Continuous Rapid Quantification of Stroke Volume Using Magnetohydrodynamic Voltages in 3T Magnetic Resonance Imaging

T. Stan Gregory, MS; John Oshinski, PhD; Ehud J. Schmidt, PhD; Raymond Y. Kwong, MD, MPH; William G. Stevenson, MD; Zion Tsz Ho Tse, PhD

Background—To develop a technique to noninvasively estimate stroke volume in real time during magnetic resonance imaging (MRI)-guided procedures, based on induced magnetohydrodynamic voltages (VMHD) that occur in ECG recordings during MRI exams, leaving the MRI scanner free to perform other imaging tasks. Because of the relationship between blood flow (BF) and VMHD, we hypothesized that a method to obtain stroke volume could be derived from extracted VMHD vectors in the vectorcardiogram (VCG) frame of reference (VMHD_{VCG}).

Methods and Results—To estimate a subject-specific BF–VMHD model, VMHD_{VCG} was acquired during a 20-s breath-hold and calibrated versus aortic BF measured using phase-contrast magnetic resonance in 10 subjects (n=10) and 1 subject diagnosed with premature ventricular contractions. Beat-to-beat validation of VMHD_{VCG}-derived BF was performed using real-time phase-contrast imaging in 7 healthy subjects (n=7) during 15-minute cardiac exercise stress tests and 30 minutes after stress relaxation in 3T MRIs. Subject-specific equations were derived to correlate VMHD_{VCG} with BF at rest and validated using real-time phase-contrast. An average error of 7.22% and 3.69% in stroke volume estimation, respectively, was found during peak stress and after complete relaxation. Measured beat-to-beat BF time history derived from real-time phase-contrast and VMHD was highly correlated using a Spearman rank correlation coefficient during stress tests (0.89) and after stress relaxation (0.86).

Conclusions—Accurate beat-to-beat stroke volume and BF were estimated using VMHD_{VCG} extracted from intra-MRI 12-lead ECGs, providing a means to enhance patient monitoring during MR imaging and MR-guided interventions. (Circ Cardiovasc Imaging, 2015;8:e003282. DOI: 10.1161/CIRCIMAGING.115.003282.)

Key Words: electrocardiogram ■ interventional magnetic resonance imaging ■ magnetic resonance imaging ■ stroke volume

Left ventricular stroke volume (SV) is a measure of the amount of blood ejected into the aortic arch during the systolic phase of the cardiac cycle. Real-time or beat-to-beat SV, measured over successive cardiac cycles, is used commonly to evaluate left ventricular mechanical function, which can detect the pathological response to stress and arrhythmias.1-5 In practice, SV quantification is often performed using invasive transesophageal echocardiography6-8 or invasive blood pressure catheters.9 Conventional cine phase-contrast magnetic resonance imaging (MRI; PCMR)10 typically provides only an averaged SV during the course of 10 to 20 successive cardiac cycles.11 A method to quantify beat-to-beat SV noninvasively within the MRI scanner, which would not increase the duration of invasive procedures, could serve to complement existing physiological monitoring information (SPO₂, ECG) during imaging or interventional procedures performed within an MRI scanner. This is particularly relevant for higher risk patients, such as those patients with a history of myocardial or cerebral ischemia, those who are intubated during imaging, or those undergoing cardiac stress testing within the MRI scanner.

See Clinical Perspective

The ECG signal is required for cardiac synchronization during cardiovascular MRI despite the presence of magnetohydrodynamic voltages (VMHD) that significantly alter the appearance of the ECG trace inside the bore (Figure 1A and 1B).12-14 VMHD becomes significant during systole when rapidly ejected blood from the left ventricle into the aortic arch interacts with the strong magnetic field (B₀) of the MRI.15-17 The uniformity of the magnetic field within the diameter spherical volume of the MRI allows for uniform and constant exposure of flow in the aortic arch to B₀, minimizing variations in induced VMHD because of off-center positioning and variances in the displacement of the heart from the isocenter of the MRI.18,19 Because of this relationship, we hypothesized that blood flow,
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MHD-Derived Flow and Stroke Volume

as a function of time in the cardiac cycle, and left ventricular SV could be derived using VMHD extracted from intra-MRI ECG (Figure 1C). This method would allow for noninvasive beat-to-beat SV estimation that can monitor patient condition during conventional cardiac MRI routines and potentially replace invasive monitoring during complex interventional procedures.

