

High-Resolution High-Speed Panoramic Cardiac Imaging System

Dale W. Evertson, Mark R. Holcomb*, Matthew D. C. Eames, Mark-Anthony Bray, Veniamin Y. Sidorov, Junkai Xu, Holley Wingard, Hana M. Dobrovolny, Marcella C. Woods, Daniel J. Gauthier, and John P. Wikswo, *Fellow, IEEE*

Abstract—A panoramic cardiac imaging system consisting of three high-speed CCD cameras has been developed to image the surface electrophysiology of a rabbit heart via fluorescence imaging using a voltage-sensitive fluorescent dye. A robust, unique mechanical system was designed to accommodate the three cameras and to adapt to the requirements of future experiments. A unified computer interface was created for this application—a single workstation controls all three CCD cameras, illumination, stimulation, and a stepping motor that rotates the heart. The geometric reconstruction algorithms were adapted from a previous cardiac imaging system. We demonstrate the system by imaging a polymorphic cardiac tachycardia.

Index Terms—Cardiac arrhythmias, cardiac electrophysiology, optical mapping, panoramic, 3-D reconstruction.

I. INTRODUCTION

Cardiac tissue is an electrically excitable medium that can support either normal or abnormal patterns of activation. The initiation of

Manuscript received May 17, 2006; revised August 21, 2007. This work was supported in part by the National Institutes of Health under Grant R01-HL58241, in part by the Vanderbilt Institute for Integrative Biosystems Research and Education (Vanderbilt University), in part by the National Science Foundation under Grant PHY-0243584, and in part by the National Institutes of Health under Grant 1R01-HL-72831 (Duke University). Asterisk indicates corresponding author.

D. W. Evertson, deceased, was with the Department of Mechanical Engineering, Vanderbilt University, Nashville, TN 37235 USA.

*M. R. Holcomb is with the Department of Physics and Astronomy, 6301 Stevenson Center, Vanderbilt University, Nashville, TN 37235 USA (e-mail: mark.r.holcomb@gmail.com).

M. D. C. Eames was with the Department of Biomedical Engineering, Vanderbilt University, Nashville, TN 37235 USA. He is now with the Department of Biomedical Engineering, University of Virginia, Charlottesville, VA 22908 USA (e-mail: matte@virginia.edu).

M.-A. Bray was with the Department of Biomedical Engineering, Vanderbilt University, Nashville, TN 37235 USA. He is now with the Division of Engineering and Applied Sciences, Harvard University, Cambridge, MA 02138 USA (e-mail: braymp@deas.harvard.edu).

V. Y. Sidorov and M. C. Woods are with the Department of Biomedical Engineering, Vanderbilt University, Nashville, TN 37235 USA (e-mail: v.sidorov@vanderbilt.edu; marcella.woods@vanderbilt.edu).

J. Xu is with the Department of Physics and Astronomy, Vanderbilt University, Nashville, TN 37235 USA (e-mail: junkai.xu@vanderbilt.edu).

H. Wingard is with the Department of Mechanical Engineering, Vanderbilt University, Nashville, TN 37235 USA (e-mail: hewingard@alltel.net).

H. M. Dobrovolny is with the Department of Physics and the Center for Nonlinear and Complex Systems, Duke University, Durham, NC 27708 USA (e-mail: hdobrovo@phy.duke.edu).

D. J. Gauthier is with the Department of Physics and the Department of Biomedical Engineering, Duke University, Durham, NC 27708 USA (e-mail: gauthier@phy.duke.edu).

J. P. Wikswo is with the Departments of Biomedical Engineering, Physics and Astronomy, and Molecular Physiology and Biophysics, and the Vanderbilt Institute for Integrative Biosystems Research and Education, Vanderbilt University, Nashville, TN 37235 USA (e-mail: john.wikswo@vanderbilt.edu).

Color versions of one or more of the figures in this paper are available online at <http://ieeexplore.ieee.org>.

