Title
Left Ventricular Pressure Gating in Ovine Cardiac Studies: A Software-Based Method

Journal
Journal of Biomechanical Engineering, 135(3)

ISSN
0148-0731

Authors
Acevedo-Bolton, Gabriel
Suzuki, Takamaro
Malhotra, Deepak
et al.

Publication Date
2013-03-01

DOI
10.1115/1.4023370

Peer reviewed

Left Ventricular Pressure Gating in Ovine Cardiac Studies: A Software-Based Method

Gabriel Acevedo-Bolton
Department of Radiology,
University of California,
San Francisco, CA 94143

Takamaro Suzuki

Deepak Malhotra

Zhihong Zhang

Department of Surgery,
Department of Veterans Affairs Medical Center,
San Francisco, CA 94121

Arthur W. Wallace
Department of Anesthesia,
University of California,
San Francisco, CA 94143;
Department of Veterans Affairs Medical Center,
San Francisco, CA 94121

Julius M. Guccione
Department of Surgery,
University of California,
San Francisco, CA 94143;
Department of Veterans Affairs Medical Center,
San Francisco, CA 94121

David A. Saloner
Departments of Radiology,
University of California,
San Francisco, CA 94143;
Department of Veterans Affairs Medical Center,
San Francisco, CA 94121

Mark B. Ratcliffe[1]
Department of Surgery,
University of California,
San Francisco, CA 94143;
Department of Veterans Affairs Medical Center,
San Francisco, CA 94121
e-mail: mark.ratcliffe@med.va.gov

Cardiac imaging using magnetic resonance requires a gating signal in order to compensate for motion. Human patients are routinely scanned using an electrocardiogram (ECG) as a gating signal during imaging. However, we found that in sheep the ECG is not a reliable method for gating. We developed a software based method that allowed us to use the left ventricular pressure (LVP) as a reliable gating signal. By taking the time derivative of the LVP (dP/dt), we were able to start imaging at both end-diastole for systolic phase images, and end-systole for diastolic phase images. We also used MR tissue tagging to calculate 3D strain information during diastole. Using the LVP in combination with our digital circuit provided a reliable and time efficient method for ovine cardiac imaging. Unlike the ECG signal the left ventricular pressure was a clean signal and allowed for accurate, nondelay based triggering during systole and diastole.
[DOI: 10.1115/1.4023370]

Keywords: left ventricular pressure gating, MRI, tissue tagging, strain

1 Introduction

Cardiac imaging using magnetic resonance (MR) requires several heart beats to reconstruct one cardiac cycle because of limitations in temporal resolution. One can imagine the cardiac cycle being divided into a number of bins, each bin representing a time-frame within the cycle. With each heartbeat, a few lines of k-space data are collected for each bin. This continues until all the k-space lines for each bin have been collected. To ensure that data collection occurs at the right timepoint and that the data is placed in the correct bin, a gating signal is required. The electrocardiogram (ECG) signal is routinely used in human studies for this purpose. Current MR compatible ECG technology utilizes a 3 or 4-lead R-wave detecting vectorial analysis technique [1] that is quite robust in humans.

However, in our experience, the ECG signal in sheep studies is not as reliable. In a series of experiments in sheep hearts using MR tissue tagging [2,3] to calculate strain, we found that the ECG was problematic once the animal was placed in the bore of the scanner. Problematic ECG signals may be related to a number of factors such as skin preparation, the magnetohydrodyanmic effect [4,5], orientation of the heart, position of the aorta relative to the heart and general anatomy.

Problematic ECG signals lead to image problems such as blurring because data from different time-frames can be incorrectly grouped. Long imaging times can also occur when the scanner has difficulty recognizing the peak of the R-wave and thus failing to trigger a scan. Algorithms that can correct for the magnetohydrodynamic effect and other noise sources have been created and are optimized for human anatomy. However, sheep anatomy is different enough that the nonstandard induced currents from the magnetohydrodynamic effect, and resultant ECG signals, tend not to be corrected for. Pulse pressure monitors are not a viable alternative because of limited signal stability and the ability to only trigger away from peak systole due to the delay in the pressure pulse reaching the sensor location.

