HHS Public Access

Author manuscript

IEEE Trans Ultrason Ferroelectr Freq Control. Author manuscript; available in PMC 2020 March 01.

Published in final edited form as:

IEEE Trans Ultrason Ferroelectr Freq Control. 2019 March ; 66(3): 433–441. doi:10.1109/TUFFC.2018.2885777.

Improved Visualization in Difficult-to-Image Stress Echocardiography Patients Using Real-Time Harmonic Spatial Coherence Imaging

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Abstract

Stress echocardiography is used to detect myocardial ischemia by evaluating cardiovascular function both at rest and at elevated heart rates. Stress echocardiography requires excellent visualization of the left ventricle (LV) throughout the cardiac cycle. However, LV endocardial border visualization is often negatively impacted by high levels of clutter associated with patient obesity, which has risen dramatically worldwide in recent decades. Short-lag spatial coherence (SLSC) imaging has demonstrated reduced clutter in several applications. In this work, a computationally-efficient formulation of SLSC was implemented into an object-oriented GPU-based software beamformer, enabling real-time (>30 fps) SLSC echocardiography on a research ultrasound scanner. The system was then used to image 15 difficult-to-image stress echocardiography patients in a comparison study of tissue harmonic imaging (THI) and harmonic spatial coherence imaging (HSCI). Video clips of four standard stress-echocardiography views acquired with either THI or HSCI were provided in random shuffled order to three experienced readers. Each reader rated the visibility of 17 LV segments as “invisible”, “suboptimally

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visualized”, or “well-visualized”, with the first two categories indicating a need for contrast agent. In a symmetry test unadjusted for patient-wise clustering, HSCI demonstrated a clear superiority over THI ($p < 0.0001$). When measured on a per-patient basis, the median total score significantly favored HSCI with $p < 0.001$. When collapsing the ratings to a two-level scale (“needs contrast” vs. “well-visualized”), HSCI once again showed an overall superiority over THI, with $p < 0.0001$ by McNemar test adjusted for clustering.

Index Terms—

Ultrasound; Image enhancement/restoration (noise and artifact reduction)

I. Introduction

Transthoracic echocardiography is the second-most commonly utilized imaging modality for the heart. Transthoracic echocardiography allows for quantitative measurements of ventricular and atrial mass and volume, estimation of ejection fraction, assessment of wall motion, and measurement of chamber flow velocities to aid in the evaluation of both systolic and diastolic function [1], [2]. Stress echocardiography is a transthoracic technique used to detect myocardial ischemia in the left ventricle (LV) that may not manifest at rest. The wall motion of the LV is first observed at rest, and then again in response to cardiac stress induced with either exercise or a pharmacological agent. A lack of increase in wall motion is indicative of a restricted blood supply to the heart caused by ischemia in the coronary arteries.

Visualization of the endocardial border is essential in determining LV function. In stress echocardiography, visualization is deemed inadequate when two or more segments of the LV (using the 16- or 17-segment model [2]–[4]) are not visualized. Transthoracic echocardiography is reported to have inadequate visualization of the left ventricular endocardial border in 12–17% of patients [5]–[7]. However, echocardiography is significantly and negatively impacted by patient obesity. A study by Finkelhor et al. [8] found that 49.7% of patients referred to the Case Western Reserve University Medical Center outpatient echocardiography laboratory were obese, and that obese patients had image quality ratings of poor in 14% of cases, compared to 3.9% of cases for normal weight patients. They also found that obese patients more frequently required use of ultrasound contrast agents to assess LV ejection fraction, and their exams required significantly more time than those of normal-weight patients. Unfortunately, the prevalence of obesity has risen dramatically in recent decades. It is estimated that the proportion of adults that are overweight (BMI 25.0–29.9) or obese (BMI ≥ 30.0) is as high as 69.3% in the United States [9]–[11], as high as 50.2% in the European Union [12], and is also increasing in Asia [13].

Inadequate visualization with transthoracic echocardiography incurs additional costs through the use of contrast agents or additional imaging procedures such as transesophageal echocardiography, x-ray computed tomography, or magnetic resonance imaging. A major source of image degradation in transthoracic echocardiography is clutter, appearing as an overlying haze that fills in anechoic regions and obscures anatomical features that are critical

to diagnosis [14], [15]. In apical views acquired in transthoracic echocardiography, for example, clutter is generally strong near the apex of the heart, thereby obscuring it. We have previously shown that much of this clutter is a result of reverberation among tissue layers [16]–[18]. Reverberation clutter occurs when an acoustic wave reflects multiple times between the subcutaneous tissue layers and creates a diffuse speckle-like texture that overlies the image [17].

Current clinical practices aimed at reducing image clutter involve the use of tissue harmonic imaging (THI) and the use of contrast agents. In THI, images are formed at the second harmonic frequency of the transmitted pulse. Because second harmonic frequencies are not generated in tissue until the pulse has propagated a sufficient distance, the reflections from second harmonics generally avoid reverberation in the subcutaneous tissues. We have previously shown that the major mechanism leading to improvement in image quality with THI is associated with the reduction in reverberation clutter from the proximal tissue layers [16]. However, THI does not always eliminate reverberation clutter and is still degraded by it [19]. The addition of a contrast agent to transthoracic echocardiography has shown improved visualization of the endocardial border, decreasing the number of inadequate exams to less than 1% [5], [6], [20]. However, contrast agents increase cost and extend exam times. In a small percentage of patients, contrast agent is not recommended due to allergic reaction [21].

