Transthoracic Ultrafast Doppler Imaging of Human Left Ventricular Hemodynamic Function

Bruno-Félix Osmanski, David Maresca, Emmanuel Messas, Mickael Tanter, and Mathieu Pernot

***Abstract*—Heart diseases can affect intraventricular blood flow patterns. Real-time imaging of blood flow patterns is challenging because it requires both a high frame rate and a large field of view. To date, standard Doppler techniques can only perform blood flow estimation with high temporal resolution within small regions of interest. In this work, we used ultrafast imaging to map in 2-D human left ventricular blood flow patterns during the whole cardiac cycle. Cylindrical waves were transmitted at 4800 Hz with a transthoracic phased-array probe to achieve ultrafast Doppler imaging of the left ventricle. The high spatio-temporal sampling of ultrafast imaging permits reliance on a much more effective wall filtering and increased sensitivity when mapping blood flow patterns during the pre-ejection, ejection, early diastole, diastasis, and late diastole phases of the heart cycle. The superior sensitivity and temporal resolution of ultrafast Doppler imaging makes it a promising tool for the noninvasive study of intraventricular hemodynamic function.**

I. Introduction

Major cardiovascular diseases including congestive heart failure, coronary artery disease, hypertension and cardiomyopathies are associated with left ventricular dysfunction [1]. The accurate assessment of ventricular function during all phases of the heart cycle is therefore a central issue in cardiac imaging. Since its introduction in the late 1970s, Doppler echocardiography [2], [3] has emerged as an important tool for the noninvasive hemodynamic characterization of the heart and the management of cardiac patients. Intracardiac blood flow, pressures, and pressure gradients can be derived from Doppler examinations to assess systolic and diastolic performance, as well as valve function. Overall, Doppler echocardiography provided new insights into the pathophysiology of myocardial diseases [4]–[7] and contributes to clinical decision making [8].

Conventional Doppler echocardiography relies on line per line focused beam transmissions to scan the medium of interest [2]. Transthoracically, the left ventricle is typically imaged at a rate of 20 to 100 frames per second, which leads to a tradeoff between the field of view and the temporal resolution achievable. Color flow imaging (CFI) has been introduced in clinical practice to map blood flow in a large region of interest, but is currently limited by its low frame rate and angle dependency, whereas pulse wave (PW) Doppler relies on a much higher number of time samples along a single line to characterize local hemodynamics. The evaluation of left ventricular blood flow pattern is currently limited given the need for the practitioner to choose one of these two Doppler modalities.

An alternative technique is contrast-enhanced echocardiography, mostly used for left ventricle endocardial border detection in patients with suboptimal echocardiograms [9], or to assess myocardial perfusion [10]. It was shown that ultrasound contrast agents can be used as reporters of intraventricular blood motion using particle imaging velocimetry [11]. However, the US Food and Drug Administration only approves ultrasound contrast perfusion for left ventricular opacification and contrast-enhanced ultrasound strategies disrupt the noninvasive character of echocardiography.

Recently, the introduction of ultrafast scanners has offered new insight in medical ultrasonic imaging [12]–[17]. Ultrafast plane wave imaging allows for the acquisition of hundreds of temporal samples per second over a large field of view, therefore breaking the usual tradeoff between field of view and temporal resolution. The high spatio-temporal resolution of ultrafast ultrasound acquisitions offers the possibility of imaging and quantifying blood flow simultaneously over a larger region of interest, hence providing more accurate hemodynamic information. This ultrasound imaging approach gathering the advantages of CFI and PW Doppler in a single mode was introduced under the terminology ultrafast Doppler imaging [18], [19].

Here, we report the implementation of ultrafast Doppler imaging (UFD) on a transthoracic phased-array probe using cylindrical waves [20]–[24], and present its application to the characterization of human left ventricular hemodynamics. We provide a detailed temporal analysis of all phases of the heart cycle (ejection phase, early diastole, diastasis, late-diastole, pre-ejection phase) by processing the UFD data in terms of both CFI and PW Doppler. Results demonstrate the capacity of UFD to describe intraventricular transient flows with a millisecond resolution, in agreement with earlier findings [18], [25]–[27]. UFD provides an enhanced characterization of left ventricular hemodynamic function without the use of ultrasound contrast agents.

