Fully-Automated Diagnosis of Aortic Stenosis Using Phonocardiogram-Based Features*

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***Abstract*— The irreversible damage and eventual heart failure caused by untreated aortic stenosis (AS) can be prevented by early detection and timely intervention. Prior work in the field of phonocardiogram (PCG) signal analysis has provided proof of concept for using heart-sound data in AS diagnosis. However, such systems either require operation by trained technicians, fail to address a diverse subject set, or involve unwieldy configuration procedures that challenge real-world application. This paper presents an end-to-end, fully-automated system that uses noise-subtraction, heartbeat-segmentation and quality-assurance algorithms to extract physiologically-motivated features from PCG signals to diagnose AS. When tested on n=96 patients showing a diverse set of cardiac and non-cardiac conditions, the system was able to diagnose AS with 92% sensitivity and 95% specificity.**

I. Introduction

Timely diagnosis of aortic stenosis (AS) improves long-term patient outcomes by lowering the risk of comorbidity [1][2]. Current diagnostic techniques such as cardiac auscultation and echocardiography require operation by physicians or trained technicians and involve high screening costs [3]. The associated clinical and financial burden can be mitigated by adopting a fully-automated, low-cost system capable of early and reliable AS diagnosis.

Prior studies have focused on developing and validating screening tools that use patient phonocardiogram (PCG) data to detect the presence of systolic heart murmurs [4][5]. These tools operate on PCG signals by extracting temporal, spectral or other features and supplying these as inputs to classification engines such as k-nearest neighbors, support-vector machines, or artificial neural networks [6][7][8].

The heart sounds used to develop and evaluate these tools are collected from carefully-controlled sources such as online databases, volunteer participants, clinical subjects presenting a specific set of medical conditions, or completely healthy individuals [9][10][11]. The data collection protocol requires the subject to remain quiet or motionless and may additionally call for voluntary apnea [6]. Manual PCG heartbeat-segmentation and feature-extraction processes also require time-intensive visual or auditory inspection by trained technicians [4][8].

Although prior studies in this emerging field provide good proof of concept, there is still a need for an end-to-end, fully-automated system that can provide clinically significant diagnoses at the point-of-care without expert supervision. To enable widespread adoption, such a system would require training and validation across a large heart-sound dataset collected in a clinical setting consisting of adult subjects showing diverse medical histories.

This paper presents a fully-automated PCG-based system that leverages heartbeat segmentation and data-quality assurance to extract physiologically-motivated features for AS diagnosis.

Section II introduces the subject population and describes the data collection, noise subtraction, heartbeat segmentation and feature extraction framework. Section III presents diagnostic results and demonstrates clinical significance of the proposed system.

II. Methods

A. Data Collection

Synchronous PCG and electrocardiogram (ECG) signals were acquired after obtaining informed consent from adult inpatients (n=96) at Ronald Reagan University of California Los Angeles (UCLA) Medical Center (Los Angeles, CA, USA) between March 2016 and September 2017. This clinical study was approved by the UCLA Office of the Human Research Protection Program (Study Identifier: 14-000670). Subjects included males and females between 19 and 95 years old (mean age of 57±18 years), between 40 and 116 kg in weight (mean weight of 79±17 kg) and exhibited one or more of 81 types of cardiac and non-cardiac afflicted conditions in their medical history. 12 of these 96 subjects were diagnosed as having AS by a medical sonographer using echocardiography, and these diagnoses were independently confirmed through auscultation by a physician.

PCG signals were acquired at the aortic auscultation region on the anterior chest wall at a sample rate of 512 Hz using an electret microphone housed in an ABS-plastic body with a membrane made of 0.4 mm-thick nitrile elastomer [12][13]. The membrane provided coupling with the patient's skin and allowed for transfer of acoustic signals into the sensor chamber for measurement by the microphone. The location for sensor placement was determined relative to the suprasternal notch and did not require physician intervention.