Magnetic resonance tissue tagging has become a widespread method for measuring cardiac deformation *in vivo*. In humans, obtaining tissue tagging data is generally straightforward during systole. However, due to fading over time, following the tags is difficult during diastole. To overcome this difficulty, methods such as using a fixed temporal delay after R-wave detection have been proposed; however they can suffer from the variability in the heart rate during imaging [6]. Another method, CSPAMM [7] offers longer tag presence, but imaging time is increased. 3D-CSPAMM [8] offers longer lasting tags and an extremely rapid acquisition, but is not widely available for all MRI platforms.

In animal studies, where the internal cardiac pressure is being monitored, the left ventricular pressure (LVP) has previously been used as a gating signal. Pirolo and colleagues [6] constructed an analog circuit that used the LVP as a gating signal for cardiac MR studies in canines. The circuit computed the time derivative of the LVP (dP/dt) and sent a trigger signal to the scanner when a threshold was exceeded. By changing the sign of

[1]Corresponding author.

Contributed by the Bioengineering Division of ASME for publication in the Journal of Biomechanical Engineering. Manuscript received July 3, 2012; final manuscript received December 14, 2012; accepted manuscript posted January 10, 2013; published online February 11, 2013. Assoc. Editor: Ender A. Finol.

the dP/dt threshold, the circuit allowed myocardial tagging to trigger in either systole or diastole.

Inspired by the analog LVP gating circuit, we built a software-based triggering circuit to provide a versatile alternative to ECG-gating for our sheep studies. Advantages of this method over an analog circuit were simpler control over timing values, the ability to add or change features, and ease of implementation. We tested the hypothesis that using the LVP as a gating signal would improve image quality and reduce total imaging time as compared to ECG-based triggering in our sheep cardiac studies. In addition, by using MR-Tagging with negative dP/dt triggering, the 3D strain of the heart during diastole was calculated.

2 Method of Approach

Animals used in this study were treated in compliance with the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources, National Research Council, and published by the National Academy Press (revised 1996).

2.1 Software-Based Triggering Circuit. The analog LVP signal was digitized with a 14 bit multifunction board (USB-6009, National Instruments, Austin, TX). The time derivative of the LVP (dP/dt) was calculated in real time using a custom C# based program (Visual Studio 2005, Microsoft, Redmond, WA). When the dP/dt exceeded the user defined threshold, a 5 V signal (trigger pulse) was sent to the MR scanner.

The program utilized a customizable dP/dt-threshold level at which the trigger pulse was created, as well as a blank-out period during which incoming signals were ignored. The trigger pulse was sent to the external-trigger input on the scanner and used as the gating signal. For systolic triggering (beginning at end-diastole), the threshold was set at a positive value of dP/dt. In order to capture the diastolic phase (beginning at end-systole), the threshold for triggering was set at a negative value of dP/dt.

The software can be freely obtained by contacting the corresponding author.

2.2 Radio-Frequency-Noise. Electrical cables entering an MRI suite can act as antennas for all radio frequency (RF) signals present in the surrounding environment. If these signals enter the MRI suite, they appear as noise in the resultant images. To test for the introduction of RF noise, the cables connecting the pressure transducers to the signal amplifiers and the computer were run two different ways. In the first one, cables were run through waveguide ports in the wall to connect the computer and pressure transducer. In the second one the cable from the LV pressure transducer was connected to the amplifier within the scan room. The output from the amplifier was sent via a twisted-pair cable to a panel of low-pass RF filters in the MR room wall. On the other side of the filters, the cable was connected to the A/D converter (Fig. 1). The trigger pulse from the computer was also passed through the low-pass RF filters and back to the scanner. The low-pass filters are designed to attenuate signals with frequencies starting slightly below the range of the scanner, approximately 50 Mhz, and higher

2.3 MR Tissue Tagging. Scanning was performed on a Siemens Avanto 1.5 T MR scanner (Siemens Healthcare Erlangen, Germany). A prospectively gated breath-hold tagging sequence was used. Parameters used include TE = 3.92 ms, TR = 40.45 ms matrix = 256 × 102 pixels, FOV = 280 mm × 230 mm, 6 mm thick slices and a flip angle of 20 deg and nine segments. Two orthogonal sets of tagged images were acquired following the injection of a gadolinium contrast agent (Omniscan (Gadiomide), GE Healthcare, Princeton NJ) to better differentiate the lumen from the myocardium. The first set consisted of six slices along the long axis rotated 30 deg relative to each other, centered in the midpoint of the left ventricle. These slices included horizontal tags to measure deformation in the apex-base direction. These same slices were imaged a second time with the tags turned off to facilitate contour drawing in post-processing. The second set consisted of a series of short axis slices covering the left ventricle, acquired with a tagged grid to measure in-plane deformation in the slice. As part of our standard protocol, a nonferromagnetic transducer-tipped pressure catheter (model SPC-320; Millar Instruments, Houston, TX) was inserted into the LV to ensure that the LV pressure, a measure of animal health, was maintained at appropriate levels during the study. The details of the surgery and image post-processing have previously been described [9].