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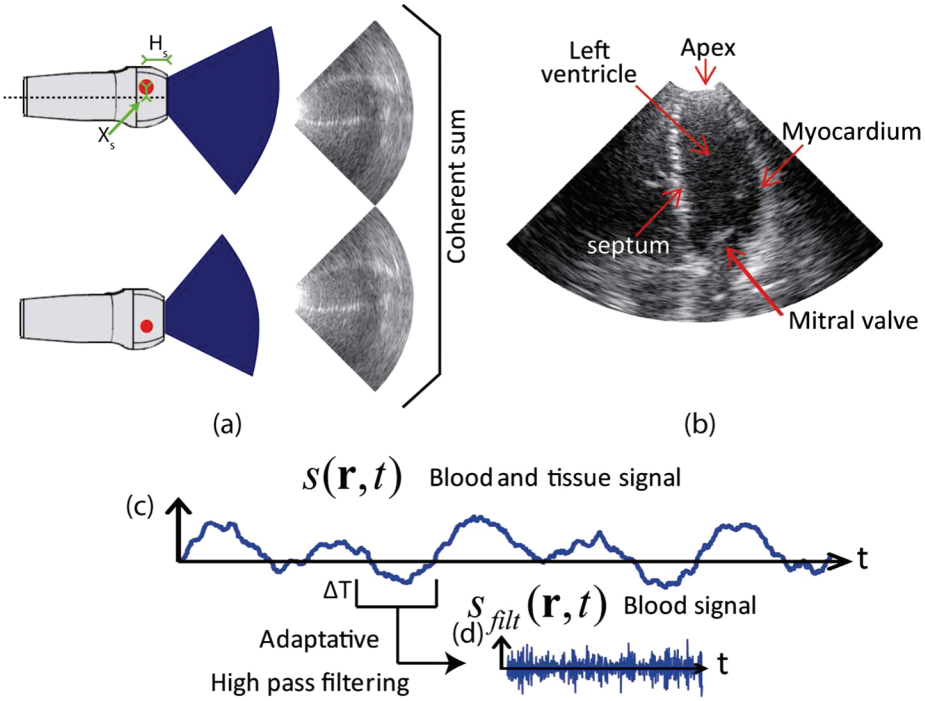

Fig. 1. (a) Two cylindrical wave ultrasound images of the left ventricle arising from two different virtual sources. (b) Enhanced ultrasound image of the left ventricle resulting from the spatial compounding of the pair of cylindrical wave images. (c) Time signal of a spatial pixel containing blood and tissue signal. (d) Blood signal of a time window obtained after wall filtering ($\Delta T = 25$ ms).

II. Methods

A. Experimental Setup

We made use of an ultrasound phased-array probe (2.75MHz, 60% bandwidth, 64 elements, Vermon, Tours, France) connected to an ultrafast scanner (Aixplorer, SuperSonic Imagine, Aix-en-provence, France). Data were acquired on a 27-year-old healthy male volunteer who displayed a normal echocardiogram and did not report any cardiac history. To show the robustness of UFD, a second set of data was acquired on a patient with poor echogenicity. The patient was a 62-year-old male with ischemic cardiomyopathy and left ventricular apical akinesis. An experienced cardiologist held the probe against the patient's chest to obtain a 4-chamber apical view of the left ventricle. The patient's heart cycle was monitored using an electrocardiography (ECG) device. The ultrasound acquisitions were triggered on the R-wave of the ECG signal.

The study was approved by the Comité de Protection des Personnes (CPP) and the national agency for health (ANSM); authorization number 2009-A01324–53. The subject was informed of the nature and aims of the study and signed a consent form.

B. Ultrafast Cylindrical Wave Imaging

To image the heart with a high frame rate over a large field of view, we used cylindrical (diverging) waves emerging from a virtual source placed behind the probe [24]. We used spatial compounding to improve the resolution of B-mode images. Fig. 1(a) illustrates spatial compounding with two virtual sources generating two cylindrical wave images. Each image individually has poor quality in term of contrast and resolution, but their coherent sum provides an ultrasound image of superior quality [see Fig. 1(b)].

Ultrafast ultrasound imaging presents the advantage of being tunable, because the operator can adjust the tradeoff between ultrasound image quality and frame rate for a given investigation depth. In this manuscript, two different imaging sequences were used: one for UFD and one for B-mode imaging. For UFD imaging, the heart was insonified at a 4800 Hz frame rate during 1.5 s with cylindrical waves arising from a single virtual source position. Subsequently, the heart was insonified for ultrafast B-mode imaging for 1.5 s with 21 virtual sources, leading to a frame rate of 229 Hz after spatial compounding. Both sequences had the same pulse repetition frequency (4800 Hz) but the first UFD sequence, using a single virtual source position, was designed to maximize frame rate, whereas the second sequence dedicated to B-mode imaging was designed to maximize imaging quality via spatial compounding.