We hypothesized that development of VMHD-derived SV estimation method could allow for continuous beat-to-beat blood flow (BF) determination, requiring only a software plugin in MRI-conditional ECG recording systems for VMHD–SV model calibration. The presented method provides a noninvasive physiological measure of BF for free in standard cardiac MRI routines, leaving the scanner free to perform other imaging tasks. This study forms an extension of previous work on the correlation between MHD and SV.

Methods

Study Population
Ten healthy volunteers (n=10) and 1 patient diagnosed with premature ventricular contractions (PVCs; n=1) were studied with Institutional Review Board approval. A GE digital-IT 12-lead ECG recording system modified to be MRI conditional was installed at Brigham and Women’s Hospital and used to record 12-lead ECG traces in 3 healthy volunteer subjects in an Siemens Skyra 3T scanner. A similar 12-lead ECG recording system was installed at Emory University Hospital and was used to record 12-lead ECG traces in 7 healthy volunteer subjects in an Siemens Trio 3T scanner. Conventional cine PCMR and real-time PCMR (RTPC) with a repetition time of 44 ms and an acquisition window of 20 s were used to validate VMHD-based metrics for each test subject.

ECG Recording System
The ECG recording system modified to be MRI conditional has a nonmagnetic coaxial ECG cable fitted with 10 carbon lead clips and inline radiofrequency filters for radiofrequency suppression. An electronic switching circuit synchronized with the MRI-gradient cabinet was connected to the ECG front-end amplifier to block out MRI gradient-induced noise to ECG traces during MR imaging. The MRI-conditional ECG recording system only records physiological signals in the absence of gradient activity, removing the potential for variations in induced VMHD because of alterations in the MRI magnetic field.

VMHD-derived metrics were derived and validated in 4 parts (Figure 2): (1) derivation of cine PCMR equation of fit, (2) vectorial MHD processing, (3) patient-specific model calibration using PCMR, and (4) RTPC model validation under varying heart rates (HRs).

(1) Derivation of Cine PCMR Equation of Fit
Relationship of VMHD With Aortic FlowWe developed a patient-specific multiple parameter linear regression model that is able to obtain a subject-specific approximation of volumetric BF (mL/s) using the correlation with extracted VMHD in the vectorcardiogram (VCG) reference frame (VMHD\textsubscript{VCG}). VMHD\textsubscript{VCG} is to be contrasted with the conventional VCG (Figure 3A), which records the magnitude and direction of the heart’s electric activity (Figure 3B), as it illustrates the direction and magnitude of induced VMHD in the same frame of reference (Figure 3C). The current regression model was improved from previous methodology based on MHD signals extracted from a single ECG lead, whereas the derived BF was not in the standard unit and was lacking quantitative validation.

As VCG provides vectorial information, it provides a frame of reference for describing the heart’s electric activity during the development of this model. The BF gold standard, as a function of time, was obtained using a conventional cine PCMR scan in the aortic arch. VMHD\textsubscript{VCG}-derived volumetric BF, flow \((t)\), was then time integrated over the systolic phase to estimate SV (SV\textsubscript{VCG}; Equation 1), which was compared with SV derived from PCMR (SV\textsubscript{PC}).

\[
SV = \int_0^{t_{\text{sys}}} \text{flow}(t) \, dt \quad \text{(1)}
\]

A solution of the proposed model can be derived by first considering the spatial components of the extracted VMHD\textsubscript{VCG} at any given time (Equation 2) and their relationship to the volume of moving aortic blood in the static magnetic field (\(B_0\)) over the length of the aortic arch at this time.

\[
\text{VMHD}(t) = |\text{VMHD}(t)_x, \text{VMHD}(t)_y, \text{VMHD}(t)_z| \quad \text{(2)}
\]

The flow, as a function of induced MHD voltages, may be represented as a linear summation of experimentally derived linear regression coefficients (Equation 3).
After a patient-specific model calibration was established using conventional cine PCMR (detailed in Methods—Section 3), the success of the MHD-derived SV $\text{MHD}$ and BF ($\text{BF}_\text{MHD}$) was, thereafter, evaluated by comparison with results obtained from cine RTPC during a series of exercise stress testing (detailed in Methods—Section 4). Correlation between $\text{VMHD}$ and MRI-derived BF was calculated.

\begin{equation}
\text{BF}_{\text{MHD}}(t) = A_0 + A_1 \times \text{VMHD}(t)_X + A_2 \times \text{VMHD}(t)_Y + A_3 \times \text{VMHD}(t)_Z
\end{equation}

