Fiber-Optic Stethoscope: A Cardiac Monitoring and Gating System for Magnetic Resonance Microscopy

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A fundamental problem associated with using the conventional electrocardiograph (ECG) to monitor a subject's cardiac activity during magnetic resonance imaging (MRI) is the distortion of the ECG due to electromagnetic interference. This problem is particularly pronounced in MR microscopy (MRI of small animals at microscopic resolutions (< 0.03 mm³)) because the strong, rapidly-switching magnetic field gradients induce artifacts in the animal's ECG that often mimic electrophysiologic activity, impairing the use of the ECG for cardiac monitoring and gating purposes. The fiber-optic stethoscope system offers a novel approach to measuring cardiac activity, unlike the ECG, is immune to electromagnetic effects. The fiber-optic stethoscope is perorally inserted into the esophagus of small animals to optically detect pulsatile compression of the esophageal wall. The optical system is shown to provide a robust cardiac monitoring signal in rats and mice during routine cardiac MR microscopy. Magn Reson Med 47: 314–321, 2002. © 2002 Wiley-Liss, Inc.

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The development of transgenic small-animal models of cardiac disease has focused attention in recent years on MR microscopy as a tool to characterize cardiac structure and function (1–5). A crucial component of in vivo MR microscopy is the ability to continuously assess the animal's cardiac activity, for purposes of both cardiac monitoring and cardiac gating (the careful synchronization of imaging to the heart cycle). However, the method conventionally used to measure cardiac function, the electrocardiograph (ECG), is corrupted during MR microscopy by the imaging process itself. According to Faraday's Law, the time-varying magnetic field gradients applied during imaging induce an electromotive force (EMF) in the conductive medium through which magnetic flux lines pass and induce an EMF. Alternative measures of cardiac activity could be used, including peripheral blood pressure and blood perfusion techniques. In general, however, such superficial measurements suffer from low sensitivity, particularly in small animals (9). Moreover, the arterial pulse from peripheral tissue can vary over the course of an experiment due to temperature- or drug-induced vasoconstriction/dilation. Legnere et al. (10) successfully detected cardiac activity in rats using a fiber-optic reflectometer; however, their technique was invasive, requiring arterial catheterization. Thus, none of the existing techniques have been shown to provide reliable, noninvasive cardiac monitoring ability, much less gating ability, in small animals.

The purpose of this study was to design and implement a cardiac monitoring and gating system that was immune to electromagnetic interference during MR microscopy. The system was required to be: 1) inherently nonelectrical, 2) MR-compatible, 3) noninvasive (requiring no surgery), and 4) small enough for use on rats and mice.

METHODS

Fiber-Optic Stethoscope System Design

As shown in the MR image of the mouse thorax (Fig. 1), the mammalian esophagus shares close anatomical proximity with the heart, lying dorsal to the aortic arch (AA) and left atrium (LA), then adjoining the descending aorta until emptying into the stomach. As a result of this proximity, the heart imposes significant pulsatile compression of the esophagus, as has been observed in humans both directly via endoscopy (11) and indirectly via esophageal pressure signals (12). The premise for this work was that this me-
Mechanical esophageal compression could be detected optically as an indication of cardiac activity. Optical displacement sensors have previously been employed for respiratory gating in MRI (13,14), and techniques such as transesophageal ECG monitoring and echocardiography have exploited the heart–esophagus proximity for closer access to the heart; however, to the authors’ knowledge, esophageal wall motion has never before been detected as a means to gauge cardiac activity.

A fiber-optic “stethoscope” was created that could be inserted into the esophagus of a small animal to optically detect esophageal wall pulsations related to cardiac activity. A schematic of the fiber-optic stethoscope system is shown in Fig. 2. Two step-index multimode optical fibers (OFs) (Thorlabs, Newton, NJ) were used: one for transmission and the other for detection of light. These silica fibers had numerical apertures (NA) of 0.37, and were 5 m in length. The last 8 cm of each fiber were stripped of buffer to a diameter of 125 µm, and then the two bare (core + cladding) fibers were bundled together with epoxy for a total diameter of 250 µm. The fiber tips were cleaved and polished to maximize light detection. In some experiments, polyethylene tubing (inner diameter = 1.2 mm) filled with a 1:500 concentration of Magnevist (gadopentetate dimeglumine; Berlex Laboratories, Wayne, NJ) was secured along the length of the OFs with the tubing tip at the same level as the OF tips. While the OFs themselves do not yield signal in MR images, the Magnevist-filled tubing generates a strong signal and therefore provides a distinct marker of stethoscope position.