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ECG signals were acquired using 3 electrodes placed proximally on the two upper limbs and abdomen at a sample rate of 300 Hz. 1 to 16 minutes of signals (mean duration of 7±3 minutes) were acquired per subject and stored for offline analysis in Matlab (MathWorks, MA, USA).

B. Automated Heartbeat Segmentation

Noise artifacts from speech, motion and other disturbances were minimized in the PCG signal using a spectral noise subtraction algorithm commonly used in speech processing. As described in [14], the spectral noise estimate was subtracted from raw signal to generate the denoised PCG signal. A fourth-order Butterworth band-pass filter with cutoff frequencies of 25 and 140 Hz was then applied to obtain a PCG signal of improved audio quality.

ECG signals were band-pass filtered using a fourth-order Butterworth filter with cutoff frequencies of 1 and 30 Hz and subsequently processed to detect the start and end times for individual beats for the purpose of heartbeat segmentation [15]. The short-term periodicity of successive cardiac cycles was then leveraged to segment the corresponding noise-subtracted PCG signal for each heartbeat into diastolic interval, first heart sound (S1), systolic interval, and second heart sound (S2) [16][17].

A support-vector machine classifier trained on temporal, spectral and model-based features was used to select beats of high signal quality. The individual high-quality heartbeats selected for further analysis met the following additional criteria:

- Both S1 and S2 sounds were successfully identified
- Systolic interval was free of any signal excursions greater than 50% of S1 or S2 peak amplitude
- Beat duration was within ±20% of the median beat duration for that subject

2 to 484 eligible beats per subject (mean beat-count of 127±121 beats) satisfied the above criteria and were included in the final heart-sound dataset.

C. Feature Extraction

For each eligible heartbeat, the PCG signal corresponding to the second half of S1 sound, systolic interval, and first half of S2 sound was extracted and band-pass filtered using a fourth-order Butterworth filter with cutoff frequencies of 38 and 154 Hz (Fig. 1). The resulting data vector, d_{sys}, was used to extract features to identify systolic murmurs unique to AS (Fig. 2).

First, an amplitude-based feature was developed to detect systolic murmurs regardless of their physiological origin. The absolute value of the Hilbert transform [18] was used to compute the signal envelope of d_{sys}, and the resulting envelope was low-pass filtered using a fourth-order Butterworth filter with a cutoff frequency of 51 Hz to faithfully recreate its shape. The 10th percentile value of the filtered envelope provided a good approximation of the fluctuating noise level and was used to estimate the noise floor for that systolic interval. Then, the first 25% and last 15% of the envelope were removed to ensure that S1 and S2

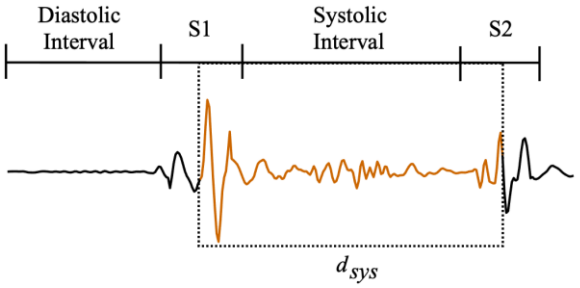

Figure 1. Example of segmentation and d_{sys} extraction in a heartbeat. The PCG signal extracted as d_{sys} corresponds to the second half of S1, systolic interval and first half of S2.