(3) Patient-Specific Model Calibration Using PCMR

Conventional cine PCMR was obtained to derive the subject-specific equations of fit in each healthy subject (men; age, 20–40 years; $n=10$) and a patient (man; age, 25 years) diagnosed with mild interpolated PVCs ($n=1$; Equation 3) using a transverse slice, perpendicular to the direction of flow in the ascending aorta, and to quantify the BF volume and SV using an Siemens Skyra 3T MRI with the following parameters: VENC, 150 cm/s; TR/TE/flip, 37.00 ms/4.00 ms/15°; field of view, 300 mm by 243 mm; and slice thickness, 3 mm. $\text{SV}_{\text{PC}}$ was calculated from measured BF by time integration of measured BF across the aortic lumen within the region of interest (Equation 1). Twelve-lead ECG recordings were performed during a 20-s breath-hold to reduce artifacts associated with bulk patient motion and alterations in breathing patterns. Normal breathing patterns produced a minimal effect on acquired ECGs, with baseline variations being removed using a 2-pole 0.05 Hz to 0.67 Hz linear digital high-pass filter with phase compensation to induce zero phase distortion as per American Heart Association standards. \(25\) Twelve-lead ECG and conventional cine PCMR baseline recordings were used to train the multiple parameter linear regression equation to obtain fit coefficients ($A_0, A_1, A_2, A_3$) at a resting HRs.

(4) RTPC Validation Under Varying HRs

Method accuracy was evaluated in 7 subjects during a series of 15-minute exercise stress tests designed to increase patient HR during...
RTPC cine scans recorded with the following parameters: VENC, 150 cm/s; TR/TE/flip, 44.08 ms/5.76 ms/30°; field of view, 268 mm by 330 mm; and slice thickness, 10 mm. Blood velocity was measured from cine images using Segment version 1.9, a medical image analysis package, and used to calculate the flow rate.

The accuracy of SVMHD and BF MHD was tested during changes in HR in 7 subjects during an exercise stress test using a resistance band and an MRI-compatible exercise bike (Figure 4), at peak stress, after 15 minutes of exercise, and during the HR's subsequent return to baseline (full relaxation 30 minutes after induced stress). The exercise elevates each subject's HR above baseline by ≈40%. Once the subjects reached peak stress, with an SpO2 sensor measuring the instantaneous HR, RTPC scans were performed for 30 frames, and 12-lead ECG recordings were subsequently recorded during a 20-s breath-hold. Once the subject’s HR returned to rest, ECG baseline data were acquired again.

A Bland–Altman analysis comparing VMHD- and MRI-derived SV (mL) and peak flow (mL/s) was performed using the subject data set (during baseline, elevated, and a return to baseline HR) to assess the clinical relevance of results obtained through exercise stress testing and quantify the bias of the measurements.

Results

Patient-Specific Model Calibration Using PCMR

Subject VMHD-derived BF and SV were compared with PCMR results (Figure 5A) to evaluate fit (Table 1), with correlation determined through a Spearman rank correlation coefficient, found to be >0.84. VMHD-based SV was estimated with a <5% error when compared with PCMR in all subjects. On the basis of the SE achieved in SVMHD when compared with SVPC, a sample size of 10 subjects has been used in this study to achieve a margin of error of 1 mL with 95% confidence interval and a statistical power of 0.95.

Figure 4. Depiction of a human subject undergoing an exercise stress test using an ergometer on the magnetic resonance imaging (MRI) scanner table. The relationship of the MRI coordinate plane with the position of the subject can be viewed.

Figure 5. Stroke volume (SV) estimation using magnetohydrodynamic voltages vectors in the vectorcardiogram frame of reference (VMH-DVCG) and phase-contrast magnetic resonance (PCMR)–based methodology in human subject 1. MRI indicates magnetic resonance imaging; and VCG, vectorcardiogram.
Conventional cine PCMR scans were obtained for each subject and used to extract BF as a function of time (Figure 5A). Using the previously described coefficients ($A_0$, $A_1$, $A_2$, and $A_3$; Equation 3), the patient-specific relationship between extracted VMHD and BF was estimated, and an appropriate fit was computed (Figure 5B). Using this methodology, real-time beat-to-beat BF and SVMHD, as well as the associated HR, were estimated (Figure 5C), providing continuous flow and SV monitoring.