Collimated continuous-wave light from a 40-mW, 650-nm laser diode (Thorlabs) was focused into the transmit fiber using an optical lens. As light from the transmit fiber impinged upon a moving surface, such as the esophageal wall, the amount of diffusely reflected and backscattered light detected by the receive fiber increased as the surface moved closer to the probe tip and decreased as it moved away from the tip. The detected light was conveyed by the receive fiber to an amplified p-i-n photodiode (gain ≤ 125 dB) (Thorlabs) outside the imaging magnet. The resulting electrical signal was passed to a custom-built signal-processing circuit for further amplification, and then to a physiologic monitor for recording and display.

Unlike the ECG, the more slowly-varying optical signal did not contain a high-frequency spike from which to trigger cardiac-gated imaging. Instead, a second signal—a 5-ms, 5-V square-wave pulse—was generated by the circuit whenever the slope of the optical signal exceeded a certain threshold. This signal, similar to the ECG in appearance but fundamentally different in origin, was used to trigger cardiac-gated imaging and to measure the animal’s heart rate.

Animal Preparation
All animal studies were conducted at the Duke Center for In Vivo Microscopy (CIVM) in accordance with institu-
tional animal care regulations. Twenty-eight rats (Charles River, Wilmington, MA) weighing 150–250 g, and one C57BL/6J mouse (Jackson Lab, Bar Harbor, ME) weighing 40 g were anesthetized with methohexital (45 mg/kg, Brevital; Eli Lilly, Indianapolis, IN) and placed prone in a plexiglas cradle. Following intubation, anesthesia was maintained with 2–3% isoflurane (IsoFlo; Abbott Laboratories, North Chicago, IL) delivered by a computer-controlled, MR-compatible pressure ventilator set at 40–80 breaths/min (15). A solid-state pressure transducer on the breathing valve measured airway pressure. Pediatric electrodes were taped to the animal’s footpads to acquire a reference ECG signal. Body temperature was measured using a rectal thermistor. In some experiments, arterial pressure was measured by inserting a pressure transducer into the AA via the right carotid artery. All physiologic signals were processed (Coulbourn Instruments, Allentown, PA) and displayed on a computer using LabVIEW software (National Instruments, Austin, TX) for continuous monitoring throughout the experiments.

An 8-cm length of plastic tubing, slightly larger in diameter than the bundled OFs, was lubricated with Surgilube (Altana Inc., Melville, NY) and perorally inserted into the animal’s esophagus to the mid-thorax. The purpose of the tubing was to protect the walls of the esophagus from perforation as the OFs were inserted. The protective tubing was then withdrawn to expose the fibers to the esophageal wall. The laser diode was turned on and the ambient room lights were turned off to reveal a red glow emanating from inside the animal’s body, permitting easy positioning of the fiber tip near the heart. Photothermal effects were negligible because tissue absorption of 650-nm light is minimal (16). The probe was then secured to the cradle to remain stationary throughout the experiment. Figure 3 shows a rat anesthetized by ventilator-delivered isoflurane, with the fiber-optic stethoscope shown in front, prior to insertion in the animal’s esophagus.

Imaging Setup

For this study, cardiac-gated imaging using the fiber-optic stethoscope was performed on rats only. The animal in the cradle was placed inside a 7-cm-diameter birdcage RF coil and positioned in a 30-cm bore 2.0 T magnet (Oxford Instruments, Oxford, UK) with shielded gradients (up to 0.18 T/m) controlled by a Signa console (General Electric Medical Systems, Milwaukee, WI). Body temperature was maintained by a feedback system that controlled heated airflow through the magnet (17). The combination of closely regulated body temperature and anesthesia delivery kept the animal’s heart rate to within 5% of its baseline rate. Baseline heart rates averaged 300 beats/min. To minimize image motion artifacts from breathing, data acquisition was enabled by a 600-ms window during end-expiration of the respiratory cycle. Cardiac-gated, radial-acquisition (RA) cine imaging (18) was then triggered by the fiber-optic gating pulse rather than the conventional ECG.