We have recently introduced a clutter-reducing beamforming technique called short-lag spatial coherence (SLSC) [22]. Whereas B-mode images display the magnitude of the backscattered echo, SLSC images display its spatial coherence. Spatial coherence is a generic term that describes the overall similarity of the echo wavefront as measured between two points on the aperture. In SLSC imaging, wavefront similarity is quantified using the average correlation coefficient between any two points with a given spacing, referred to as their lag. In particular, it is the average correlation coefficient for small spacings, i.e. “short” lags. Clutter characteristically exhibits low SLSC values as compared to tissue even when it is similar in magnitude, allowing SLSC imaging to distinguish between tissue and clutter in instances where B-mode cannot. *In vivo* application of SLSC has been used to suppress clutter in the liver [23] and in fetal imaging [24], [25] as well as to improve visualization in blood flow estimation [26] and ultrasound molecular imaging [27]. SLSC imaging with second harmonics, referred to as harmonic spatial coherence imaging (HSCI), has been investigated in simulations and *in vivo* [19], [23], demonstrating further clutter reduction beyond SLSC imaging at the fundamental frequency or THI alone.

The computational load of spatial coherence estimation is several orders of magnitude greater than delay-and-sum (DAS) beamforming [28], presenting an obstacle to the translation to real-time imaging. We have previously proposed several algorithmic modifications to improve the computational throughput of SLSC up to 20-fold [28]. Despite these improvements, a CPU-based implementation remained insufficient for achieving real-time imaging at frame rates adequate for cardiac imaging, which requires roughly 30 frames per second (fps). Earlier studies of cardiac SLSC imaging [15], [29] and HSCI [30] were not real-time.

Recently, graphics processing units (GPUs) have been used to substantially accelerate scientific computing. GPUs, originally designed for rendering computer graphics, are programmable devices that are composed of hundreds to thousands of computational cores that operate in parallel. GPUs are particularly well-suited for applications where the same operations are applied to multiple data. This includes ultrasound beamforming algorithms such as DAS and SLSC, where magnitude or coherence estimation is applied on a pixel-by-pixel basis. Using GPU-based beamforming, we have previously demonstrated the feasibility of achieving real-time cardiac SLSC imaging [31] and real-time HSCI [32]. Others have also demonstrated beamforming with GPUs for DAS [33], [34] and Capon beamforming [35].

In this study, we demonstrate the clinical translation of HSCI in a study of stress echocardiography patients using a GPU-based software beamformer. We describe in detail the methodology used in developing the software beamformer and in implementing it on a research ultrasound scanner to achieve real-time THI and HSCI at over 30 fps. The custom scanner is used to assess the visibility of LV segments in difficult-to-image stress-echocardiography patients in a comparison study of THI and HSCI.

II. Methods

A. Beamforming Methods

THI and HSCI images were reconstructed using channel signals received from second harmonic echoes using the standard procedures for B-mode and SLSC imaging [19]. Denote the N analytic channel signals focused at a field point x as $s_i(x)$, $i = 1, \dots, N$. THI images were formed via summation, envelope detection, and logarithmic compression:

$$I_{\text{THI}}(x) = 20 \log_{10} \left| \sum_{i=1}^N s_i(x) \right| \quad (1)$$

The original SLSC beamformer [22] estimates the spatial coherence as a function of lag m as the average correlation coefficient:

$$\hat{\rho}(x, m) = \frac{1}{N-m} \sum_{i=1}^{N-m} \frac{\sum_k s_i(x+k) s_{i+m}^*(x+k)}{\sqrt{\sum_k |s_i(x+k)|^2 \sum_k |s_{i+m}(x+k)|^2}} \quad (2)$$

where k iterates over an axial kernel, typically of length 1λ . To improve computational throughput and reduce estimator variance, an efficient implementation of the SLSC beamformer introduced by Hyun et al. [28] was used:

$$\hat{\rho}(x, m) = \frac{\sum_{i=1}^{N-m} s_i(x) s_{i+m}^*(x)}{\sqrt{\sum_{i=1}^{N-m} |s_i(x)|^2 \sum_{i=1}^{N-m} |s_{i+m}(x)|^2}}. \quad (3)$$

This estimator does not utilize an axial kernel, which improves computational throughput and maintains axial resolution, and computes a single ensemble correlation coefficient rather

than the average over all element pairs. The HSCI pixel value at x was then computed as the average correlation coefficient over “short lags”, defined as $1 \leq m \leq M$:

$$I_{\text{HSCI}}(x, M) = \frac{1}{M} \sum_{m=1}^M \hat{\rho}(x, m), \quad (4)$$

The threshold was selected as $M = 10$, corresponding to 16% of the aperture. HSCI images were displayed on a linear scale.

B. GPU-Based Software Beamforming

A GPU-based software beamformer was utilized to achieve customizable real-time ultrasound beamforming and image display for THI and HSCI. An object-oriented library was written in C++ and CUDA (NVIDIA, Santa Clara, CA), and was composed of classes that performed tasks ranging from parsing the raw channel data buffer to estimating the spatial coherence to form HSCI images. To maintain consistency, each beamforming class was derived from a common parent abstract base class called **DataProcessor**, illustrated in Figure 1. A **DataProcessor** was designed to accept a pointer to GPU memory, perform some class-specific processing via CUDA kernels, and output a pointer to GPU memory containing the processed output.

Real-time THI and HSCI imaging was achieved using subclasses derived from **DataProcessor**, listed below along with a brief description of their purpose:

- **DataFormatter** – Format the raw data into a form acceptable by other classes. Optionally align the direct quadrature sampling performed by a Verasonics research scanner (Verasonics Inc., Kirkland, WA, USA) to obtain demodulated channel data.
- **HilbertTransform** – Convert real radiofrequency data into complex analytic data via the Hilbert transform.
- **Focus** – Demodulate channel data to baseband and apply focusing time delays.
- **Bmode** – Sum focused complex channel data, detect magnitude, and apply logarithmic compression.
- **SLSC** – Compute the short-lag spatial coherence.