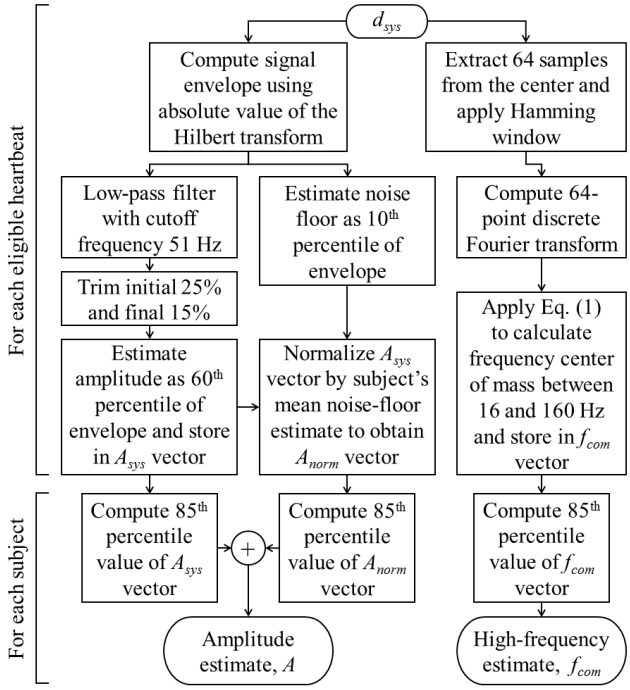

Figure 2. Summary of feature extraction from the d_{sys} vector of a heartbeat. One amplitude estimate (A) and one high-frequency estimate (f_{com}) is extracted for each of the 96 subjects.

sound signals did not influence systolic amplitude computation. The 60th percentile value of the remaining envelope provided a reliable measure of signal amplitude independent of any outlier excursions caused by non-cardiac signals and was used to estimate the systolic interval amplitude, A_{sys}. All A_{sys} values for a subject were stored in a vector, and a corresponding A_{norm} vector was created by normalizing each element of the A_{sys} vector by the mean noise-floor estimate for that subject.

Not all heartbeats in an AS subject were expected to exhibit systolic murmurs due to variations in underlying physiology and sensor coupling. The final systolic amplitude features for each subject were therefore set to the 85th percentile value of their A_{sys} *and* A_{norm} vectors to reduce the impact of systolic intervals that did not demonstrate murmurs.

Next, a frequency-based feature was developed to differentiate AS subjects from others with elevated systolic amplitude estimates. It was expected that the proximity of the aortic auscultation site to the stenosed aortic valve would

allow for the recording of minimally-attenuated broadband systolic murmurs with greater high-frequency amplitude in AS subjects [12][19]. To this end, a 64-point discrete Fourier transform (DFT) was computed for a 64-sample (125 ms) subvector extracted from the center of d_{sys} after application of a Hamming window. The center of mass, f_{com}, of the systolic interval frequency distribution was then calculated as

$$f_{com} = \sum_{i=3}^{21} x_i p_i \; / \; \sum_{i=3}^{21} p_i \;, \qquad (1)$$

where x_i and p_i were the frequency and amplitude of the i^{th} bin in the single-sided DFT, and limits 3 and 21 on i corresponded to 16 and 160 Hz respectively. All f_{com} values for a subject were stored in a vector and, similar to the systolic amplitude estimation process, the final systolic spectral feature for each subject was also set to the 85th percentile value of the f_{com} vector.

The individual A_{sys}, A_{norm} and f_{com} feature values for all 96 subjects were then standardized by subtracting the mean and dividing by standard deviation. Finally, A_{sys} and A_{norm} values were summed to yield a single systolic amplitude feature, A.

Subjects with systolic murmurs were expected to have elevated systolic amplitudes, and subjects with systolic murmurs due to AS were expected to have elevated levels of high-frequency systolic content [19].

An example of feature extraction in AS and non-AS subjects is shown in Fig. 3. The AS subject's systolic interval had feature values of A=3.4 (Fig. 3a) and f_{com}=0.4 (Fig. 3b). In comparison, the non-AS subject's systolic interval had feature values of A=0.41 (Fig. 3c) and f_{com}= –1.06 (Fig. 3d). The AS subject had elevated systolic amplitude and high-frequency content relative to the non-AS subject.

For diagnostic purposes, a subject was classified as having AS if their A and f_{com} values exceeded thresholds of 0.7 and -1.0 respectively (Fig. 4).