C. Wall Filtering for UFD Sequence

CFI was computed with the data set of the first (high-frame-rate) UDF sequence. For each spatial pixel $\mathbf{r}$, we can compute a 7200-sample-point temporal signal $s(\mathbf{r}, t)$ containing blood and tissue signal [see Fig. 1(c)]. For each time window of 120 sample points ($\Delta T = 25$ ms) that we slide every 30 sample points (6.25 ms), we applied a wall

filter (high-pass fourth-order Butterworth) with an adaptive cutoff frequency to remove the tissue signal [see Fig. 1(d)]. The heart cycle was analyzed into 5 phases (see Section III). For the ejection phase and the early diastole phase, the cutoff frequency was set to 400 Hz, whereas in the other phases, the cutoff frequency was set to 250 Hz. PW Doppler spectra were computed along the whole heart cycle with a 400 Hz cutoff frequency.

D. Color Flow Imaging Processing

For each spatial pixel and for each time window of size ΔT, we computed the Doppler frequency using the first moment of the power Doppler spectrum:

$$f_{\mathrm{d}}(\mathbf{r}) = \frac{\int_f f \left| \int_0^{\Delta T} s_{\mathrm{filt}}(\mathbf{r},\tau) e^{-2j\pi f\tau} d\tau \right|^2 \mathrm{d}f}{\int_f \left| \int_0^{\Delta T} s_{\mathrm{filt}}(\mathbf{r},\tau) e^{-2j\pi f\tau} d\tau \right|^2 \mathrm{d}f}. \quad (1)$$

We obtained a set of 221 color Doppler images describing one heart cycle. We used the color mode convention that flow coming toward the probe was colored red and flow going away from the probe was colored blue.

E. Spatio-Temporal Analysis of the Blood Flow

The transient transmitral flow propagation during early filling was analyzed to show how spatial and temporal information can be combined using UFD. Flow propagation velocity has been investigated extensively with color M-mode to characterize the early filling of the left ventricle. Using UFD, the 2-D acquisition allows us to compute the propagation velocity not only in the direction of an M-mode line, but also along an arbitrary direction in the 2-D plane. The local axial acceleration field was computed by differentiating the mean velocity in each pixel of the map as a function of time. Then, the time of the acceleration peak during the early filling of the left ventricle was computed at each location. Finally, the direction of the flow propagation was determined as the direction of the lowest gradient of the timing map.

III. Results

Color flow maps and PW Doppler spectrum of the healthy volunteer are shown in Fig. 2 for the main phases of the cardiac cycle [28]. During the ejection phase [Fig. 2(b)], the blood is expulsed in the aorta after the opening of the aortic valve and the mitral valve is closed; the blood is flowing downward in the direction of the aorta. Ultrafast Doppler permits the same acquisition to be used to compute a post-processed PW Doppler spectrum [see Fig. 3(g)]. We noticed a high axial velocity (high frequency on the PW Doppler spectrum) of the blood approaching the aortic valve.

Fig. 2(c) shows the early diastole phase that takes place after the closing of the aortic valve and the opening of the mitral valve. The first part of the filling of the left ventricle begins with a flow of high velocity in the direction of the apex resulting from low pressure inside the left ventricle. Computing a PW Doppler spectrum in a spatial window located at the maximum blood velocity of this phase [see Fig. 2(h)] indicated that the maximum blood flow velocity during the diastole is reached during this phase. In addition, the magnitude of the transmitral flow velocity in early diastole was of the same order as the blood velocity through the aortic valve during the ejection phase.

In the diastasis phase, the filling of the left ventricle continues and a vortex starts to form. Fig. 2(d) shows flow distribution inside the entire left ventricle. The late diastole phase is observed just before the closure of the mitral valve and corresponds to the final part of the left ventricle filling. Fig. 2(e) shows a global motion of the blood flow toward the apex; the vortex has disappeared. We performed a standard evaluation of the mitral valve inflow and measured an E/A ratio of 1.4.

