction. These parameters were also generated using conventional pressure transducer respiratory gating which did not defer from the ECG-derived respiratory gating data. Therefore, the authors concluded that ECG-derived respiratory gating was a feasible alternative to dedicated hardware-based gating.
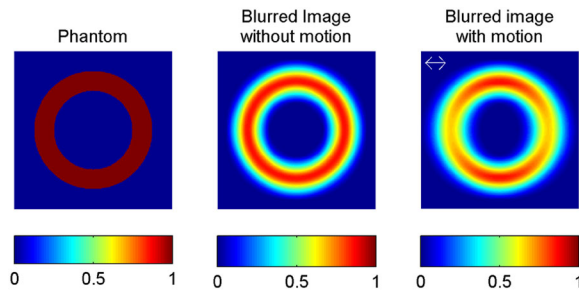
Figure 1. Simulation of a phantom image (*left*) and with an image acquisition, reconstruction, and cardiac motion mimicking blur, both without (*center*) and with (*right*) the presence of sinusoidal horizontal motion. A symmetric partial volume loss due to motion is demonstrated. The magnitude of motion is equal to the wall thickness as illustrated by the *white arrow*.

Preliminary human data were also included, indicating ability to translate the technology to clinical and human research applications. While these conclusions have exciting implications, some critical analysis is warranted.

The phenomenon of respiratory sinus arrhythmia (RSA), or fluctuation of heart rate with respiration, was described as far back as 1847.[3] RSA has been exploited for a wide range of applications including patient ambulatory monitoring, intensive care monitoring, biomedical and psychophysiological research, and deception detection. RSA has even been demonstrated to persist, albeit at reduced amplitudes, in heart transplant patients,[4] supporting the notion that heart rate modulation is not entirely dependent on vagal tone. As early as the 1980's RSA-derived respiratory triggering has been demonstrated,[5] and has since been applied in medical imaging applications.[6,7]

Several potential limitations exist with RSA-derived respiratory triggers from ECG signals. Primarily, the magnitude of RSA has been shown to have negative correlation with age, obesity, diabetes, hypertension, cardiovascular disease, and smoking.[8] Thus RSA may be less reliable for derivation of respiratory triggers in cardiac and lung oncology target populations. Psychological states that are associated with cardiac disease and aging such as depression have likewise been associated with reduced RSA,[8] while mental stress (e.g., anxiety) can also attenuate RSA.[9] While RSA has been demonstrated to be robust during exercise in healthy volunteers,[10] the effect of pharmacologic stressors commonly used in myocardial perfusion imaging is unclear. Whether in a clinical setting or in disease/ therapy models, drugs and other interventions may adversely impact RSA response. In cases where RSA response is attenuated, dedicated markers of respiration may prove to be more robust trigger sources.

As with other external markers of respiratory motion, RSA-derived phases may also have limited correlation with actual organ motion.[11] No information exists in the trigger signal to indicate the magnitude of each individual respiration or the duration of inhalation or expiration, and it is assumed that the respiration pattern is quite repeatable from one breath to the next. Todica et al, noted previous work which demonstrated that in healthy mice virtually no motion is present in 75% respiratory cycle. Thus, they divided the respiratory cycle into large fractions (thirds) to accept a large portion of the motion free data while increasing robustness against fluctuations in inhalation and expiration durations. In subjects with shorter end-exhalation periods, shorter acceptance intervals (more gates) may be preferable to ensure respiratory motion-free images, at the expense of further reducing count statistics.

As with other respiratory triggering technologies, a robust implementation must filter out erratic breathing cycles including coughing and gasping and deviations from tidal volume. In this case ad-hoc classifiers were applied to reject abnormal respiratory cycles as detailed in the appendix. The results reported in this work relate to healthy female rats and healthy human volunteers. It is reasonable to assume that these classifiers would need to be optimized for other species, disease models and patient populations to ensure accurate rejection anomalous respiratory data.

While this work dealt with producing respiratory triggering signals, it is important to keep in mind that dedicated respiratory triggering systems may produce additional information. Analog devices that track respiratory motion may be used as surrogates for organ or lesion localization in a continuous fashion, and therefore offer the potential to drive motion correction, as opposed to motion rejection, with the benefit of maintaining high count statistics. Furthermore, these devices may be used to monitor the subject's respiratory function during the imaging experiment which is especially important in the context of anesthetized animals, and more so in those which had undergone invasive interventions. Absence of adequate real-time respiratory information may lead to elevated fatality rates along with associated costs and ethical considerations. While Figures 1 to 4 in the appendix illustrate derived respiratory curves, it remains unclear if RSA provides sufficient information to fill the need for monitoring respiratory function.

A final point for contemplation is that for ECG-derived respiratory triggering to become widespread, system integration is essential. In the work of Todica et al, ECG data were processed off-line to embed the triggers into the list-mode data prior to image reconstruction, recognizing that accurate temporal synchronization between the ECG and the PET scanner is essential.[12] Their implementation is vendor specific due to the unique list-mode file format; utilization of a

universal respiratory triggers interface (i.e., TTL port) may be advantageous for vendor-independent real-time insertion of respiratory triggers into the list-mode file.

While several technologies are currently available for respiratory gating in medical imaging, RSA is not commonly utilized and may offer unique advantages. Most important of these is the ability to use existing ECG equipment with recording capabilities as either a primary or backup respiratory trigger source without the need for additional instrumentation. Having an additional tool in our imaging arsenal enables discovery of new applications.

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