III. Results and Discussion

The noise-subtraction algorithm enabled processing of low signal-to-noise-ratio data collected without physician intervention in the non-controlled and fast-paced environment of a preoperative holding area [20]. Noise-subtracted PCG signals were found to be of qualitatively higher audio fidelity than raw signals. The heartbeat-selection algorithm enabled detection of high-quality beats even in severely-afflicted subjects or those with abnormal sinus rhythm. The end-to-end AS diagnosis system operated in a fully-automated fashion with a per-subject computational runtime of 6 to 125 seconds on a 2.3 GHz Intel Core i7 processor (mean runtime of 52±22 seconds).

Mean and standard deviation values of the two features for AS and non-AS subjects are summarized in Table I. Two-sample t-test p-values of $2.2\text{x}10^{-8}$ and 0.069 for A and f_{com} respectively indicated that the amplitude feature was strongly correlated with AS in the diverse population set, whereas the spectral feature appeared less significantly linked across the same set. However, such an analysis for the spectral feature was misleading because while the amplitude feature was intended to identify subjects with systolic murmurs, the

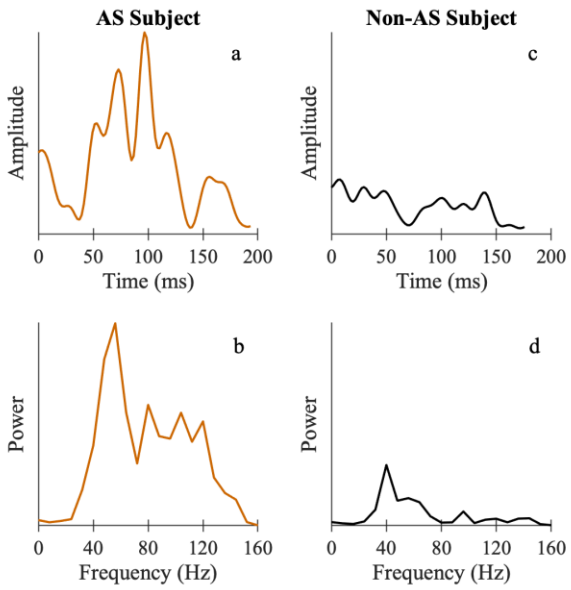

Figure 3. Illustration of feature extraction from the systolic interval of an AS subject (a,b) and a non-AS subject (c,d). a) AS subject systolic signal envelope showing mid-systolic murmur and A=3.4. b) AS subject systolic DFT showing elevated high-frequency content and f_{com}=0.4. c) Non-AS subject systolic signal envelope with A=0.41. d) Non-AS subject systolic DFT with f_{com}= –1.06.

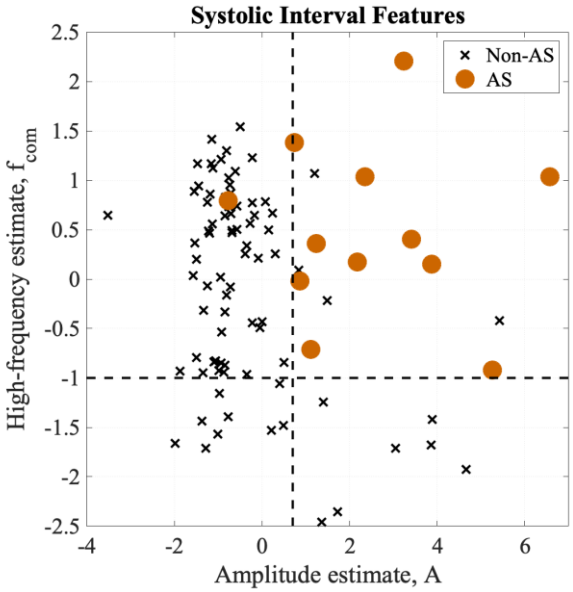

Figure 4. Standardized center-of-mass of systolic frequency distribution (f_{com}) vs. standardized systolic envelope amplitude (A) for n=96 subjects. Diagnostic criteria are shown as dashed lines. 11 of 12 AS subjects and 4 of 84 non-AS subjects show $f_{com} > -1$ and $A > 0.7$. AS subjects visibly cluster in the top-right quadrant, whereas non-AS subjects exhibiting other systolic-murmur inducing conditions exceed threshold on A but not on f_{com}, and hence appear in the bottom-right quadrant.