2.4 Strain Calculations. The techniques used for calculating 3D strain have been previously described [10], but in brief: The two orthogonal sets of MR tagged images were combined in a slightly modified version of FindTags (Laboratory of Cardiac Genetics, National Institutes of Health, Bethesda, MD) [11].

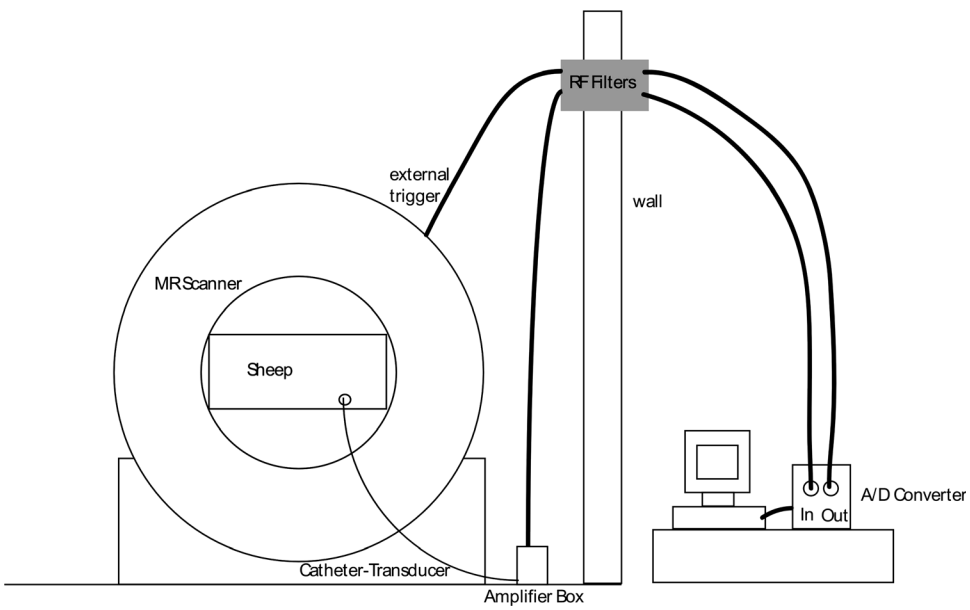

Fig. 1 Schematic of experimental setup. Note that cables pass through RF filters.