Digital Object Identifier 10.1109/TBME.2007.912417

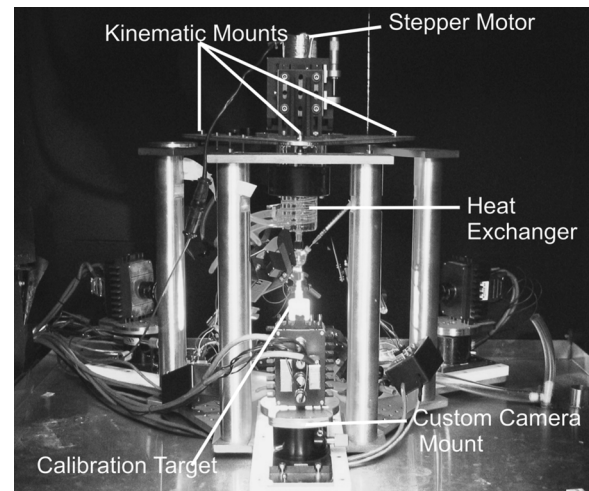


Fig. 1. System as seen from outside the Faraday cage through one of three sets of double doors.

activation and its subsequent propagation bear significant importance in the design of pacemakers, defibrillators, and antiarrhythmic drugs. By studying the cardiac electrophysiology of rabbit hearts, researchers may extrapolate the acquired data and apply it to human heart electrophysiology. Panoramic cardiac optical mapping using a voltage-sensitive dye to report the time-dependence of the transmembrane potential has been used previously to record and analyze cardiac electrical activity. This technique, described in preliminary form by Lin *et al.* [1] and further expanded by Bray *et al.* [2], involves 1) imaging an excised, Langendorf-perfused rabbit heart from three points of view; 2) numerically reconstructing the heart surface features; and 3) texture-mapping the acquired fluorescence images of the heart's electrical activity onto the virtual surface. The result is a movie of the electrical activity across the entire 3-D epicardial surface. Subsequently, panoramic systems for studying hearts have been developed by Kay *et al.* [4], and Qu *et al.* [5]. Rogers *et al.* describe the use of the Kay system for imaging the lifetime of multiple phase singularities in the fibrillating swine heart [6]. In addition to a more extended discussion than presented in this communication, the supplement contains detailed descriptions of the surface reconstruction, and the custom kinematic mount, base plate, and computer control.

II. CAMERAS

The system shown in Fig. 1 uses three high-speed, low noise, CCD cameras spaced 120 degrees around the heart on the horizontal plane. The three synchronized 14-bit CCD cameras (CardioCCD-SMQ, RedShirt Imaging) are used to image the electrical activity across the surface of a heart. Each camera is capable of recording up to 2000, 3000, and 5000 fps at resolutions of 80×80 , 40×40 , and 26×26 pixels, respectively. We also have an alternate configuration which uses 128×128 pixel cameras running at 490 fps (DS-12-16K5H, Dalsa). All cameras are controlled by a single workstation (Precision 650, Dell) equipped with 2 GB of RAM. Both camera configurations use 12-mm C-mount lenses (LM12JCM, Kowa).

Qu *et al.* [5] make use of 16×16 element photodiode arrays (PDA) operating at 5000 fps in a panoramic system with similar experimental goals. The RedShirt cameras match the PDA frame rate while offering 250% more pixels. The 40×40 3000 fps mode is only 60% as fast, but offers 625% more pixels. Fig. 2 shows raw (unfiltered) data from single pixels. The signal-to-noise ratio (SNR) for the RedShirt (~ 30) is