Finally, when the heart starts contracting, the mitral valve is closing and the aortic valve is still closed. This phase is called the pre-ejection phase. Fig. 2(f) shows the appearance of a vortex which starts to redirect the blood toward the aortic valve to prepare for the ejection phase. Note that because the mitral valve is hyperechogenic and moving quickly during this phase, it produces an artifact in the CFI image, as seen in Fig. 2(f).

The same analysis was performed on the patient's data. Despite the low echogenicity, CFI maps were computed successfully (see Fig. 3). Both flow patterns and velocities were found to be very different compared with the healthy volunteer case. A much lower velocity was measured in the ejection phase (mean velocity of 0.15 m/s), and the filling flow in early diastole was very high (mean velocity of 0.5 m/s). Unlike the healthy patient, we observed the establishment of the vortex during the early filling phase. Moreover, the vortex pattern in diastasis was found to remain during the entire diastole. No early systole phase could be observed.

Finally, the transient transmitral flow propagation during early filling was analyzed as an example of how spatial and temporal information can be combined using ultrafast Doppler imaging. Fig. 4 shows several acceleration maps at 13.3 ms intervals during the early filling of the left ventricle. The propagation of the acceleration peak is visualized in 2-D: the peak is initially located at the output of the mitral valve, as seen in Fig. 4(a), then the acceleration peak propagates in all directions at various velocities. The largest distance reached after 40 ms was identified in Fig. 4(d), determining the direction of maximum velocity propagation [indicated by the black arrow in Fig. 4(d)]. Fig. 4(e) displays the acceleration progression along this direction as a function of time. We derived an average velocity of 0.68 ms from the slope of the peak acceleration position as a function of time. A similar analysis was