A full beamforming pipeline was constructed by concatenating instances of each beamforming class such that the output of one **DataProcessor** was immediately the input of the next.

A two-stage procedure was employed to achieve real-time processing. All time-intensive and non-repeating tasks (e.g., memory allocation, loading delay tables into GPU memory) were performed on the first invocation to “initialize” a pipeline. Initialized pipelines then processed the raw data in real time by executing the respective computations of each **DataProcessor** object in order, with the last object outputting the final processed image. Costly CPU-GPU memory transfers were minimized by keeping the data in GPU memory and passing data pointers between objects. The class structure of the library additionally

allowed objects to be interchanged according to the imaging task at hand (e.g., using a **HilbertTransform** versus **DataFormatter** to obtain complex data), promoting flexibility in the computational pipeline and simplifying memory management and multi-GPU operation. Two GPUs were used in parallel to simultaneously execute two computation pipelines by utilizing POSIX threads, with each GPU reconstructing a subset of the output THI and HSCI image. Scan conversion was performed after stitching the beamforming outputs of the GPUs together. The dual-GPU workflow is depicted in Figure 2. The computational throughput for a single pipeline was measured on an NVIDIA GeForce GTX 1080 Ti GPU using the NVIDIA Visual Profiler tool.

C. Real-Time Imaging System

The GPU beamformer was used in conjunction with a Verasonics Vantage 256 ultrasound research scanner to perform real-time THI and HSCI. Pulse-inversion harmonic imaging was performed with a Verasonics P4-2v transducer using two focused 2 MHz transmissions with 180° phase offset. The transmit focus (6–8 cm) and imaging depth (14–16 cm) were adjusted on a per patient-basis. The echoes were summed and bandpass filtered at 4 MHz. Demodulated channel data were obtained by aligning the direct quadrature sampling of the Verasonics with **DataFormatter** objects. Each frame consisted of 65 lines scanned in a 72° sector. The raw channel signals were transferred in real-time at 32 frames per second (fps) to a Linux workstation where the software beamformer was used to reconstruct THI and HSCI images in real-time using two NVIDIA Quadro K2200 GPUs [31]. Each GPU processed half of the output image independently (see Figure 2).

D. Acoustic Output Safety Measurements

Acoustic output measurements were performed prior to commencing the study to ensure adherence to FDA safety guidelines [36]. The acoustic output was measured in a degassed water tank with a membrane hydrophone (polyvinylidene fluoride with a 0.6-mm spot size, Sonic Technologies, Wyndmoor, PA, USA) for a range of focal depths (6 cm–12 cm) and transmit voltages (7 V–15 V). For each configuration, the mechanical index (MI), thermal index (TI), derated spatial-peak temporal-average intensity (I_{SPTA}) and derated spatial-peak pulse-average intensity (I_{SPPA}) were computed. The thermal index was measured as the thermal index in soft tissue (TIS).

E. Study Design

The goal of this study was to investigate the impact of spatial coherence imaging on the ability to visualize LV segments in stress echocardiography patients with high levels of clutter. The study included only patients who required contrast agents as part of their normal standard of care due to poor image quality. Fifteen subjects undergoing stress-echocardiography exams were recruited under the institutional review board protocol Pro00030455 at Duke University and provided written informed consent. Imaging was performed at the Duke Echocardiography Clinic at the Duke Medical Center.

Matched THI and HSCI scans were reconstructed from the same channel data and displayed side-by-side in real-time to the sonographer. During live scanning, the raw channel data were recorded for 100 frames at 32 frames per second for each of four standard imaging views:

parasternal short-axis (PSA), parasternal long-axis (PLA), apical two-chamber (A2C), and apical four-chamber (A4C). Figure 3 shows an example of each view in a B-mode image, annotated with the segments visible within each view as defined by the standardized nomenclature in echocardiography [3]. Additionally, a simple spatiotemporal clutter filter [37], [38] was applied in post-processing, where the filter weights were adaptively selected such that only the most significant singular values (accounting for 60% of the total sum) were retained for all THI and HSCI scans to suppress thermal noise.

F. Data Analysis

A total of 30 image sets (15 THI, 15 HSCI) consisting of PSA, PLA, A2C, and A4C views from the 15 patients were shuffled in random order and presented to one cardiologist and two sonographers. Each reviewer scored the visibility of the 17 LV segments across the four views. Each segment was rated with a score of 0 (invisible), 1 (suboptimally visualized), and 2 (well visualized), where two or more contiguous segments of scores of 0 and 1 indicate a need for contrast agent. The readers were allowed to adjust the dynamic range of the images as desired. Four statistical tests were performed:

1. *Reader agreement:* The agreement between the three readers was assessed by a quadratically weighted kappa statistic, such that exact matches received a score of 1, adjacent values a score of 0.75, and non-adjacent values a score of 0.
2. *Global performance:* The THI and HSCI ratings for all segments for all three readers were compared using an exact test of symmetry.
3. *Patient-wise performance:* For each patient, a score was computed as the total of pairwise differences in ratings across segments, with negative scores favoring THI and positive scores favoring HSCI. A one-sided Wilcoxon signrank test was used to test for a median score greater than zero.
4. *Well-visualized segments:* Across all patients and segments, the ratings were collapsed to well-visualized (score of 2) vs. suboptimally visualized (score of 0 or 1) and tested for superiority of HSCI by a one-sided McNemar test adjusted for clustering within patients.