RESULTS AND DISCUSSION

Initial benchtop experiments revealed that the optical signal detected by the fiber-optic stethoscope exhibited periodic amplitude oscillations matching the frequency of the cardiac cycle as measured by the ECG. The shape and
Timing of these variations were observed to vary with the position of the stethoscope tip in the thorax, indicating that the nature of esophageal compression depended greatly on the surrounding tissue. To further examine this point, the OFs were inserted to several different esophageal depths and the resulting optical signal was recorded and compared to the ECG and aortic pressure waveforms. The relative timing of the optical signal with respect to these other known metrics of cardiac activity helped to elucidate the anatomical relationship between the heart and the stethoscope tip in the esophagus. As a secondary verification of fiber-tip position, a series of MR images was acquired at incremental axial levels through the thorax from head to tail, and the path of the Magnevist tubing (MT) was followed to its end to pinpoint the exact position of the stethoscope tip and therefore the site of optical signal detection.

Figure 4a and b shows sample results from an experiment in which the fiber-optic stethoscope was inserted to a depth of 7 cm in the esophagus of a 250-g rat. The ECG, detected optical signal, and aortic pressure waveforms are plotted in Fig. 4a. The optical signal amplitude decreases suddenly after the R-wave of the ECG, reaching a minimum just before the peak in aortic pressure. Because it occurs between ventricular depolarization and peak aortic pressure, the optical signal trough is likely due to contraction of the ventricles. Systolic ventricular contraction involves a decrease in chamber volume (19), which then causes the neighboring tissue, including the esophagus, to experience a corresponding expansion. An expanded esophageal diameter lengthens the distance between the esophageal wall and stethoscope tip and decreases the amount of reflected light detected by the receive fiber. As the ventricles fill again in diastole, the heart expands and compresses the esophagus, causing the amount of detected light to steadily increase.

The corresponding axial MR image (Fig. 4b) shows the position of the OF tips relative to the cardiac ventricles. The OF tips are visible as two dark circular regions directly below the bright MT. The ECG, detected optical signal, and aortic pressure waveforms are plotted in Fig. 4b. The OF tips are at the same axial level as the LV and RV. The data in a and b indicate that, at a depth of 7 cm, ventricular contraction causes the variations in optical signal, while in c and d, at a depth of 6 cm, aortic pulsation appears to modulate the signal.

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The fiber-optic stethoscope was then withdrawn 1 cm to an esophageal depth of 6 cm, and a very different optical signal was detected, as shown in Fig. 4c. Whereas in Fig. 4a the optical signal troughs precede peaks in aortic pressure, in Fig. 4c the optical signal troughs coincide with aortic pressure peaks (the two signals essentially mirror each other), suggesting that aortic rather than ventricular motion was being detected in this case. In addition, the signal-to-noise ratio (SNR) of the optical signal is greater in c than in a, suggesting that the extent of cardiac-induced esophageal compression has increased because of closer proximity. Indeed, the corresponding axial MR image in Fig. 4d confirms that the OF tips border the AA at this level. It is known that just below the tracheal bifurcation, the AA partially encircles the esophagus and, together with the left main bronchus, causes left-sided compression of the esophagus known as the aortic narrowing. Significant pulsatile motion has been observed at the site of aortic narrowing due to dorsal shifting of the aorta (11). Thus, systolic aortic shifting may momentarily increase esophageal diameter and decrease the amount of light detected by the receive fiber at this depth.

The optimal OF position for cardiac gating purposes in the rat was found to be at an intermediate esophageal depth of 6.5 cm. At this level, the detected optical signal had the greatest SNR and provided a cardiac trigger pulse that consistently coincided with the R-wave of the ECG. The recorded waveforms are shown in Fig. 5a. The amplitude of the optical signal increases in end-diastole, reaching a maximum coincident with the R-wave, and then decreases again just after the R-wave. This behavior suggests that atrial contraction, which occurs immediately prior to ventricular contraction to supply 20–30% additional filling of the ventricles, is responsible for decreasing esophageal diameter and causing the optical signal peaks in end-diastole. The corresponding axial MR image in Fig. 5b reveals the proximity of the OFs to the LA, supporting the idea that atrial activity is detectable at this depth.