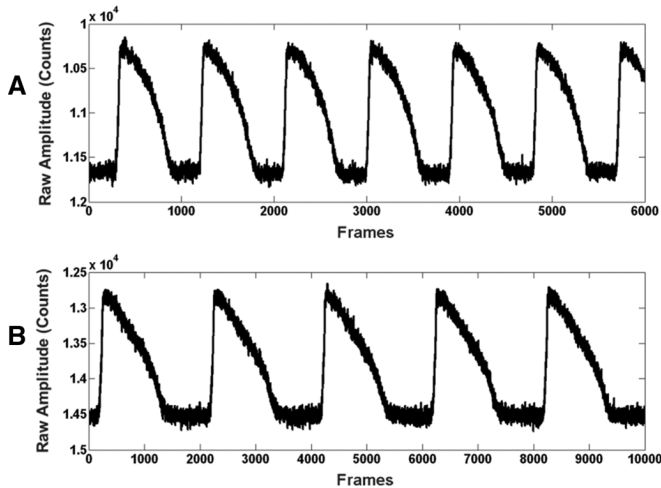


Fig. 2. Single pixel pacing data. (a) Raw data (unfiltered) acquired at 3000 fps at a resolution of 40×40 pixels. (b) Raw data (unfiltered) acquired at 5000 fps at a resolution of 26×26 pixels. LEDs were used for (a) and laser illumination (Verdi, Coherent) for (b). The SNR for A and B are 31 and 35, respectively, based on $SNR = (S1 \text{ Amplitude}) / (\text{Standard deviation during diastolic interval})$. The pixels used were on the left ventricle, but from different hearts. The recordings shown were taken shortly after the hearts were first stained but are not atypical signals.

slightly less than that of the PDAs but is fully acceptable for quantitative imaging of cardiac arrhythmias and fibrillation. Additionally, spatial filtering down to the resolution of PDAs would increase the SNR substantially. In this application, the higher spatial resolution, along with the flexibility to change binning modes easily with a software setting, makes the RedShirt an arguably superior choice over both PDAs and the Dalsa CCDs. Advanced complementary metal oxide semiconductor (CMOS) cameras, although expensive, may prove even better [7]. In contrast to the large-heart system for which rotation of the heart is impractical [4] and PDA-based system with its low imaging resolution [5], we do not require the use of an additional video or CCD camera to obtain the high-resolution images required to create the wire frame model of the heart.

Each of the three cameras in the new system may be independently positioned and directed at the target object. The camera mounts (PO80N, Newport) shown in Fig. 3 allow easy adjustment of the pan, tilt, and roll of the camera to optimize the position of the heart in the field-of-view.

III. ILLUMINATION

We excite the voltage-sensitive dye with an illumination system comprising six high-intensity green LEDs (LXHL-LM5C, Luxeon) arranged about the heart and centered on the faces of a virtual cube aligned with its diagonal (1 1 1) axis oriented along the vertical axis of the system.

We mounted the LEDs on CPU heat sinks and fans (SKU 275016, COMPUSA). A custom bracket secures a lens (LXHL-NX05, Luxeon) to the front surface of each LED. The LEDs are powered by three dual-mode power supplies (E3610A, Agilent). The shutter motors on a custom mount (Standard Servo Stock#: 900-00005, Parallax) are controlled by simple pulse-width modulation and open and close automatically before and after data acquisition. The shutter system allows the LEDs to remain on continuously at steady-state intensity while preventing photobleaching by only exposing the heart to light during data acquisition. The fluorescence response from the LED

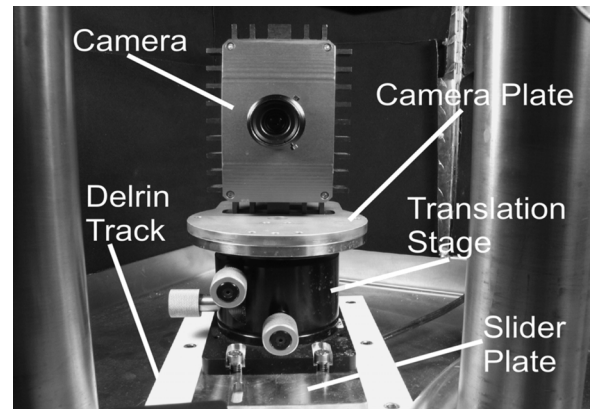


Fig. 3. One of the three cameras and its mount on the Delrin track, as seen from the perspective of the heart.

illumination is capable of saturating the cameras. The entire LED illumination system, including power supplies, costs approximately \$2000, making it much more cost-effective than the \$50 000 frequency-doubled Nd:YAG lasers (Verdi, Coherent) used in the previous system and also available for use with this system.

IV. PERFUSION SYSTEM

The pumps and heat exchangers used in this experimental setup are identical to or are updated versions of those used in our previous system [1], [2]. For the purposes of this paper, the key function of the perfusion system is to maintain the viability of the heart *ex vivo* while the experiment is performed and data recorded. The perfusion system is also used to administer the voltage-sensitive fluorescent dye, di-4-ANEPPS, (Molecular Probes, Inc.) to the cardiac tissue.