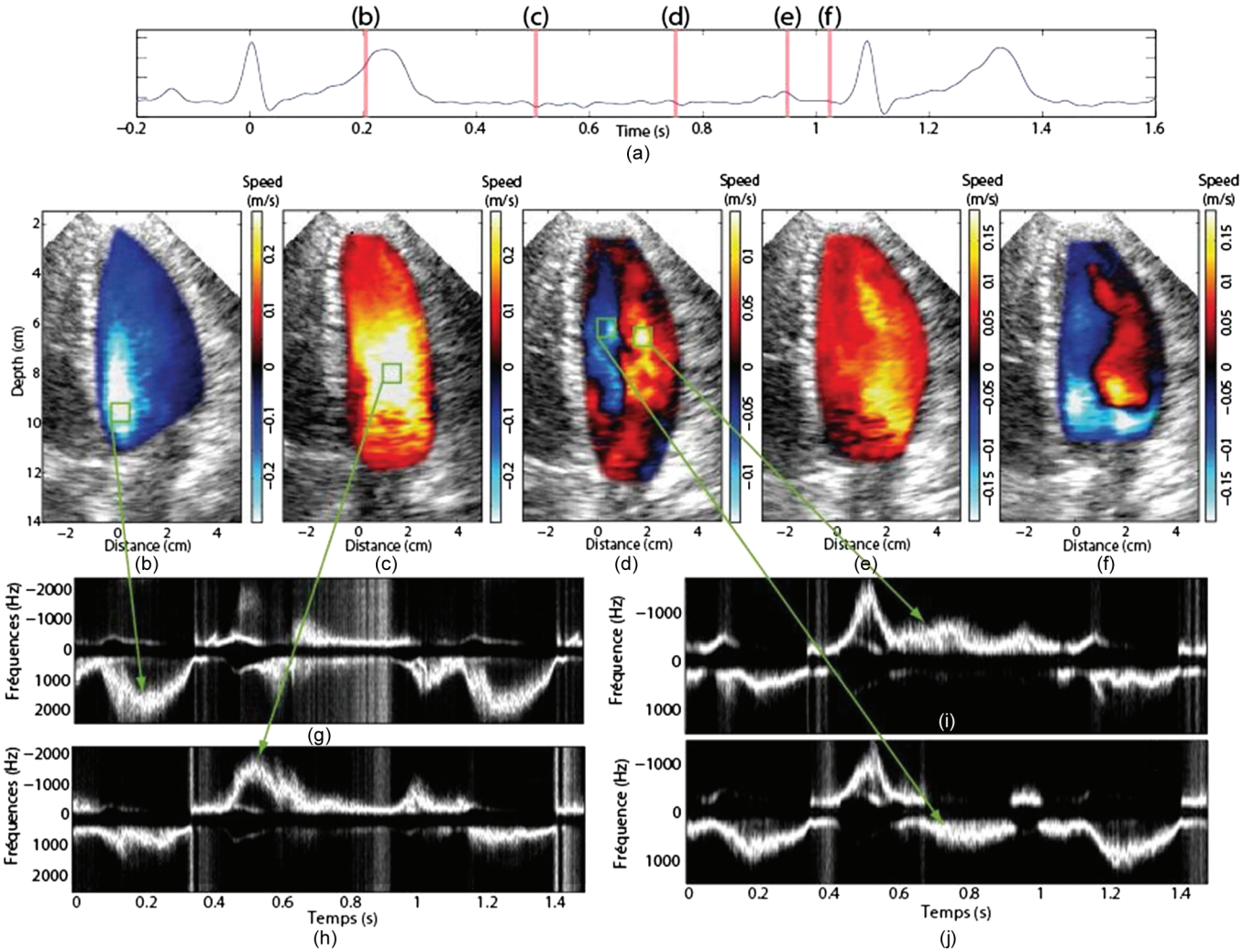

Fig. 2. Ultrafast color flow images of the healthy volunteer displayed at several phases of the cardiac cycle. (a) ECG signal. CFI of the left ventricle during (b) the ejection phase, (c) early diastole, (d) diastasis, (e) late diastole, and (f) early systole. PW Doppler spectra were computed at four locations indicated by the green square boxes.

performed using only one line of the acquisition, which is equivalent to a so-called color M-mode. A flow propagation velocity of 0.62 m/s was measured with the M-mode. This analysis assumes the flow propagation to be in the direction of the M-mode line, which is wrong, as shown on Fig. 4(d). Therefore, an error of 9% exists on the flow propagation velocity. In this example, the error was small, but it could be larger if the angle between the two directions is higher.

IV. Discussion and Conclusions

In this study, we investigated the ability of ultrafast Doppler imaging to map ventricular blood flow with high temporal resolution over a full two-dimensional sector view. A conventional transthoracic imaging probe was used to acquire the apical view of the left ventricle of a healthy volunteer. Two ultrafast imaging sequences were implemented with cylindrical wave transmits on a programmable scanner to acquire 2-D ultrasound images at a frame rate of 4800 images/s.

Ultrasound data were analyzed over small temporal sliding windows to provide quantitative information on the blood flow, and two types of quantitative information were computed. The full Doppler spectrum was obtained at each pixel of the 2-D image, and the mean velocity was extracted from the Doppler spectrum to compute 2-D color flow maps. It should be noted that PW Doppler information and color flow maps were provided by the same acquisition at every location in the image simultaneously and at high frame rate. This is a major advantage of the technique, because it can provide quantitative spatio-temporal information on the blood flow velocity. To illustrate this capability, we have presented both examples of color flow maps at different periods of the cardiac cycle (ejection, filling and diastasis phases) and examples of PW Doppler at different locations (transaortic and transmitral flows and mid-ventricular flows). Ultrafast Doppler imaging was capable of mapping and quantifying high blood

