33rd Annual International Conference of the IEEE EMBS
Boston, Massachusetts USA, August 30 - September 3, 2011

Development of an Interactive Coronary Doppler Vibrometry System for Detection of Coronary Artery Disease

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***Abstract*— Coronary artery disease is a deadly and costly condition and represents an important public health issue globally. Coronary Doppler vibrometry (CDV), a new noninvasive coronary artery stenosis detection technique, showed encouraging results in our recent clinical study. However, the CDV system required lengthy offline data analysis, thus it did not provide any feedback during examination on the quality of data, not to mention analysis results. To overcome these limitations, we have developed a new CDV system that interactively performs acquisition, analysis and display of a complete data set while a subject is still on the examination table. Our system is based on a commercial ultrasound machine, and it will be a useful tool for CDV research and clinical studies in the future.**

I. INTRODUCTION

Coronary artery disease (CAD) caused by coronary artery stenosis (CAS) constitutes a major public health issue and creates a major financial burden not only in the industrialized countries with their aging populations but also in developing countries. It is a leading cause of death and disability. In 2005, for example, 7.6 million people died from CAD [1]. In the U.S., more than 400,000 deaths were attributed to CAD in 2006 [2]. In 2010, the estimated direct cost of CAD was $96 billion in the U.S. [2]. To control these public health and financial problems, a new CAS detection technique, which is simple to use, inexpensive, low-risk and accurate, is needed for efficient CAD screening, diagnosis and management.

As a new noninvasive CAS detection technique, coronary Doppler vibrometry (CDV) was developed. Audio-frequency vibrations are generated from turbulences in stenosed artery (in case of complete occlusion, there would be no vibrations). CDV detects these vibrations in the left ventricular myocardium and in the tissue adjacent to the left coronary cusp of the aortic valve using pulse-wave (PW) Doppler [3][4]. In our recent clinical study, CDV showed encouraging results in detecting stenoses of $\geq$25%, $\geq$50% and $\geq$70% with a sensitivity higher than 80%. With the wide availability and safe nature of diagnostic ultrasound, CDV has potential to be a low-risk and efficient technique for CAD screening, diagnosis and monitoring.

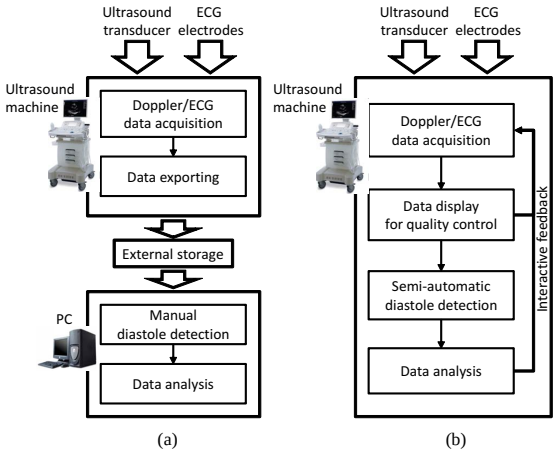

Fig. 1. CDV examination: (a) previously and (b) with a new interactive system.

A key limitation with the previous CDV method is lack of interactive feedback on analysis results and data quality during examinations. Figure 1(a) shows the CDV examination process used in our recent study [4]. Data were acquired using a commercial ultrasound machine. Subsequently, data analysis was performed offline using a separate PC, requiring a total examination time of at least 3 hours. As a result, data quality and analysis results could not be assessed nor available during the examination. During offline analysis, we found the data from four patients (out of 35) unusable for CDV analysis because PW Doppler data had been incorrectly saved or electrocardiogram (ECG) data were poor in quality [4]. As these patients had already left the hospital when this was discovered, we could not reacquire the data. Furthermore, additional data acquisition, such as more detailed interrogation of the suspected myocardium area based on the CDV results made available to the operator interactively, was not possible because the analysis results were not generated while scanning the patient.