III. Results

A. Real-Time THI and HSCI

Table I lists the computation time used for each beamforming task. GPU-related tasks took 4.23 ms to compute a single frame of both B-mode and SLSC from the raw Verasonics channel data buffer, corresponding to a theoretical maximum achievable frame rate of 236 fps. Although CPU to GPU transfers were minimized so as to occur only once at the beginning of each frame, they still accounted for most of the overall computation time (76%), followed by SLSC (10.9%) and focusing (5.7%). The overhead non-GPU tasks, which includes the acoustic travel time of the waves, data transfer from the Verasonics to CPU memory, and display in a MATLAB figure, took a total of 27.07 ms to complete (640% of the total GPU time). The overall time per frame was 31.30 ms, corresponding to a framerate of 32 fps.

B. Acoustic Output Safety Measurements

Table II lists the measured acoustic outputs for the two focal depths at the maximum transmit voltage of 15 V. The highest measured values of MI, TI, I_{SPTA} , and I_{SPPA} are denoted in bold. Each of these values were within the FDA recommendations. It was also observed that deeper focal depths and lower transmit voltages resulted in lower values for each quantity.

C. Qualitative Imaging Results

Figure 4 displays THI and HSCI images of an example A2C view of the heart from patient #5. THI is logarithmically compressed and shows a dynamic range of 50 dB, whereas HSCI is shown on a linear scale. Clutter is visible in the THI image proximal to the transducer face, appearing as a hyperechoic haze and partially obscuring the endocardial border near the apex (segment 17). The clutter is suppressed in the HSCI image, revealing the extension of the pointed tip of the LV apex into the cluttered region of the THI image. Figure 5 shows example THI and HSCI images of the PSA view from patient #1. The outline of the LV is not cleanly delineated in the THI image. In the HSCI image, the LV border is apparent in the region highlighted by arrows. The endocardium is visualized to be more coherent than the blood within the chamber. We have included two supplementary multimedia AVI format movie clips from which Figures 4 and 5 were formed, showing side-by-side THI and HSCI throughout the cardiac cycle at 32 fps. These will be available at <http://ieeexplore.ieee.org>.

D. Data Analysis

The median scores for LV segment visibility across the three readers are presented in Fig. 6a, and the net change in scores from THI to HSCI are presented in Fig. 6b. Overall, HSCI improved segment visibility in 156 segments, did not alter visibility in 82 segments, and reduced visibility in 17 segments compared to THI. Additionally, HSCI improved the average score for basal segments (#1 to #6) by 0.21, mid-cavity segments (#7 to #12) by 0.40, and apical segments (#13 to #17) by 0.35. In patient #5, HSCI improved visualization sufficiently such that no two contiguous LV segments were suboptimally visualized, eliminating the need for contrast agents altogether.

1. *Reader agreement:* Table III lists the inter-reviewer agreement statistics for the THI and HSCI methods. The overall agreement among readers had a Kappa statistic of .48 for both the THI and HSCI methods, indicating a moderate level of agreement [39], [40].
2. *Global performance:* The summarized segment visibility scores are presented in Table IV. Overall, a greater proportion of the 765 total LV segments were well-visualized by HSCI (35%) than THI (20%), and a smaller proportion were rated as not visible by HSCI (25%) than THI (42%). There were a total of 9 instances in which a well-visualized THI segment was degraded by HSCI, but 120 instances in which a suboptimally visualized THI segment was well-visualized by HSCI. In a symmetry test unadjusted for patient-wise clustering, HSCI demonstrated a clear superiority over THI with $p < 0.0001$.

3. *Patient-wise performance:* Figure 7 plots the net score per patient (sum of HSCI scores minus THI scores for all segments). Across 15 patients and 3 readers, there were only two readings with a net score that favored THI. A subset of the patients accounted for the majority of the improvement: 36% of readings accounted for 65% of the net improvement in total score per patient due to HSCI. When measured on a per-patient basis, only two patients had a net score that favored THI. The median score across 15 patients was significantly greater than zero with $p < 0.001$.
4. *Well-visualized segments:* When collapsing the ratings to a two-level scale (well-visualized or not well-visualized), HSCI once again showed an overall superiority over THI, with $p < 0.0001$ by McNemar test adjusted for clustering.

IV. Discussion

Strong reverberation clutter cannot be distinguished from endocardial echoes with a similar magnitude using DAS beamforming alone. In these cases, spatial coherence beamforming can be used to suppress reverberation clutter while retaining the endocardial echoes because the clutter characteristically exhibits little to no spatial coherence, whereas human tissue generates echoes with moderate levels of coherence [18]. These effects were particularly noticeable in Figure 4, where the apex of the LV was visualized beneath the clutter by HSCI, and in Figure 5, where the LV chamber and the endocardium were distinguished more clearly by HSCI. Across three readers, HSCI increased the number of visible and well-visualized LV segments over THI by a statistically significant margin. The results indicate that HSCI provides additional clutter reduction beyond that afforded by harmonic imaging, which is consistent with previous findings [19], [23]. In particular, the greatest improvements in per-segment visibility score were observed in the apical (+0.35) and mid-cavity (+0.40) segments, which are generally more strongly affected by reverberation clutter than the deeper basal segments (+0.21). When using the median score across the 3 reviewers, the HSCI image quality for patient #5 was high enough that no two contiguous LV segments were suboptimally visualized, meaning that contrast agent was no longer necessary under HSCI.