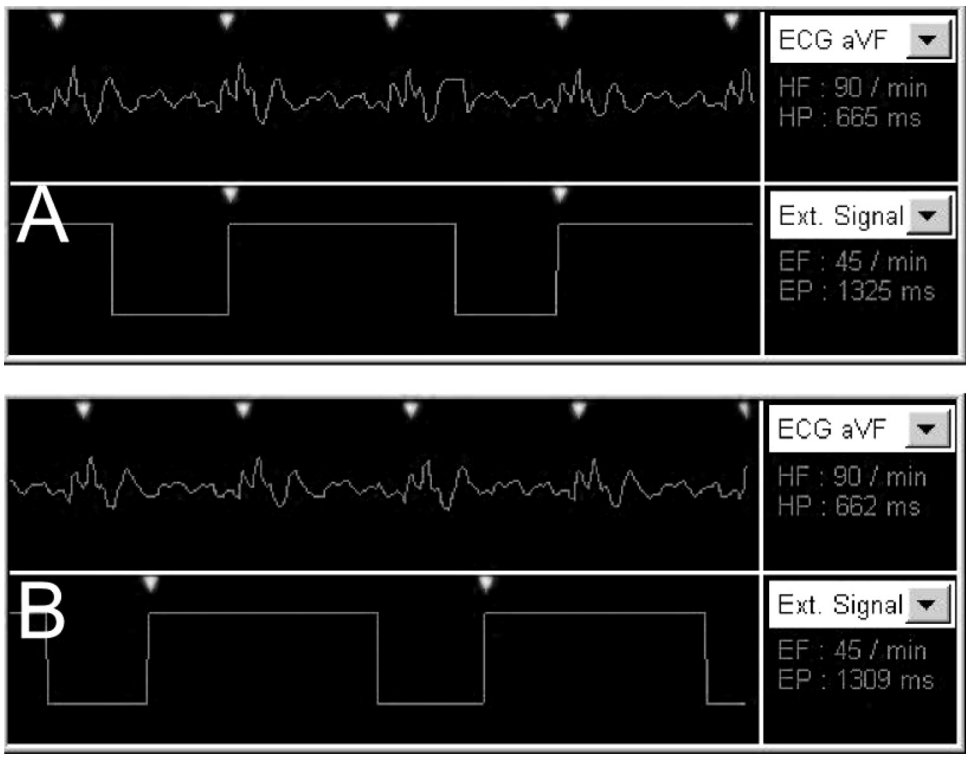

Fig. 2 Comparison of optimal ECG and trigger pulse from software-based timing circuit. Figure 2(*a*) shows the ECG trace on the top panel and systolic triggering from the dP/dt trigger in the bottom. Arrows, indicating where the scanner is detecting the trigger point, coincide at the R-wave as seen on the ECG. Figure 2(*b*) shows the ECG trace on the top panel and diastolic triggering from the dP/dt trigger in the bottom. In this case, the trigger point is offset from the R-wave peak shown on the ECG. These plots also show that the dP/dt signal triggers on every other heartbeat.

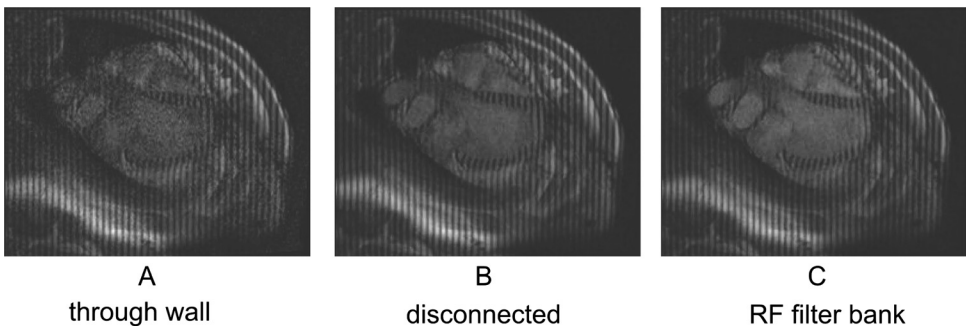

Fig. 3 The same image acquired with three different cabling methods. (*a*) Transducer cables passed through physical ports in wall, (*b*) Transducer cables disconnected from computer, and (*c*) Transducer signals passed through low-pass RF filters.

Epicardial and Endocardial contours as well as tag lines were initially drawn by hand and then automatically propagated through the rest of the time-frames. Errors in the propagation were manually corrected. The output of the FindTags software was passed into Tag Tissue Tracker (TTT) [12] which then computed the Lagrangian strain tensor components throughout the volume.

3 Results

Comparison with ECG results obtained with the animal outside the bore of the magnet showed a high degree of correlation between the R-wave and the digital signal during systole and a noticeable offset from the R-wave during diastolic triggering (Fig. 2).

Figure 3 shows the effect of cable routing on RF noise. The first image (Fig. 3(*a*)) where the cables were run through ports in the wall, has the highest amount of noise. Since the case using the RF filters (Fig. 3(*c*)) has much less visible noise, this suggests that the RF filters are effective in blocking the introduction of RF noise from the cables. All cardiac images from this and subsequent figures were acquired using our software method.

3.1 Systolic and Diastolic Triggering. Systolic and diastolic phase tagged images of the left ventricle were acquired by setting the threshold to positive and negative values of dP/dt, respectively. A sequence of images, obtained during diastole, from a short-axis slice approximately 30 mm from the apex is shown in Fig. 4.