TABLE I. Statistical Measures for Individual Features

Feature	Mean and Standard Deviation Values			p-value
	All subjects	*AS subjects*	*Non-AS subjects*	
A	0.00 ± 1.78	2.50 ± 2.08	–0.36 ± 1.43	$2.2\text{x}10^{-8}$
f_{com}	0.00 ± 1.00	0.49 ± 0.87	–0.07 ± 1.00	0.069

spectral feature was intended to differentiate between subjects with AS and non-AS murmurs within this subset and its relatively high *p*-value across the diverse population set was therefore unimportant.

11 of 12 AS subjects and 4 of 84 non-AS subjects had standardized feature values above both diagnostic thresholds, corresponding to 92% sensitivity and 95% specificity. Standard receiver operating characteristic (ROC) analysis did not apply directly to these results because two diagnostic thresholds were used on two features. The complementary nature of the two features was instead observed by applying either threshold first, and then performing ROC analysis of the other feature for the remaining set of subjects. For example, applying the $f_{com} > -1$ criterion removed 16 subjects, and ROC analysis of the amplitude feature for the remaining 80 subjects yielded an area under the curve (AUC) value of 0.94 (Fig. 5a). This indicated that the amplitude feature provided significant complementary information to the spectral feature. Similarly, ROC analysis of the spectral feature for the set of 22 subjects with $A > 0.7$ yielded an AUC value of 0.87 (Fig. 5b), further confirming the complementary nature of the two features.

The importance of combining A and f_{com} for AS diagnosis was especially seen in the case of non-AS subjects afflicted by other systolic-murmur-inducing conditions such as ventricular and atrial septal defect, mitral regurgitation, mitral valve prolapse, tricuspid regurgitation and hypertrophic cardiomyopathy [21]. These subjects typically exceeded the threshold on A, but not on f_{com}, which indicated that the two features were independently informative and specific to AS.

The noise-subtraction, beat-selection and feature-extraction algorithms along with clinically significant classification results demonstrate the real-world applicability of the AS diagnosis system and suggest that similar fully-automated systems could also be leveraged to diagnose other murmur conditions.

IV. Conclusion

This paper presented an end-to-end, fully-automated and clinically-relevant AS diagnosis system leveraging temporal and spectral features. PCG signals were collected without physician intervention in real-world conditions of a hospital using a single acoustic sensor from adult subjects exhibiting a diverse set of conditions. Noise-subtraction and beat-selection algorithms were applied to select high-quality heartbeats. Features were extracted from the systolic interval of these beats to determine the presence of systolic murmurs and to estimate their high-frequency content. Subjects with systolic intervals showing elevated amplitude and high-frequency content were classified as having AS with 92% sensitivity and 95% specificity.

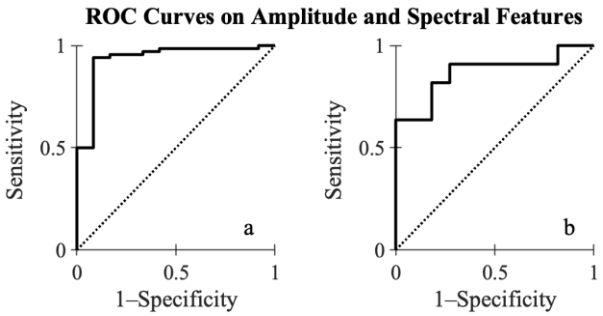

Figure 5. ROC curves on amplitude and spectral features. a) ROC curve on amplitude feature (A) for subjects with $f_{com} > -1$, yielding AUC = 0.94. b) ROC curve on spectral feature (f_{com}) for subjects with $A > 0.7$, yielding AUC = 0.87.