The current study addresses the effects of SLSC beamforming in the context of stress echocardiography under clinically relevant imaging conditions. Prior studies have also shown an improvement in LV visibility using SLSC beamforming over DAS; however, these studies were performed with protocols that do not reflect clinical usage of ultrasound [41] due to the use of fundamental imaging [15], [29], [31] or lack sufficient frame rate [15], [29], [30]. Here, harmonic images were acquired in four standard views as per the current clinical standard of care, permitting a complete visibility assessment of all 17 LV segments. The patient population was specifically selected as “difficult-to-image” stress echocardiography patients who required contrast agents as part of their standard of care. Within this clinically relevant context, HSCI resulted in clear and significant improvements over THI, demonstrating its potential for improving LV imaging in difficult-to-image patients without using contrast agents.

Image degradation in echocardiography can be caused via a multitude of mechanisms beyond that of reverberation clutter. One indication of this is that HSCI did not improve image quality uniformly across all patients, with 36% of the readings accounting for 65% of the net improvement in total score per patient due to HSCI. A possible explanation is that HSCI is more effective at tackling one particular mechanism (e.g., in-coherent clutter) and less effective for others, such as physical obstructions that limit ultrasound penetration (e.g., scar tissue, high attenuation). We also did not consider the effects of post-processing aside from using a simple spatiotemporal filter, which eliminated salt-and-pepper noise throughout the video clip. Commercial systems utilize extensive post-processing to reduce degradation caused by thermal and speckle noise. Commercial systems may also be able to more accurately produce inverted pulses, which could improve harmonic image quality. A future study employing a commercial system and incorporating optimized post-processing techniques for both THI and HSCI would potentially have greater clinical value.

In addition to demonstrating the clinical potential of HSCI, this study highlights its feasibility for real-time echocardiography from a computational perspective. Prior work [28] showed that even with a six-fold improvement in computational throughput from the original SLSC estimator in (2) to the efficient SLSC estimator in (3), a CPU-based C++ implementation required approximately 380 ms to reconstruct an image with 65000 pixels, corresponding to a maximum frame rate of 3 fps, which is well below the 30 fps needed for real-time cardiac imaging. In contrast, the GPU-based SLSC computation on a single NVIDIA GTX 1080 Ti GPU required 4.23 ms to reconstruct an image of the same size, an improvement of 90× corresponding to a theoretical frame rate of more than 230 fps, well above the real-time threshold. This improvement was achieved by leveraging the parallelized computational architecture of GPUs to perform the highly parallelizable task of ultrasound beamforming.

Two major challenges that were encountered in the GPU implementation of HSCI included the slow data transfer between CPU and GPU memory devices and the difficulty in optimizing algorithms that execute on GPUs. The former challenge was circumvented by keeping all intermediate data structures on the GPU and seamlessly handing pointers from one **DataProcessor** to the next. The latter challenge was addressed by utilizing optimized libraries and hardware whenever possible. For instance, the **HilbertTransform** class invoked NVIDIA's cuFFT library to perform the forward and inverse fast Fourier transforms, while the **Focus** class utilized built-in hardware texture fetching to perform fast linear interpolation. Other algorithms, such as spatial coherence estimation, were implemented as CUDA kernels and required manual tuning and optimization for the specific GPU architectures that were used in this study.

The technologies used in this study comprise the first real-time implementation of cardiac HSCI, and have implications for further clinical translation. The software beamformer used here can be implemented on any system with compatible GPUs and with access to real-time channel signals, including both research and commercial clinical scanners. We have implemented a modified form of this beamformer on a Siemens Acuson SC2000 scanner in a fetal imaging study of real-time B-mode and SLSC imaging [25]. The object-oriented approach promotes flexibility throughout the beamforming pipeline and can serve as a

template for achieving scalable and fully customizable software beamforming for a wide range of techniques.

V. Conclusion

We have demonstrated a real-time implementation of HSCI suitable for echocardiography applications. Frame rates of greater than 30 fps were achieved using an efficient formulation of spatial coherence estimation and a GPU-based software beamformer. A flexible object-oriented framework was developed to maximize the computational throughput of the beamformer and to enable real-time imaging. In this study, THI and HSCI were compared in a clinical study in stress echocardiography patients with poor image quality. Imaging performance was quantified by an experienced cardiologist, scoring the visibility of 17 LV segments on a 3-point scale: 0=invisible, 1=suboptimally visualized, and 2=well visualized. HSCI demonstrated a clear superiority over THI via symmetry test ($p < 0.0001$), improved the median score across 15 patients ($p < 0.001$), and when comparing the number of well-visualized segments with McNemar test adjusted for clustering ($p < 0.0001$). While contrast agent imaging remains the gold standard, HSCI provided additional information to the clinician that was previously inaccessible with THI alone by leveraging the spatial coherence properties of tissue and clutter.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgment

The authors would like to thank the Duke Echocardiography Clinic for their clinical support and Gregg Trahey from Duke University for providing access to imaging equipment for the study.

This work is supported by the National Institute of Biomedical Imaging and Bioengineering through grants R01-EB015506 and R01-EB013661.

Biographies

Dongwoon Hyun was born in Seoul, South Korea in 1988. He received the B.S.E. and Ph.D. degrees in biomedical engineering from Duke University, Durham, NC, USA, in 2010 and 2017, respectively. He is currently a Research Engineer in the Department of Radiology at Stanford University, Stanford, CA, USA.

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Anna Lisa C. Crowley received the M.D. degree from the Ohio State University in Columbus, Ohio. She completed Internal Medicine Residency and Cardiology Fellowship training at Duke University, Durham, NC.