In this study, we developed an interactive CDV system as shown in Fig. 1(b) to overcome the limitations of the previous CDV system. By providing the CDV operator with immediate feedback on data quality and analysis results using software running on an ultrasound machine (instead of a separate PC), our system offers flexibility to the operator and makes sure that a complete and usable data set has been

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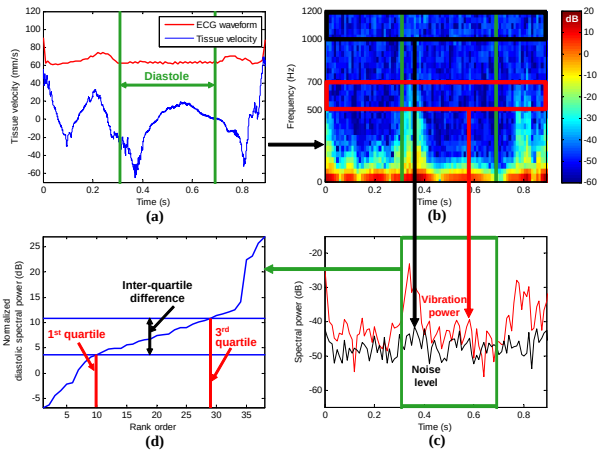

Fig. 2. An example of myocardial vibration analysis for a single cardiac cycle. (a) Myocardial tissue velocity derived from the PW Doppler data and synchronized ECG waveform. The diastolic period is marked by the green vertical lines. (b) Power spectral amplitude (color in dB) of tissue velocity oscillations vs. time. The red box is the 500 to 700 Hz vibration frequency band, and the black box is the 1000 to 1200 Hz reference noise frequency band. (c) Integrated vibration power and noise level. (d) Vibration power values within the diastolic period divided by the corresponding noise level for normalization are sorted in ascending order to derive the inter-quartile difference. The median inter-quartile difference over multiple cardiac cycles in one acquisition is the tissue vibration difference (TVD).

acquired and analyzed in one examination while the subject is still on the examination table.

II. CDV ALGORITHM AND PERFORMANCE

To analyze myocardial vibrations in PW Doppler data, our CDV algorithm uses the tissue vibration difference (TVD) and TVD index (TVDI) [4]. TVD and TVDI are derived using the PW Doppler data only in diastole, when heart movements are reduced and the coronary artery blood flow is maximum. Thus, ECG data were used to delineate diastolic periods, and TVD/TVDI analysis was performed during the detected diastolic periods. An example of TVD calculation process is shown in Fig. 2. Once PW Doppler and ECG data were acquired, myocardial velocity was derived from PW Doppler data while diastole was detected from ECG data (Fig. 2(a)). The myocardial velocity was converted into the frequency domain where Fig. 2(b) shows the calculated power spectrum of the tissue velocity. Power spectral values between 500 and 700 Hz were integrated to estimate the vibration power, and those between 1000 and 1200 Hz were averaged to create a noise level (Fig. 2(c)). The diastolic vibration power values, divided by the noise level values, were sorted in ascending order to determine the inter-quartile difference for each cardiac cycle (Fig. 2(d)). TVD is the median value over multiple cardiac cycles in one acquisition. A high TVD value represents the presence of diastolic vibrations that would be caused by CAS. TVDI is defined as the maximum TVD among multiple acquisitions taken along each coronary artery including left anterior descending (LAD), left main (LM), circumflex (CRX) and right coronary artery (RCA). An abnormal level of vibrations in the corresponding myocardium is detected for each coronary

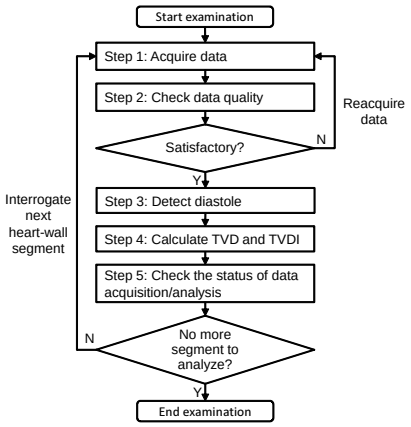

Fig. 3. New CDV examination protocol.

artery by comparing its TVDI to a threshold value. In our recent clinical study, we examined 31 patients with known or suspected stenosis using coronary angiography and CDV and 83 normal volunteers using CDV [4]. In this study, the optimal TVDI threshold value that maximized CAS detection performance was determined for each coronary artery. Sensitivity for detecting $\geq$25% stenosis was 89%, 87%, 83% and 100% in LAD, RCA, CRX and LM, respectively. These results suggest that CDV could permit more refined risk stratification of normals and CAS patients due to its capability of separating true normal ($<$25% stenosis) from subclinical (25%-49%) and clinical ($\geq$50%) CAS in a manner analogous to CT-based coronary artery calcium screening. We also successfully detected stenoses of $\geq$50% and $\geq$70% in LAD and of $\geq$50% in RCA with a sensitivity of higher than 85%.