Because the optical signal began to drop in amplitude just after the R-wave of the ECG, the falling edge was used to generate a cardiac gating pulse that would closely track the R-wave. As illustrated by the dotted line in Fig. 5a, the optically-derived gating pulses generated in this manner do, in fact, consistently coincide with the R-wave. The standard deviation between the two signals was measured to be less than 1% of the cardiac cycle, and over 95% of the falling edges of the optical signal were detected. While the coincidence of the optically-derived gating pulse and the R-wave makes the gating pulse easily interpretable, it is not necessary for purposes of cardiac gating. Cardiac gating can be achieved no matter where the trigger pulse occurs in the cardiac cycle—as long as the position of the pulse remains consistent throughout the scan.

An interesting feature of the system is its ability to detect breathing motion in addition to cardiac motion. As seen in Fig. 5a, the optical signal amplitude increases during inspiration, indicating that increased lung volume further compresses the esophagus and increases the amount of detected light. If desired, the slower-frequency breathing signal could be filtered out to measure the animal’s respiratory rate, further extending the capability of the system.

Screen saves of the physiologic monitor taken during cardiac-gated MR microscopy of a rat demonstrate the value of the fiber-optic stethoscope over the ECG (Fig. 6). In Fig. 6a, imaging gradients are off, the ECG appears normal, and the optically-derived gating pulses are coincident with the R-wave. In Fig. 6b, however, imaging gradients are turned on and the ECG is visibly distorted by induced voltage artifacts, whereas the optically-derived gating pulse is unaffected and continues to provide a robust signal for cardiac gating.

The fiber-optic stethoscope was used in a series of cardiac MR microscopy experiments to test its ability to provide a reliable cardiac gating pulse for time-resolved functional imaging. Each optically-derived gating pulse triggered the cine acquisition of data at six 30-ms intervals across the cardiac cycle, for a total imaging time of 10 min. Figure 7 shows a temporal series of the same 2-mm coronal slice of the rat thorax at six phases of the cardiac cycle. Without a consistent cardiac gating pulse, the data would...
be misregistered in time. But, as seen in Fig. 7, the distinct cardiac phases are discernible as the heart cycles through diastole (a), systole (b and c), and then returns to diastole (d and f), confirming the ability of the fiber-optic stethoscope to provide an accurate temporal reference frame for cardiac imaging.

Once the operation of the system was validated on rats, it was then tested on a 40-g mouse to verify its feasibility on an animal with one-fifth the mass and up to twice the heart rate. The results were very similar to those in the rat, with apparent detection of atrial contraction and coincidence of the optically-derived gating pulse to the R-wave of the ECG. This finding demonstrates that cardiac-induced esophageal compression is not species-dependent, and that the fiber-optic stethoscope can be used with rats, mice, and (potentially) other small animals.

FIG. 6. Screen saves of the physiologic monitor taken during ventilatory- and cardiac-gated MR microscopy of a rat. The physiologic signals, graphed from top to bottom, are the ECG, optically-derived gating pulse, and ventilatory pressure waveform (unlabeled). a: Imaging gradients are off and optically-derived gating pulses are coincident with the R-wave of the ECG. b: Imaging gradients are on and the ECG is visibly distorted by induced voltage artifacts, whereas the optically-derived gating pulses continue to provide a reliable trigger for cardiac gating.

CONCLUSIONS

It is important to note that the ECG and the fiber-optic stethoscope provide fundamentally different kinds of information about cardiac activity. Whereas the ECG assesses electrical aspects of impulse generation and conduction, the fiber-optic stethoscope provides a measure of mechanical cardiac contractility; both types of information are useful in monitoring cardiac activity. Therefore, the fiber-optic stethoscope is not meant to replace the ECG. Though virtually useless during some imaging sequences, the ECG does provide important cardiac information when imaging gradients are off. However, when imaging gradients are on, the fiber-optic stethoscope’s ability to provide a robust signal makes it a valuable tool for cardiac monitoring and gating purposes. For this reason, the system has
been incorporated into routine microscopy studies beyond those mentioned here. Furthermore, the system’s ability to detect esophageal compression from multiple sources, including the aorta, atria, ventricles, and lungs, makes it a versatile monitoring device with other possible applications not explored in this work.

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REFERENCES