She is currently an Associate Professor of Medicine at Duke University and the Director of the Durham VA Echocardiography Laboratory, Durham, NC. Her clinical expertise is cardiovascular imaging of congenital heart disease. Her research interests are optimizing cardiovascular imaging to diagnose and determine the prognosis of patients with congenital heart disease and cardiac infections.

Melissa LeFevre was born in Ft. Dix, New Jersey, on Jan. 28, 1975. She received a B.A. degree in art at the University of North Carolina in Wilmington in 1997. She went back to school and became a Registered Diagnostic Cardiac Sonographer (RDCS). She has been working at Duke University Medical center in cardiology since 2007, where she has a dual role in cardiac ultrasound and research. She is involved the American Society of Echocardiography and has been involved with multiple clinical trials and cardiac imaging studies.

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Jarrett Rosenberg is currently a Biostatistician with the Department of Radiology, School of Medicine, Stanford University, Stanford, CA, USA, where he collaborates with researchers in the design and analysis of studies on imaging modalities and imaging-based interventions.

Jeremy J. Dahl (M'11) was born in Ontonagon, Michigan, in 1976. He received the B.S. degree in electrical engineering from the University of Cincinnati, Cincinnati, OH, USA, in 1999, and the Ph.D. degree in biomedical engineering from Duke University, Durham, NC, USA, in 2004.

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References

- [1]. Gottdiener JS, Bednarz J, Devereux R, Gardin J, Klein A, Manning WJ, Morehead A, Kitzman D, Oh J, Quinones M, Schiller NB, Stein JH, and Weissman NJ, "American society of echocardiography recommendations for use of echocardiography in clinical trials," *J Am Soc Echocardiogr*, vol. 17, no. 10, pp. 1086–1119, 2004. [PubMed: 15452478]
- [2]. Armstrong WF and Ryan T, *Feigenbaum's Echocardiography*, 7th ed Philadelphia, PA: Lippincott Williams & Wilkins, 2010.
- [3]. Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, Pennell DJ, Rummerger JA, Ryan TJ, and Verani MS, "Standardized Myocardial Segmentation and Nomenclature for Tomographic Imaging of the Heart," *Journal of Cardiovascular Magnetic Resonance*, vol. 4, no. 2, pp. 203–210, 2002.
- [4]. Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, Picard MH, Roman MJ, Seward J, Shanewise JS, Solomon SD, Spencer KT, Sutton M. St. John, and Stewart WJ, "Recommendations for chamber quantification: A report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology," *J Am Soc Echocardiogr*, vol. 18, no. 12, pp. 1440–1463, 2005. [PubMed: 16376782]
- [5]. Hundley WG, Kizilbash AM, Afridi I, Franco F, Peshock RM, and Grayburn PA, "Effect of contrast enhancement on transthoracic echocardiographic assessment of left ventricular regional wall motion," *Am J Cardiol*, vol. 84, no. 11, pp. 1365–1368, 1999. [PubMed: 10614810]
- [6]. Kurt M, Shaikh KA, Peterson L, Kurrelmeyer KM, Shah G, Nagueh SF, Fromm R, Quinones MA, and Zoghbi WA, "Impact of Contrast Echocardiography on Evaluation of Ventricular Function and Clinical Management in a Large Prospective Cohort," *Journal of the American College of Cardiology*, vol. 53, no. 9, pp. 802–810, 2009. [PubMed: 19245974]
- [7]. Flynn BC, Spellman J, Bodian C, and Moitra VK, "Inadequate visualization and reporting of ventricular function from transthoracic echocardiography after cardiac surgery," *J Cardiothorac Vasc Anesth*, vol. 24, no. 2, pp. 280–284, 2010. [PubMed: 19833534]
- [8]. Finkelhor RS, Moallem M, and Bahler RC, "Characteristics and impact of obesity on the outpatient echocardiography laboratory," *Am J Cardiol*, vol. 97, no. 7, pp. 1082–1084, 2006. [PubMed: 16563921]
- [9]. Flegal KM, Carroll MD, Kuczmarski RJ, and Johnson CL, "Overweight and obesity in the United States: prevalence and trends, 1960–1994," *International Journal of Obesity and Related Metabolic Disorders*, vol. 22, pp. 39–47, 1998. [PubMed: 9481598]
- [10]. Flegal K, Carroll M, Ogden C, and Johnson C, "Prevalence and trends in obesity among us adults, 1999–2000," *JAMA*, vol. 288, no. 14, pp. 1723–1727, 2002. [PubMed: 12365955]