III. SYSTEM DESCRIPTION

A. Interactive CAD examination protocol

Our goal is to develop a new CDV system that adds interactiveness to our previous CDV method. The new CDV system would enable the examination protocol shown in Fig. 3. Once an examination is started, an operator acquires B-mode, PW Doppler and ECG data in a heart-wall segment (step 1). The operator checks the quality of the PW Doppler and ECG data (step 2). If it is not satisfactory, the operator repeats the data acquisition step. If the data quality is satisfactory, diastole periods are detected from the acquired ECG data (step 3). Using the PW Doppler data in the diastolic periods, the TVD is calculated, and the TVDI value for each artery is updated (step 4). Then, the operator checks the status of data acquisition/analysis at each heart-wall segment to determine the next heart-wall segment to interrogate (step 5). If there is no more heart-wall segment to examine, the examination ends. Otherwise, the operator repeats the data acquisition and analysis for the next heart-wall segment by going back to step 1.

B. System requirements

To support the examination protocol shown in Fig. 3, several features were needed for the new CDV system. In

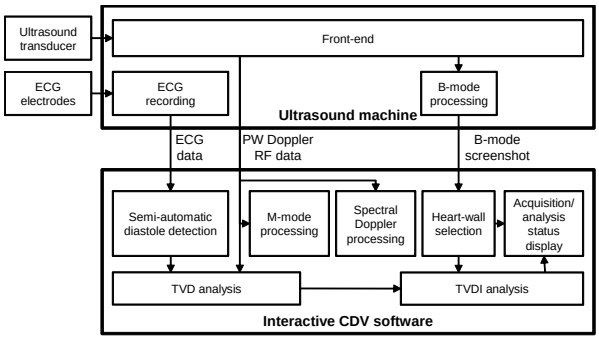

Fig. 4. Block diagram of our interactive CDV system.

step 2, the system needs to interactively display an M-mode image, Doppler spectrum and ECG waveforms, from which the operator can check whether the range-gate position and Doppler gain are set properly and the acquired ECG data are of acceptable quality and appropriate for diastole detection. For step 3, a user interface for diastole detection is required. As manually identifying the diastolic periods is time-consuming, semi-automatic detection (automatic detection with the option of manual override) is preferred in order to expedite the examination. For step 4, interactive TVD/TVDI analysis and display functions are required. As a TVD/TVDI value is assigned to the corresponding heart wall and coronary artery by the operator, an intuitive user interface for this assignment that is based on widely-used cardiac imaging conventions, such as the 17-segment model of the left ventricular myocardium [5], is important. For step 5, we need to be able to display the status of data acquisition/analysis to check whether data have been collected in each heart-wall segment and any abnormal vibrations have been detected in that segment. To promote the intuitiveness and operator efficiency, a bullseye polar plot [5], a commonly-used graphical representation of the 17-segment model, would be desired in the acquisition/analysis status display.

C. System design

To meet the system requirements presented above, we designed a new CDV system that consists of a commercially-available ultrasound machine, Ultrasonix Sonix RP (Ultrasonix, Richmond BC, Canada), and interactive CDV analysis/display software running on the machine as shown in Fig. 4. In this system, the Sonix RP machine provides B-mode, PW Doppler and ECG data. After each acquisition, PW Doppler radio-frequency (RF) and ECG data and a B-mode screenshot are saved in the ultrasound machine. The interactive CDV analysis/display software analyzes the saved data by performing semi-automatic diastole detection, M-mode and spectral Doppler processing, and TVD/TVDI analysis with appropriate user interfaces for diastole detection, heart-wall selection and data/result display. A screenshot of the interactive CDV software is shown in Fig. 5. In the following, we describe in detail several features shown in Fig. 5.