The 3D strain tensor for the entire left ventricle was computed using diastolic phase images described above. The circumferential, longitudinal and radial strain for the mid-layer of the same slice as shown above are plotted in Fig. 5. The myocardium has been divided into 12 segments (Fig. 5(*a*)) and the strain for each

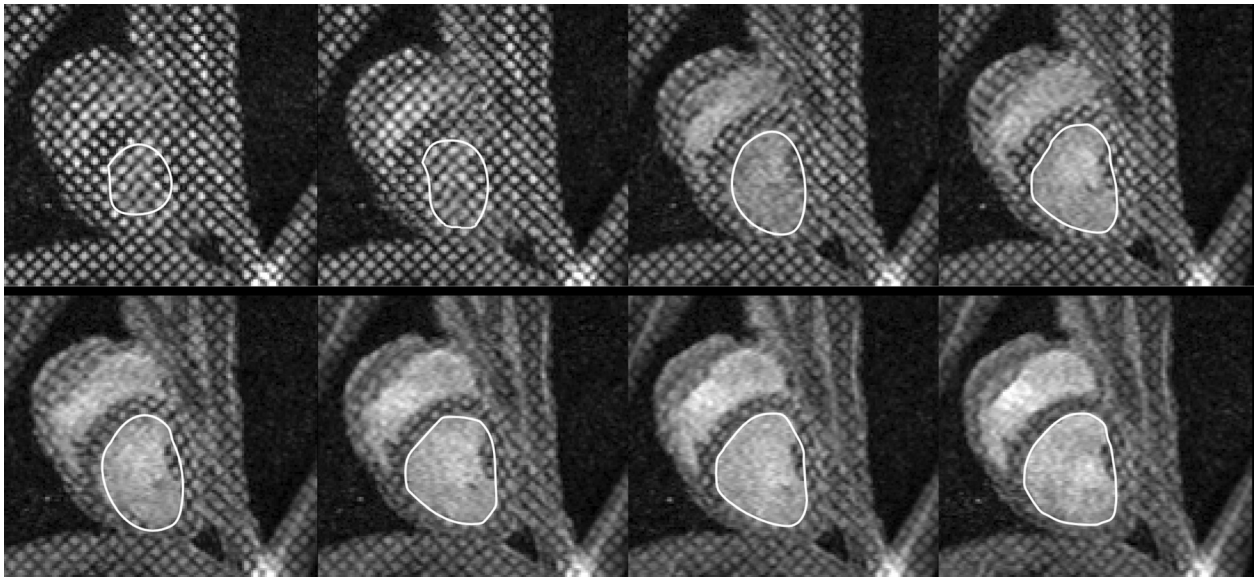

Fig. 4 Sequence of short axis slice which has been tagged, going through the first eight time frames of diastole (TR = 40 ms). The papillary muscles are seen inside the white contour.