VMHD-derived arrhythmic beats were detected in the PVC patient (Figure 6), and an 18.8% decrease in SV was observed during arrhythmic beats when compared with normal beats (Figure 6C). Induced VMHD can be seen superimposed on the PVC beat when compared with the PVC observed outside of the MRI bore (Figure 6A), increasing the difficulty in recognizing the arrhythmic beat (Figure 6B).

RTPC Model Validation Under Varying HRs

The robustness of the method to variations in subject anthropometry and electrode placement can be observed by comparing subjects 6 and 7 (Figure 7). Subjects 6 and 7 were chosen to validate the BF and SV estimation methods as they accurately represent approximately a 50th percentile male weight (weight, 68 kg; height, 168 cm; chest circumference, 94 cm) and approximately a 90th percentile male weight (weight, 127 kg; height, 185 cm; chest circumference, 135 cm) in the population. 28,29

A representative RTPC scan image is shown for each section of the exercise stress test (baseline, elevated, and return to baseline HRs). Correlation in the VMHD-derived flow waveform was shown to maintain a level of consistency with the RTPC gold standard during exercise stress testing and after the return to baseline (Table 2). The VMHD-derived method was able to estimate peak flow during each cardiac cycle with an average error of <4.59%. The mean predicted ejection period was shown to differ from the RTPC cine by an average of 31 ms, during peak stress, and 56 ms after the full relaxation, compared with the temporal resolution of the ECG traces (2 ms) and the RTPC (44 ms). VMHD-derived metrics were shown to accurately predict aortic BF and SV, with some inaccuracies that may be attributed to the low RTPC temporal resolution relative to the ECG traces. From the results in a Bland–Altman analysis (Figure 8), taken from subjects in each stage of exercise stress testing, it can be observed that the variability does not seems in a clear trend, and the error is not necessarily dependent on the average. The mean bias line calculated from SV estimation yields a value of 3.3 mL, with an average error of 6.71% calculated from the mean difference and the limits of agreement, a comparable error with those observed in conventional methods used in clinical practice. 11,30

Repeatability was assessed based on an ANOVA taken from

### Table 1. Multiple Linear Regression for Blood Flow and SV Estimation Using VMHD$_{VCG}$

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Correlation</th>
<th>SV$_{PC}$, mL</th>
<th>SV$_{VMHD}$, mL</th>
<th>Initial Fit</th>
<th>Error, %</th>
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</table>

*Weight measurements and comparison according to the Business and Institutional Furniture Manufacturers Association guidelines. 28,29

SV$_{PC}$ indicates stroke volume derived from phase-contrast magnetic resonance; VCG, vectorcardiogram; and VMHD, magnetohydrodynamic voltages.
SV difference measurements. A value of 6.95 mL was calculated, suggesting that repeat SV measurements should differ by no >6.95 mL, also a comparable error suggesting method repeatability.31,32

Discussion

Major findings of this study are the development and validation of a method for noninvasive beat-to-beat SV and BF estimation using MHD voltages extracted from 12-lead ECGs. This provides a means for enhanced patient monitoring inside the MRI bore, requiring only a relatively short cine PCMR calibration scan (≈20 s) to provide the required patient-specific parameters before continuous monitoring for the entire duration of a subject’s stay in the MRI bore.

An average error of 7.22% and 5.38% in VMHD_VCG-derived SV estimation, respectively, when compared with the
RTPC cine estimate was found during peak stress and after the full relaxation. In the future, PCMR prescans used to train an active Kalman filter for VMHD$\text{ECG}$-derived estimates could potentially result in a further increase in accuracy in BF$\text{MHD}$ and SV$\text{MHD}$ estimates. Average BF waveform correlation between the PCMR and MHD methods decreased after full relaxation from 0.89 to 0.86. VMHD$\text{ECG}$-derived estimates were shown to maintain an average error of <8% in all cases, with a marginal decrease in accuracy after full relaxation.

Beat-to-beat BF$\text{MHD}$ has a temporal resolution of 5 ms, based on the low-pass frequency used in the ECG monitor (200 Hz) from which MHD signals were extracted, when compared with the 40-ms temporal resolution of the RTPC sequence used for the BF measurements. Furthermore, the use of MRI for continuous monitoring of SV is impractical because of the need to use the scanner to image additional contrasts or other regions of the heart.

VMHD-derived SV was able to detect a change in SV during the arrhythmic beat of a patient diagnosed with PVCs. A decrease in SV of 18.8% was observed in the arrhythmic beat when compared with the healthy beat.