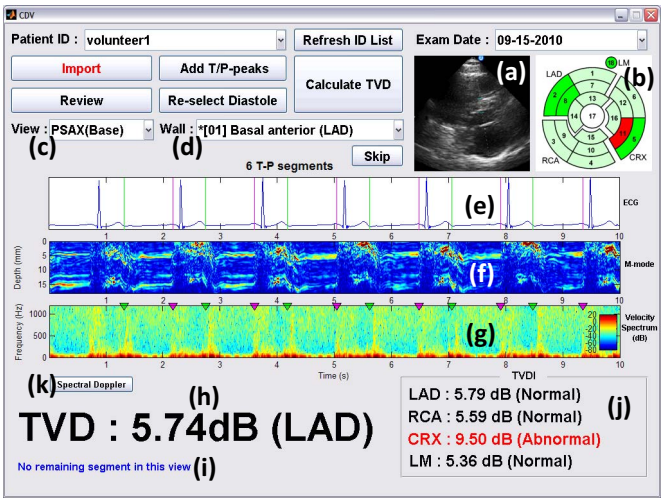

Fig. 5. A screenshot of the interactive CDV analysis/display software that shows (a) a B-mode image, (b) a color-coded bullseye plot, (c) a pull-down menu for echocardiographic view selection, (d) a pull-down menu for myocardial segment selection, (e) an ECG waveform with diastole detection results, (f) an M-mode image, (g) a tissue velocity spectrum, (h) a TVD value, (i) a list of remaining heart-wall segments in current echocardiographic view, and (j) a TVDI table.

1) Interactive data display with semi-automatic diastole detection: Our CDV software interactively displays an M-mode (Fig. 5(f)) image and ECG waveforms (Fig. 5(e)). Conventional Doppler spectrum can be displayed as well in place of the M-mode image if desired by clicking a button (Fig. 5(k)). Using the displayed image and waveforms, the operator can check the data quality. Our system also performs automatic diastole detection and displays the results overlaid on the ECG waveforms (Fig. 5(e)), which can be discarded if deemed unsatisfactory, in which case the operator identifies the diastolic periods manually.

2) Interactive TVD/TVDI analysis and display with heart-wall selection interface: Our software analyzes the PW Doppler and ECG data online and displays the TVD value interactively on the monitor of an ultrasound machine (Fig. 5(h)). For TVDI analysis, our software provides pull-down menus containing standard echocardiographic views (e.g., parasternal long axis view, PLAX) and lists of the heart-wall segments observable in each view (Figs. 5(c) and 5(d)). This lists are based on the conventional 17-segment model of the left ventricular myocardium with one additional segment that corresponds to the LM coronary artery. The bullseye polar plot in Fig. 5(b) reflects this addition to have a total of 18 segments. A B-mode image is also shown on the monitor (Fig. 5(a)) to help us select a heart-wall segment that we are currently analyzing from the pull-down menu. In addition, the CDV software automatically associates each data acquisition with the corresponding coronary artery (LAD, RCA, CRX and LM) based on the user-selected standard heart-wall segment [5] to derive the TVDI. After processing the acquired data, the TVDI value for each artery is updated and displayed in the TVDI table (Fig. 5(j)). If the TVDI value is greater than the predetermined threshold value [4], the

corresponding myocardial segment in the bullseye polar plot (Fig. 5(b)) and an entry in the TVDI table are highlighted in red. For example, Figs. 5(b) and (j) show a case where CAS is detected in CRX with the corresponding myocardial segment number of 11.

3) Data acquisition/analysis status display: To display the status of data acquisition/analysis, the CDV software provides a color-coded bullseye polar plot (Fig. 5(b)) and a list of the remaining heart-wall segments for each echocardiographic view (Fig. 5(i)). Each heart-wall segment in the bullseye plot indicates the status of data acquisition in dark green (data acquisition/analysis completed with no detected CAS) and light green (data acquisition/anslysis not yet completed with no detected CAS so far, i.e., more acquisitions are possible from different echocardiographic views). An uncolored segment indicates no data have been collected so far from that area. A red segment means that an abnormal level of vibrations has been detected there. The particular bullseye plot in Fig. 5(b) indicates that data acquisition/analysis was completed in myocardial segments 2, 5, 8 and 18, acquisition has not been made in segment 17, and an abnormal vibration was detected in segment 11. The other segments colored in light green mean that more data acquisitions are possible there.