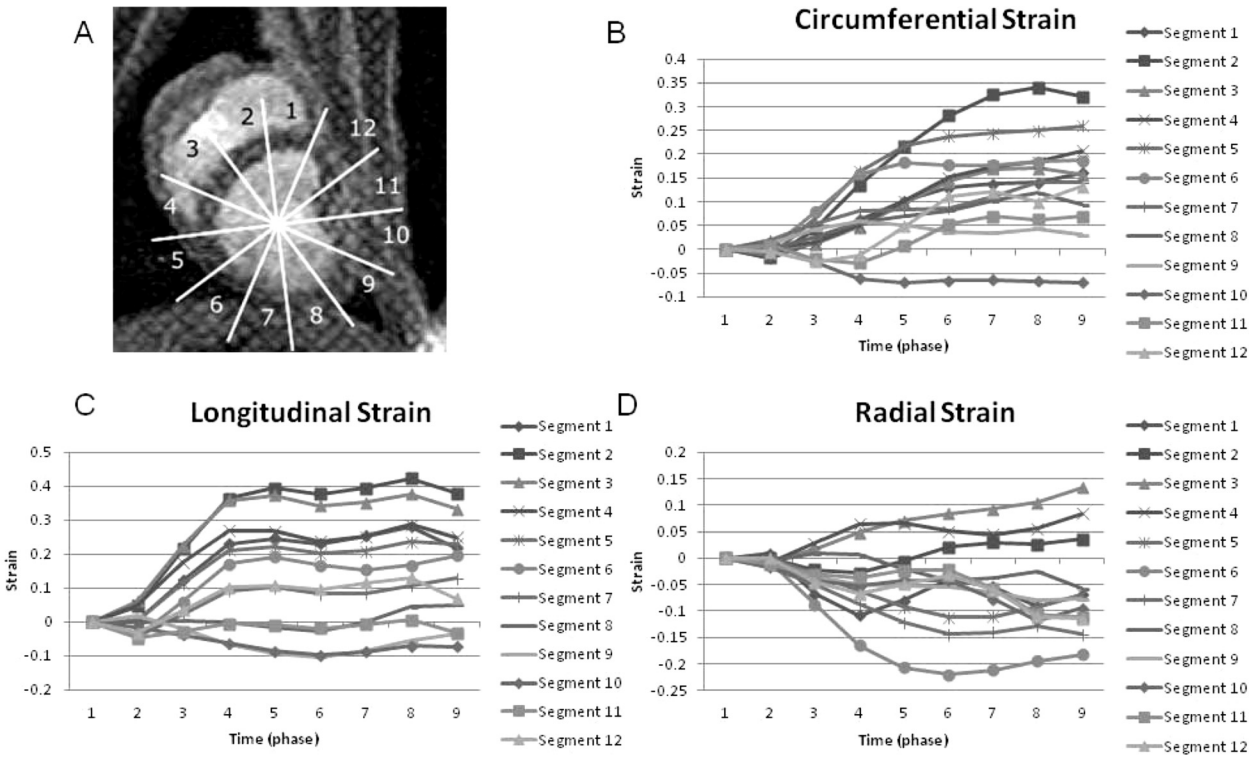

Fig. 5 (*a*) Map of segment locations in the Left Ventricle. (*b*), (*c*) and (*d*) show the circumferential, longitudinal and radial strain components, respectively.

of the segments over time (time point 1 = end-systole, time point 9 = end-diastole) is shown.

4 Conclusions

The use of the LVP in combination with a software-based signal processing and timing program provided a reliable gating signal for cardiac studies in sheep. The pressure signal provided a more reliable and consistent signal than that obtained using an ECG. By using the derivative of the pressure with respect to time (dP/dT) we were able to trigger in both systole and diastole without using a fixed timing delay.

The idea of using the LVP as a gating signal for MR based strain calculations is not a new one [13]. Here, we present a software based implementation of this idea. Our implementation is simple and rapid. Additionally, making changes to the program or adjusting parameters such as the triggering level is quite straightforward.

The use of our software-based LVP gating allowed us to acquire MR tagged images during the diastolic phase of the cardiac cycle. These MR tagged images in turn were used to calculate the 3D strain tensor during the diastolic phase. The strain analysis presented here holds the potential for further analysis using mathematical models, to estimate *in vivo* regional LV myocardial properties.

This would be a valuable way to quantitatively diagnose diastolic heart failure, as well as determine how a cardiac disease, e.g., myocardial infarction, affects myocardial properties. The longitudinal strain results show the variation of longitudinal strain over time and location, and highlight the importance of measuring longitudinal strain when trying to make 3D strain measurements.

Our method allows for the quantification of the regional differences in 3D strain with regard to position in the LV. However, since we only present the results from one sheep here, further studies will be required to draw any conclusions as to whether the strain distribution is uniform or homogenous as one moves around the LV circumference or between the base and apex.

4.1 Limitations of this Study. Due to the potential for misregistration between the two orthogonally tagged datasets, the MR-Tagging method used here is susceptible to errors.

The low-pass RF filters greatly reduced the amount of introduced noise, but did not affect spikes seen in the pressure waveform created by the magnetic gradients created during acquisition. Employing a user selectable blanking-out period in the software was necessary. The blanking-out period, the interval in which the software did not respond to any incoming signals, was set such that it covered the portion of the waveform which suffered from the gradient induced spikes. This required triggering on every other heart beat, but still proved to be faster than using a faulty ECG signal. When using the ECG as a trigger, scanning times varied greatly, a study could last between 1–3hs. Despite acquiring data on every other heart beat LVP triggering resulted in a consistent one-hour acquisition in the approximately 100 sheep studies completed since we started using this method. An improved method for dealing with the spikes in the pressure waveform would allow for even faster scan times.

The use of the LVP signal and a digital circuit produces an excellent gating signal for cardiac MR studies involving animals. The ability to trigger at different points in the cardiac cycle without the use of fixed delays and with an increased trigger reliability leads to more efficient and higher quality imaging. Although MR-Tagging was used in this work, the gating method presented here could be applied to any Cardiac MRI technique used on animals when the LV pressure is available.