- [11]. Flego K, Carroll M, Ogden C, and Curtin L, "Prevalence and trends in obesity among us adults, 1999–2008," JAMA, vol. 303, no. 3, pp. 235–241, 2010. [PubMed: 20071471]
- [12]. "Overweight and obesity - BMI statistics." [Online]. Available: http://ec.europa.eu/eurostat/statistics-explained/index.php/Overweight_and_obesity_-_BMI_statistics
- [13]. Yoon KH, Lee JH, Kim JW, Cho JH, Choi YH, Ko SH, Zimmet P, and Son HY, "Epidemic obesity and type 2 diabetes in Asia," Lancet, vol. 368, no. 9548, pp. 1681–1688, 2006. [PubMed: 17098087]
- [14]. Lediju MA, Pihl MJ, Dahl JJ, and Trahey GE, "Quantitative assessment of the magnitude, impact and spatial extent of ultrasonic clutter." Ultrasonic Imaging, vol. 30, no. 3, pp. 151–68, 2008. [PubMed: 19149461]
- [15]. Lediju Bell MA, Goswami R, Kisslo JA, Dahl JJ, and Trahey GE, "Short-Lag Spatial Coherence Imaging of Cardiac Ultrasound Data: Initial Clinical Results." Ultrasound in Medicine & Biology, pp. 1–14, 2013. [PubMed: 24210860]
- [16]. Pinton GF, Trahey GE, and Dahl JJ, "Sources of image degradation in fundamental and harmonic ultrasound imaging: a nonlinear, full-wave, simulation study." IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control, vol. 58, no. 6, pp. 1272–83, 2011.
- [17]. Dahl JJ and Sheth NM, "Reverberation Clutter from Subcutaneous Tissue Layers: Simulation and in Vivo Demonstrations," Ultrasound in Medicine & Biology, vol. 40, no. 4, pp. 714–726, 2014. [PubMed: 24530261]
- [18]. Pinton GF, Trahey GE, and Dahl JJ, "Spatial Coherence in Human Tissue : Implications for Imaging and Measurement," IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control, vol. 61, no. 12, pp. 1976–1987, 2014.
- [19]. Dahl JJ, Jakovljevic M, Pinton GF, and Trahey GE, "Harmonic Spatial Coherence Imaging: An Ultrasonic Imaging Method Based on Backscatter Coherence," IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control, vol. 59, no. 4, pp. 648–59, 2012.
- [20]. Lester SJ, Askew JW, Hurst RT, Moreno CA, Hentz JG, Wood LA, Simpson RA, Schneek SL, Tyler R, Chaliki HP, and Lynch JJ, "Contrast echocardiography: Experience in a clinical echocardiography laboratory," J Am Soc Echocardiogr, vol. 19, no. 7, pp. 919–923, 2006. [PubMed: 16825003]
- [21]. Muskula PR and Main ML, "Safety with echocardiographic contrast agents," Circ-Cardiovasc Imag, vol. 10, no. 4, p. 10:e005459, 2017, doi: 10.1161/CIRCIMAGING.116.005459.
- [22]. Lediju MA, Trahey GE, Byram BC, and Dahl JJ, "Short-lag spatial coherence of backscattered echoes: imaging characteristics." IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control, vol. 58, no. 7, pp. 1377–88, 2011.
- [23]. Jakovljevic M, Trahey GE, Nelson RC, and Dahl JJ, "In vivo application of short-lag spatial coherence imaging in human liver." Ultrasound in Medicine & Biology, vol. 39, no. 3, pp. 534–542, 2013. [PubMed: 23347642]
- [24]. Kakkad V, Dahl J, Ellestad S, and Trahey G, "In Vivo Application of Short-Lag Spatial Coherence and Harmonic Spatial Coherence Imaging in Fetal Ultrasound," Ultrasonic Imaging, vol. 37, no. 2, pp. 101–116, 2015. [PubMed: 25116292]
- [25]. Long W, Hyun D, Choudhury KR, Bradway D, McNally P, Boyd B, Ellestad S, and Trahey GE, "Clinical Utility of Fetal Short-Lag Spatial Coherence Imaging," Ultrasound in Medicine and Biology, vol. 44, no. 4, pp. 794–806, 2018. [PubMed: 29336851]
- [26]. Li YL and Dahl JJ, "Coherent flow power doppler (CFPD): flow detection using spatial coherence beamforming." IEEE transactions on ultrasonics, ferroelectrics, and frequency control, vol. 62, no. 6, pp. 1022–35, 2015.
- [27]. Hyun D, Abou-Elkacem L, Perez VA, Chowdhury SM, Willmann JK, and Dahl JJ, "Improved sensitivity in ultrasound molecular imaging with coherence-based beamforming," IEEE Transactions on Medical Imaging, vol. 37, no. 1, pp. 241–250, 2018. [PubMed: 29293430]
- [28]. Hyun D, Crowley ALC, and Dahl JJ, "Efficient Strategies for Estimating the Spatial Coherence of Backscatter," IEEE Transactions on Ultrasonics, Ferroelectrics, and Frequency Control, vol. 64, no. 3, pp. 500–513, 2017.