The presented flow and SV estimation methods provide real-time beat-to-beat monitoring, independent from scanner manufacturer of model, and do not require any additional MRI hardware development, providing a rapid method of assessing flow velocity and SV for free in a conventional cardiac MRI routine.

### Limitations

The method was only validated in a limited number of subjects. A larger patient population will be required to fully validate the method used to transform VMHD$\text{ECG}$ into BF, beyond the presented exercise stress study, as well as to further evaluate method reproducibility and repeatability. In addition, the ECG$_\text{real}$ signal was assumed to experience only minimal changes in amplitude and frequency during the training phase of the proposed method, allowing the approximation of ECG$_\text{real}$ within the MRI bore, based on previous knowledge of

<table>
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<th>No.</th>
<th>Flow Waveform Correlation</th>
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<th>Ejection Period Difference, ms</th>
<th>SV Error, %</th>
<th>BF Waveform Correlation</th>
<th>Peak Flow Error, %</th>
<th>Ejection Period Difference, ms</th>
<th>SV Error, %</th>
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<td>5.38</td>
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SV indicates stroke volume.

**Table 2. Assessment of Magnetohydrodynamic Voltages Vectors in the Vectorcardiogram Frame Of Reference—Derived Flow Metrics in Relationship With Magnetic Resonance Imaging**

**Figure 8.** Bland–Altman analysis for peak flow and stroke volume estimation. The vertical axis depicts the differences between magnetohydrodynamic voltage (VMHD)– and magnetic resonance imaging (MRI)–derived measurements, and the horizontal axis depicts the mean value for each subject. The 3 plotted lines depict upper and lower limits of agreement (red) and the average (blue).
ECG$_{real}$ obtained outside the MRI bore. This assumption may not always be valid.

The limited availability of MRI-conditional 12-lead ECG recording systems may affect the prevalence of the presented method outside of a research setting; however, the topic of acquiring ECGs during MRI scanning has been well studied in hardware-2 and software-based approaches.37-38 In cases of low repetition time or where MRI pulse sequence timing/readout may be a limitation, continuous time methods of gradient removal may be used, which rely on a short training phase and knowledge of the gradient waveform and timing used during the scan sequence.37,38 Further studies must be performed to investigate the feasibility of using this method in 4-lead ECG recording systems, available in the majority of MRI scanner suites and MRI-conditional ECG monitoring systems.

The presented pilot research shows promising results in the voluntary study of 10 healthy subjects and 1 patient diagnosed with PVCs. Further study with a large population of patients is required to evaluate the clinical effect of this work and to further optimize the current method to be accepted in a routine MRI workflow.

Conclusions

VMHD$_{VCG}$-derived SV and BF estimates allow for accurate, noninvasive, real-time cardiovascular monitoring during MRI-guided surgical procedures and interventions, leaving the scanner free to perform other imaging tasks. This method could be integrated into the clinical workflow and installed into existing ECG recording systems, requiring a simple software upgrade.

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Disclosures

None.

References


CLINICAL PERSPECTIVE

Magnetic resonance imaging (MRI) is increasingly becoming the preferred diagnostic and interventional imaging modality for a variety of diseases, commonly requested for acute stroke, acute spine, orthopedic, trauma, and cardiovascular diseases. The number of MRI-guided interventional procedures performed is growing steadily. Despite the increasing clinical merit, practical implementation of these procedures in the clinic is oftentimes limited because of the high risk associated with these patient groups and the subsequent need for advanced real-time physiological monitoring for each high-risk patient to be cleared for imaging and interventional workflows inside the MRI. In the course of MRI-guided interventions, sedated or anesthetized patients lie in the MRI for 2 to 8 hours. The risk of an acute event is larger than with conventional MR procedures, so high-fidelity physiological monitoring is required as an essential component of life support. Currently real-time high-fidelity hemodynamic monitoring, such as aortic blood flow and left ventricular stroke volume, is rarely available in MRI procedures. As a result, severally ill patients with stroke and ischemic histories and those being intubated are excluded from MRI-guided interventions, including from minor procedures, such as biopsies. The presented method for beat-to-beat SV and continuous aortic flow monitoring within the MRI bore based on magnetohydrodynamic voltages induced onto 12-lead ECG enables MR imaging and MRI-guided interventional procedures to be performed in severely ill patients who require high-fidelity real-time hemodynamic monitoring.
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