V. ROTATION SYSTEM

The heat exchanger in the perfusion system is suspended from a computer-controlled stepping motor (S57-102-MO, Compumotor), connected to a 20:1 gearhead (PG60-020-T01, Bayside) providing precise, 1° increments in the position for the sequence of 120 images necessary for creating the wire-frame reconstruction of the heart surface features with voxels no larger than 0.4 mm. The motor acceleration is chosen to minimize swinging.

VI. ENCLOSURE

A custom-built aluminum Faraday cage (Duck Welding, Nashville, TN) provides both electromagnetic isolation, a light-tight enclosure for the system, thermal control, and a tray with drain for catching spills. The enclosure is fabricated from 5-mm-thick aluminum floor plate and has double-doors on three sides to ensure convenient access to the camera system. The Faraday enclosure is cemented to a concrete-block wall that is spanned by steel-reinforced concrete lintels to minimize vibration. A metal framework suspended from the ceiling supports the perfusion system pumps and power supplies and isolates their vibrations from the camera system.

VII. RESULTS

Using the system just described, we conducted three demonstration experiments using rabbit hearts: two using the RedShirt configuration and one using the Dalsa cameras. Fig. 4 shows a sample of the results using the RedShirt cameras in their 1000-fps 80×80 pixel mode.

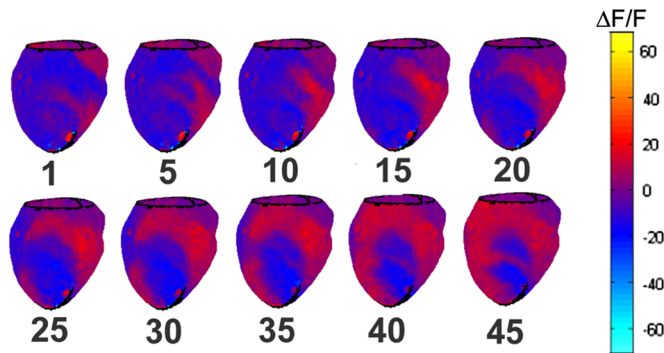


Fig. 4. Figure-of-eight reentry during polymorphic tachycardia. Every fifth frame of a 1000 fps sequence is shown. The excited tissue is red. The persistent red dot in the lower right of each image is an artifact due to the electrode.

The heart was prepared as described previously [1]. Ten frames from a 45-ms interval of a rabbit heart in polymorphic tachycardia are shown. Every fifth frame is shown, which gives a 5-ms interval between images. The sequence shows a figure-of-eight reentry, which is a common phenomenon observed in cardiac arrhythmias. We estimate the mean reconstruction error to be on the order of 1.2 mm.

VIII. DISCUSSION

We have described and demonstrated a system which allows for both high spatial and temporal resolution of the transmembrane potential over the entire epicardial surface of a rabbit heart. Our implementation of the panoramic camera is designed to optimize the mechanical stability of the system, the accuracy of the reconstruction, and ease of use. Elsewhere, we will report the use of this system to study the effects of global ischemia on propagation, and the virtual electrode distribution from intracavity defibrillation strength shocks.

ACKNOWLEDGMENT

This article is dedicated to the memory of Dale W. Everton. The authors would like to thank R. Gray of the University of Alabama at Birmingham for sharing his two RedShirt cameras for collaborative studies. They would also like to thank T. Winston and P. Park for their participation in the senior engineering design project that was associated with the development of this camera; J. Walker for her advice and guidance during that part of the effort; M. Welfel at PDM, Inc., Nashville, TN, for supervising the careful machining of the mechanical components for the system; J. Boone, K. Miller, and R. Lemaire at Duck Welding, Inc., Nashville, TN, for their design and fabrication of the Faraday shield; R. Bekele for his assistance with the illumination system; and R. Reiserer for his advice and technical support.