- [29]. Lediju Bell MA, Goswami R, and Trahey GE, "Clutter reduction in echocardiography with short-lag spatial coherence (SLSC) imaging," in 2012 IEEE International Symposium on Biomedical Imaging, 2012, pp. 1116–1119.
- [30]. Bell MAL, Goswami R, Dahl JJ, and Trahey GE, "Improved visualization of endocardial borders with Short-Lag Spatial Coherence imaging of fundamental and harmonic ultrasound data," in 2012 IEEE International Ultrasonics Symposium IEEE, 2012, pp. 2129–2132.
- [31]. Hyun D, Trahey GE, and Dahl JJ, "Real-Time High-Framerate In Vivo Cardiac SLSC Imaging with a GPU-Based Beamformer," IEEE Ultrasonics Symposium Proceedings, pp. 1–4, 2015.
- [32]. Hyun D, Crowley AL, Rosenberg J, and Dahl J, "Improved left ventricular wall visualization in stress-echocardiography using real-time gpu-based harmonic spatial coherence imaging," in 2017 IEEE International Ultrasonics Symposium (IUS), 9 2017, pp. 1–1.
- [33]. Yiu BY, Tsang IK, and Yu AC, "Gpu-based beamformer: Fast realization of plane wave compounding and synthetic aperture imaging," IEEE transactions on ultrasonics, ferroelectrics, and frequency control, vol. 58, no. 8, 2011.
- [34]. Göbl R, Navab N, and Hennersperger C, "Supra: open-source software-defined ultrasound processing for real-time applications," International Journal of Computer Assisted Radiology and Surgery, 3 2018 [Online]. Available: 10.1007/s11548-018-1750-6
- [35]. Asen JP, Buskenes JJ, Nilsen C-IC, Austeng A, and Holm S, "Implementing capon beamforming on a gpu for real-time cardiac ultrasound imaging," IEEE transactions on ultrasonics, ferroelectrics, and frequency control, vol. 61, no. 1, pp. 76–85, 2014.
- [36]. Food and Drug Administration, "Guidance for Industry and FDA Staff: Information for Manufacturers Seeking Marketing Clearance of Diagnostic Ultrasound Systems and Transducers," Silver Spring, MD, pp. 1–64, 2008.
- [37]. Gallippi CM and Trahey GE, "Adaptive clutter filtering via blind source separation for two-dimensional ultrasonic blood velocity measurement." Ultrasonic Imaging, vol. 24, no. 4, pp. 193–214, 2002. [PubMed: 12665237]
- [38]. Demeñé C, Deffieux T, Pernot M, Osmanski BF, Biran V, Gennisson JL, Sieu LA, Bergel A, Franqui S, Correas JM, Cohen I, Baud O, and Tanter M, "Spatiotemporal Clutter Filtering of Ultrafast Ultrasound Data Highly Increases Doppler and fUltrasound Sensitivity," IEEE Transactions on Medical Imaging, vol. 34, no. 11, pp. 2271–2285, 2015. [PubMed: 25955583]
- [39]. Altman DG, Practical statistics for medical research. CRC press, 1990.
- [40]. Landis JR and Koch GG, "The Measurement of Observer Agreement for Categorical Data," Biometrics, vol. 33, no. 1, pp. 159–174, 1977. [PubMed: 843571]
- [41]. Pellikka PA, Nagueh SF, Elhendy AA, Kuehl CA, and Sawada SG, "American Society of Echocardiography Recommendations for Performance, Interpretation, and Application of Stress Echocardiography," Journal of the American Society of Echocardiography, vol. 20, no. 9, pp. 1021–1041, 2007. [PubMed: 17765820]

Fig. 1.

A schematic of the **DataProcessor** abstract base class is shown. A **DataProcessor** accepts a pointer to GPU memory, executes some class member function that calls one or more CUDA kernels, and outputs the result as a pointer to GPU memory. All children of **DataProcessor** adopt this structure.

Fig. 2.

The GPU beamforming pipelines used in this study are shown. A Verasonics Vantage 256 scanner streamed raw channel data to two GPUs, labeled GPU0 and GPU1. Each GPU was assigned half of the output THI and HSCI images to reconstruct. A separate instance of the beamforming pipeline was created on each GPU to format, Hilbert transform, focus, and beamform the input data.

Fig. 3.

The four views of the LV used in this study were (a) parasternal short axis, (b) parasternal long axis, (c) apical two chamber, and (d) apical four chamber. The visible segments are labeled according to the standardized nomenclature [3].

Fig. 4. THI and HSCI images are shown of an apical two-chamber view (A2C) for patient #5. Bright clutter is visible at the apex of the LV in the THI image, but is suppressed in the HSCI image.

Fig. 5.

THI and HSCI images are shown of a parasternal short axis (PSA) view for patient #1. The LV endocardial border is highlighted using arrows. HSCI significantly enhances the visibility of the LV segments, particularly in those further from the transducer.

Fig. 6.

(a) The median visibility score across three reviewers is shown for each LV segment in each patient for THI and HSCI. Well visualized segments are plotted in light blue, poorly visualized segments in dark blue, and invisible segments in black. (b) The net visibility score accumulated across three reviewers is plotted for each segment. Possible net scores ranged from -6 (all reviewers give scores of 2 in THI, 0 in HSCI) to $+6$ (all scores of 0 in THI, 2 in HSCI).

Fig. 7.

The net score per patient (sum of all HSCI scores minus sum of all THI scores) is plotted for 15 patients and 3 reviewers in sorted order. There were two instances with negative score ($\text{THI} > \text{HSCI}$), three instances of zero score ($\text{THI} = \text{HSCI}$), and 40 instances of positive score ($\text{THI} < \text{HSCI}$).

TABLE I

Computational Profile of a Single Image Frame

Type	Operation	Execution Time	Pct. of Total GPU Time
	CPU→GPU transfer	2.80 ms	76.1%
	Formatting and alignment	0.13 ms	3.5%
	Apply focusing delays	0.21 ms	5.7%
GPU	Sum and detect envelope	0.09 ms	2.4%
	Compute spatial coherence	0.40 ms	10.9%
	Scan conversion	0.02 ms	0.5%
	GPU→CPU transfer	0.04 ms	1.0%
Other	Overhead	27.07 ms	640%
Total		31.30 ms	—

TABLE II

Acoustic Output Safety Measurements

	MI	TI	I_{SPTA}	I_{SPPA}
6 cm focus	0.87	0.25	582 mWcm ⁻²	75.9 Wcm ⁻²
8 cm focus	0.60	0.32	306mWcm ⁻²	41.7Wcm ⁻²
FDA Rec.	1.9	6.0	720mWcm ⁻²	190Wcm ⁻²

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TABLE III

Agreement Between Reviewers

Agreement	Kappa	95% CI
THI	.48	(.41 – .56)
HSCI	.48	(.39 – .57)
Overall	.50	(.46 – .58)

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TABLE IV

Comparison of LV segment visibility

		HSCI Rating			Total	Pct
		0	1	2		
THI Rating	0	161	140	23	324	42%
	1	26	165	97	288	38%
	2	5	4	144	153	20%
	Total	192	309	264	765	
	Pct	25%	40%	35%		