References

[1] Owen, Andrew, and Michael Y. Henein. "Challenges in the management of severe asymptomatic aortic stenosis." *European Journal of Cardio-Thoracic Surgery* 40.4 (2011): 848-850.

[2] Carabello, Blase A., and Walter J. Paulus. "Aortic stenosis." *The Lancet* 373.9667 (2009): 956-966.

[3] 2015 Review of recent technical advances in electronic stethoscopes - Leng, Shuang, et al. "The electronic stethoscope." *Biomedical engineering online* 14.1 (2015): 66.

[4] Gharehbaghi, Arash, et al. "A hybrid model for diagnosing sever [sic] aortic stenosis in asymptomatic patients using phonocardiogram." *World Congress on Medical Physics and Biomedical Engineering, June 7-12, 2015, Toronto, Canada*. Springer, Cham, 2015.

[5] Kang, Sukryool, et al. "Automated Identification of Innocent Still's Murmur in Children." *IEEE Trans. Biomed. Engineering* 64.6 (2017): 1326-1334.

[6] Delgado-Trejos, Edilson, et al. "Digital auscultation analysis for heart murmur detection." *Annals of biomedical engineering* 37.2 (2009): 337-353.

[7] Choi, Samjin, and Zhongwei Jiang. "Cardiac sound murmurs classification with autoregressive spectral analysis and multi-support vector machine technique." *Computers in biology and medicine* 40.1 (2010): 8-20.

[8] Ahlstrom, Christer, et al. "Feature extraction for systolic heart murmur classification." *Annals of biomedical engineering* 34.11 (2006): 1666-1677.

[9] Maglogiannis, Ilias, et al. "Support vectors machine-based identification of heart valve diseases using heart sounds." *Computer methods and programs in biomedicine* 95.1 (2009): 47-61.

[10] Thiyagaraja, Shanti R., et al. "A novel heart-mobile interface for detection and classification of heart sounds." *Biomedical Signal Processing and Control* 45 (2018): 313-324.

[11] Hu, Wei, et al. "Unsupervised Feature Learning for Heart Sounds Classification Using Autoencoder." *Journal of Physics: Conference Series*. Vol. 1004. No. 1. IOP Publishing, 2018.

[12] Karnath, Bernard, and William Thornton. "Auscultation of the heart." *Hospital Physician* 38.9 (2002): 39-45.

[13] U.S. Food and Drug Administration. June 8, 2018. Web. https://www.accessdata.fda.gov/cdrh_docs/pdf17/K173156.pdf

[14] Upadhyay, Navneet, and Abhijit Karmakar. "Speech enhancement using spectral subtraction-type algorithms: A comparison and simulation study." *Procedia Computer Science* 54 (2015): 574-584.

[15] Yeh, Yun-Chi, and Wen-June Wang. "QRS complexes detection for ECG signal: The Difference Operation Method." *Computer methods and programs in biomedicine* 91.3 (2008): 245-254.

[16] Liang, H., S. Lukkarinen, and I. Hartimo. "Heart sound segmentation algorithm based on heart sound envelogram." *Computers in Cardiology* 1997. IEEE, 1997.

[17] Ari, Samit, Prashant Kumar, and Goutam Saha. "A robust heart sound segmentation algorithm for commonly occurring heart valve diseases." *Journal of medical engineering & technology* 32.6 (2008): 456-465.

[18] Dugundji, J. "Envelopes and pre-envelopes of real waveforms." IRE *Transactions on Information Theory* 4.1 (1958): 53-57.

[19] Kim, Dosik, and Morton E. Tavel. "Assessment of severity of aortic stenosis through time-frequency analysis of murmur." *Chest* 124.5 (2003): 1638-1644.

[20] Sullivan, Ellen E. "Preoperative holding areas." *Journal of PeriAnesthesia Nursing* 15.5 (2000): 353-354.

[21] Etchells, Edward, Chaim Bell, and Kenneth Robb. "Does this patient have an abnormal systolic murmur?." *Jama* 277.7 (1997): 564-571.