REFERENCES

- [1] S. F. Lin and J. P. Wikswo, Jr., "Panoramic optical imaging of electrical propagation in isolated heart," *J. Biomed. Opt.*, vol. 4, pp. 200–207, 1999.
- [2] M.-A. Bray, S. F. Lin, and J. P. Wikswo, Jr., "Three-dimensional surface reconstruction and fluorescent visualization of cardiac activation," *IEEE Trans. Biomed. Eng.*, vol. 47, no. 10, pp. 1383–1391, Oct. 2000.
- [3] W. Niem, "Robust and fast modeling of 3D natural objects from multiple views," *Proc. SPIE*, vol. 2182, pp. 388–397, 1994.
- [4] M. Kay and J. Rogers, "Three-dimensional surface reconstruction and panoramic optical mapping of large hearts," *IEEE Trans. Biomed. Eng.*, vol. 51, no. 7, pp. 1219–1229, Jul. 2004.

- [5] F. Qu, C. M. Ripplinger, V. Nikolski, C. Grimm, and I. R. Efimov, "Three-dimensional panoramic imaging of cardiac arrhythmias in rabbit heart," *J. Biomed. Opt.*, vol. 12, pp. 044019-1–044019-9, 2007.
- [6] J. M. Rogers, G. P. Walcott, J. D. Gladden, S. B. Melnick, and M. W. Kay, "Panoramic optical mapping reveals continuous epicardial reentry during ventricular fibrillation in the isolated swine heart," *Amer. J. Physiol. Heart Circ. Physiol.*, vol. 291, pp. H1935–H1941, 2006.
- [7] Y. N. Tallini *et al.*, "Imaging cellular signals in the heart *in vivo*: Cardiac expression of the high-signal Ca²⁺ indicator GCaMP2," in *Proc. PNAS USA*, Mar. 21, 2006, vol. 103, no. 12, pp. 4753–4758.

Automatic Detection and Imaging of Ischemic Changes During Electrocardiogram Monitoring

Claudio Zizzo*, Aimen Hassani, and Delphine Turner

Abstract—A new electrocardiogram (ECG) monitor with automated ST analysis and display capability has been developed to assist healthcare professionals identify the site and severity of acute ischemic changes. The monitor displays the changes as a 3-D image of the heart in real time. The underpinning assumption is that images are easier to interpret than ECG traces. We describe here the features of two functions of the monitor, the ischemia detection and imaging function (IF). The ischemia detection function was validated using the European ST-T database, and was found to have a sensitivity of 85% and positive predictivity of 93%. Fifty doctors took part in the evaluation of the new IF and the results showed an increase in their median proficiency to diagnose ischemia from 50% to 100% and an increase in their certainty of the diagnosis from 65% to 80%. The time to reach a diagnosis for eight ECGs, dropped from 15 to 9 min.

Index Terms—Biomedical imaging, biomedical signal processing, electrocardiography, ischemic heart disease.

I. INTRODUCTION

Electrocardiography is the standard investigation for the diagnosis of ischemic heart disease. Prompt diagnosis is essential to allow early treatment and improve patient outcome [1], [2]. Although the need for skilled healthcare professionals with expertise in ECG has never been greater, the supply of such expert clinicians has never been smaller [2]. A recent study [1] on 120 medicine residents found that the median diagnostic proficiency in reading 12 electrocardiograms was 60% and the mean score for the correct diagnosis of myocardial infarction was 65%. To minimize this problem, most ECG monitors have an automated ST segment measuring capability and more sophisticated monitors have interpretative algorithms [3] to help doctors reach the correct diagnosis. The use of such monitors is limited due to their complexity, the number of false positives, and the way the information is presented [2].

To address some of these issues, we have developed a new ECG monitor. The new monitor is easy to set up, has high positive predictivity (low number of false positive when detecting ischemic changes), and

Manuscript received January 3, 2007; revised July 23, 2007. This work was supported in part by the Chelmsford Medical Education Research Trust U.K. and the Mid Essex Hospitals Services NHS Trust U.K. *Asterisk indicates corresponding author.*

*C. Zizzo is with the Computing Department, Anglia Ruskin University, Victoria Road South, Chelmsford CM1 1LL, U.K. (e-mail: claudio_zizzo@yahoo.co.uk).

A. Hassani and D. Turner are with the Broomfield Hospital, Chelmsford, U.K. (e-mail: Aimen.Hassani@meht.nhs.uk; Delphine.Turner@meht.nhs.uk).

Digital Object Identifier 10.1109/TBME.2007.909504