Acknowledgment

This work was supported in part by the National Institutes of Health (GAB: NS058573, JMG:HL077921, HL086400, HL84431, and HL63348). The authors also wish to thank Jeffry O'Hara (Siemens) for his technical assistance and Monica Sigovan for constructive comments.

References

[1] Fischer, S. E., Wickline, S. A., and Lorenz, C. H., 1999, "Novel Real-Time R-Wave Detection Algorithm Based on the Vectorcardiogram for Accurate Gated Magnetic Resonance Acquisitions," Magn. Reson. Med., **42**, pp. 361–370.

[2] Zerhouni, E. A., Parish, D. M., Rogers, W. J., Yang, A., and Shapiro E. P., 1988, "Human Heart:Tagging With MR Imaging-A Method for Noninvasive Assessment of Myocardial Motion" Radiology, **169**, pp. 59–63. Available at: http://radiology.rsna.org/content/169/1/59.abstract

[3] Axel, L., and Dougherty, L., 1989, "MR Imaging of Motion With Spatial Modulation of Magnetization," Radiology, **171**, pp. 841–845. Available at: http://radiology.rsna.org/content/171/3/841.abstract

[4] Beischer, D. E., and Knepton, J. C., Jr., 1964, "Influence of Strong Magnetic Fields on the Electrocardiogram of Squirrel Monkeys (Saimiri Sciureus)," Aerosp. Med., **35**, pp. 939–944. Available at: http://www.ncbi.nlm.nih.gov/pubmed/14198655

[5] Togawa, T., Okai, O., and Oshima, M., 1967, "Observation of Blood Flow E.M.F. in Externally Applied Strong Magnetic Field by Surface Electrodes," Med. Biol. Eng., **5**, pp. 169–170.

[6] Pirolo, J. S., Branham, B. H., Creswell, L. L., Perman, W. H., Vannier, M. W., and Pasque, M. K., 1992, "Pressure-Gated Acquisition of Cardiac MR Images," Radiology, **183**, pp. 487–492. Available at: http://radiology.rsna.org/content/183/2/487.abstract

[7] Fischer, S. E., McKinnon, G. C., Maier, S. E., and Boesiger, P., 1993, "Improved Myocardial Tagging Contrast," Magn. Reson. Med., **30**(2), pp. 191–200.

[8] Rutz, A. K., Ryf, S., Plein, S., Boesinger, P., and Kozerke, S., 2008, "Accelerated Whole-Heart 3D CSPAMM for Myocardial Motion Quantification," Magn. Reson. Med., **59**, pp. 755–763.

[9] Zhang, P., Guccione, J. M., Nicholas, S. I., Walker, J. C., Crawford, P. C., Shamal, A., Acevedo-Bolton, G., Guttman, M. A., Ozturk, C., McVeigh, E. R., Saloner, D. S., Wallace, A. W., and Ratcliffe, M. B., 2007, "Endoventricular Patch Plasty for Dyskinetic Anteroapical Left Ventricular Aneurysm Increases Systolic Circumferential Shortening in Sheep," J. Thorac. Cardiovasc. Surg., **134**, pp. 1017–1024.

[10] Guccione, J. M., Walker, J. C., Beitler, J. R., Moonly, S. M., Zhang, P., Guttman, M. A., Ozturk, C., McVeigh, E. R., Wallace, A. W., Saloner, D. A., and Ratcliffe, M. B., 2006, "The Effect of Anteroapical Aneurysm Placation on End-Systolic Three-Dimensional Strain in the Sheep: A Magnetic Resonance Imaging Tagging Study," J. Thorac. Cardiovasc. Surg., **131**, pp. 579–586.

[11] Guttman, M. A., Zerhouni, E. A., and McVeigh, E. R., 1997, "Analysis and Visualization of Cardiac Function From MR Images," IEEE Comput. Graphics Appl., **17**, pp. 30–38.

[12] Ozturk, C., and McVeigh, E. R., 2000, "Four-Dimensional B-Spline Based Motion Analysis of Tagged MR Images: Introduction and *In Vivo* Validation," Phys. Med. Biol., **45**, pp. 1683–1702.

[13] Moulton, J. M., Creswell, L. L., Downing, S. W., Actis, R. L., Szabó, B. A., and Pasque, M. K., 1996, "Myocardial Material Property Determination in the *In Vivo* Heart Using Magnetic Resonance Imaging" Int. J. Card. Imaging, **12**, pp. 153–167.