IV. IMPLEMENTATION AND TEST

An interactive CDV system was implemented using an Ultrasonix Sonix RP machine. Phased array transducers, SA4-2 and PA4-2, were used in the system. The interactive CDV software was developed in MATLAB (R2006a, 32 bit, The MathWorks, Inc., Natick, MA). We worked with a cardiologist (KAC) from the beginning of the development to get clinical feedback on usability, intuitiveness and clinical productivity. Based on this interaction and feedback, the system was improved continuously for better operator efficiency, e.g., incorporating cardiac imaging conventions into the system. After the final implementation, the cardiologist used the machine to examine volunteers under University of Washington IRB approval. Before using the machine, the cardiologist was given an introduction on the examination protocol and keystroke sequences required to operate the system and performed test acquisitions to get familiar with the system, which took around 30 minutes. After the examinations on volunteers, the cardiologist commented that the system is easy to operate and multiple safeguards, e.g., intuitive color coding on the bullseye plot and the remaining heart-wall segment list, prevented any omission in acquisition and analysis of data from all the myocardial segments he planned to interrogate from each volunteer.

V. DISCUSSION AND CONCLUSION

An interactive CDV system has been developed. Using our system, a physician who is familiar with ultrasound scanning would be able to acquire and analyze a complete Doppler/ECG data set while the subject is still on the examination table, which is very convenient and important for CDV research. With our system, more reliable clinical studies could be performed because the system helps us acquire a complete and usable data set from each subject without any omission. Furthermore, as the operator gets CDV results interactively during examination, new possibilities could open up in the future, e.g., repeated and/or more in-depth data acquisition/analysis in high TVD regions. Thus, our system can be used as an efficient platform for CDV research and additional clinical studies.

Although our current system is based on a Sonix RP machine, the CDV software is portable to other ultrasound machines that offer access to its beamformed RF or demodulated in-phase/quadrature (IQ) data for PW Doppler with ECG data and can run our software. For example, we were able to port the CDV software to an Ultrasonix Sonix MDP with relative ease. It was also ported to a standalone PC for offline analysis.

Reduction in CDV examination time is our current goal. With our new interactive system, it takes about two minutes to acquire and analyze one PW Doppler set. Thus, if we want to cover all four major coronary arteries (LAD, RCA, CRX and LM), a minimum of 36 minutes per subject is required in order to acquire and analyze the data obtained from 18 myocardial segments. To improve the reliability of the CDV analysis results, the number of data acquisitions could increase up to 40 by interrogating some myocardial segments from multiple echocardiographic views. In this case, the examination time would increase up to 80 minutes per subject. This CDV examination time (36-80 minutes) is comparable to that of current noninvasive CAD diagnostic methods, such as stress ECG, echocardiography and nuclear medicine study. We believe that the CDV examination time could be reduced in the future by using multiple range gates simultaneously or using unfocused ultrasound transmit beams insonifying a large region at once [6].

REFERENCES

[1] S. Mendis et al., "World Health Organization (WHO) and International Society of Hypertension (ISH) risk prediction charts: assessment of cardiovascular risk for prevention and control of cardiovascular disease in low and middle-income countries," J. Hypertens., vol. 25, pp. 1578-1582, 2007.

[2] D. Lloyd-Jones et al., "Heart disease and stroke statistics 2010 update: A report from the American Heart Association," Circulation, vol. 121, pp. e46-e215, 2010.

[3] S. Sikdar, J. C. Lee, J. Remington, X.-Q. Zhao, S. L. Goldberg, K. W. Beach, and Y. Kim, "Ultrasonic Doppler vibrometry: Novel method for detection of left ventricular wall vibrations caused by poststenotic coronary flow," J. Am. Soc. Echocardiol., vol. 20, pp. 1386-1392, 2007.

[4] K. Comess, J. H. Choi, Z. Xie, S. Achenbach, W. Daniel, K. Beach, and Y. Kim, "Transthoracic coronary Doppler vibrometry in the evaluation of normal volunteers and patients with coronary artery stenosis," Ultrasound Med. Biol., vol. 37, pp. 679-687, 2011.

[5] M. D. Cerqueira, N. J. Weissman, V. Dilsizian, et al., "Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart: A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association," Circulation, vol. 105, pp. 539-542, 2002.

[6] M. Fink, L. Sandrin, M. Tanter, S. Catheline, S. Chaffai, J. Bercoff, and L. Gennisson, "Ultra high speed imaging of elasticity," Proc. IEEE Ultrasonics Symposium, pp. 1811-1820, 2002.