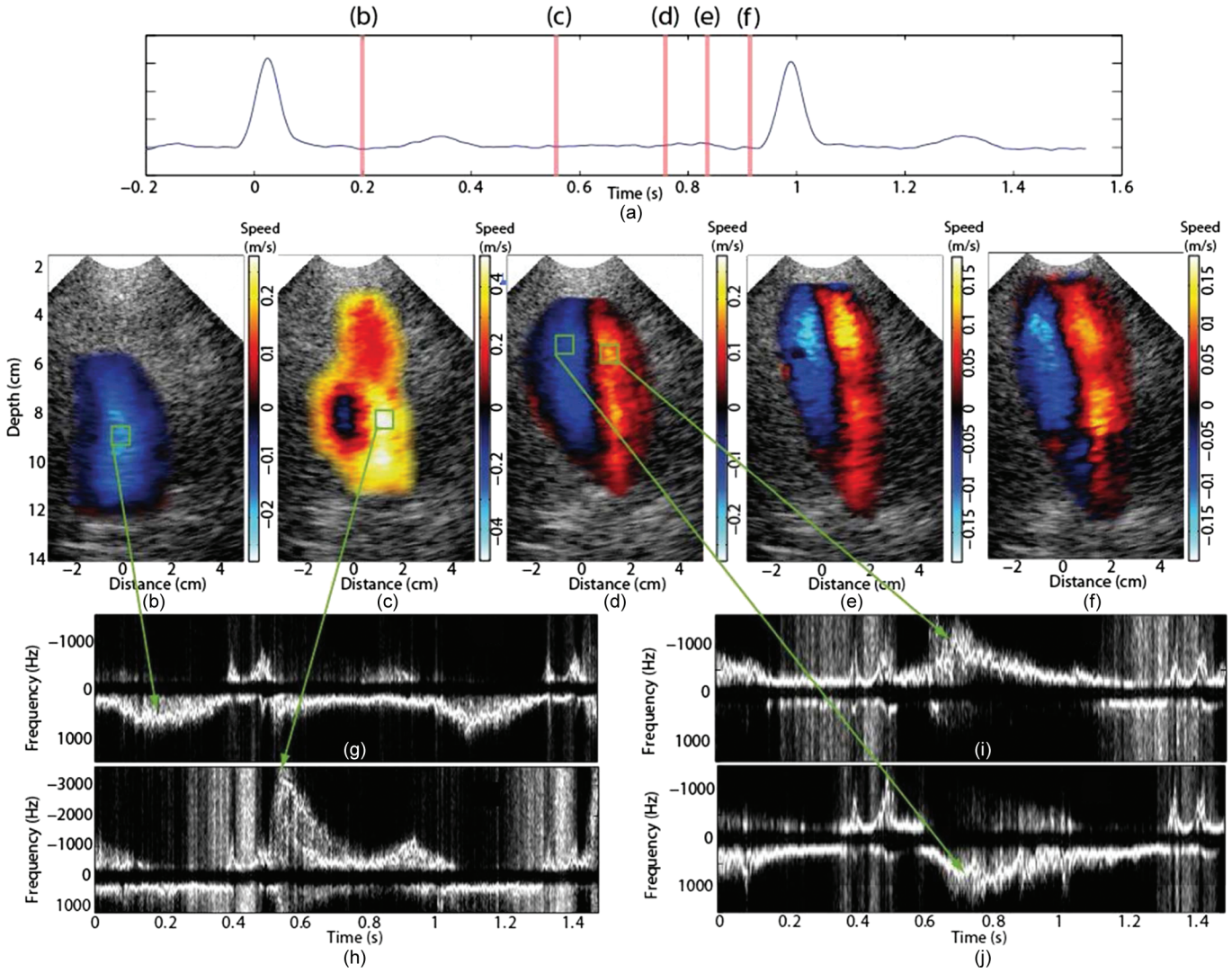

Fig. 3. Ultrafast color flow images of the patient displayed at several phases of the cardiac cycle. (a) ECG signal. CFI of the left ventricle during (b) the ejection phase, (c) early diastole, (d) diastasis, (e) late diastole, and (f) early systole. PW Doppler spectra were computed at four locations indicated by the green square boxes.

flow velocities (ejection and filling phases), and also complex flow patterns during diastasis. Flow patterns observed during the diastolic filling of the left ventricle revealed the presence of turbulences and vortices. Several studies have highlighted the importance of vortex patterns to minimize energy dissipation during ventricular filling [28] and have suggested that vortices may be impaired in patients with abnormal heart filling [29]. Ultrafast Doppler imaging may emerge as a new tool to better analyze these vortex patterns with high-temporal-resolution color flow imaging. Ultrafast Doppler data could also be further analyzed to provide vector flow mapping of the vortex [30].

In addition to CFI and PW Doppler, ultrafast Doppler imaging can also provide spatio-temporal analysis of transient flow propagation. For example, the flow propagation velocity has been investigated extensively over the past decades to analyze the spatio-temporal pattern of the transmitral flow [31]. This index quantifies the rate of propagation of the early filling flow velocity peak and was shown to change in patients with abnormal ventricular filling. With conventional echocardiography, this index is obtained by color M-mode, which provides the 1-D propagation of peak velocity along this M-mode beam. This is an important limitation, because the M-mode beam is not necessarily parallel to the flow direction, which can lead to important errors on the flow propagation velocity. In this study, we have shown the possibility of obtaining 2-D information on the flow propagation and quantifying the flow propagation in the direction of maximum velocity.

This study focused on the analysis of blood flow velocities acquired with an ultrafast imaging sequence. However, tissue velocities can also be computed from the same acquisition data set, as described by Papadacci *et al.* [24]. Tissue velocity analyses were already reported in several studies [21], [24], [32] to map tissue velocities or strain at very high frame rate and measure electromechanical and mechanical wave speed. Therefore, such an ultrafast imaging sequence can provide at very high frame rate both

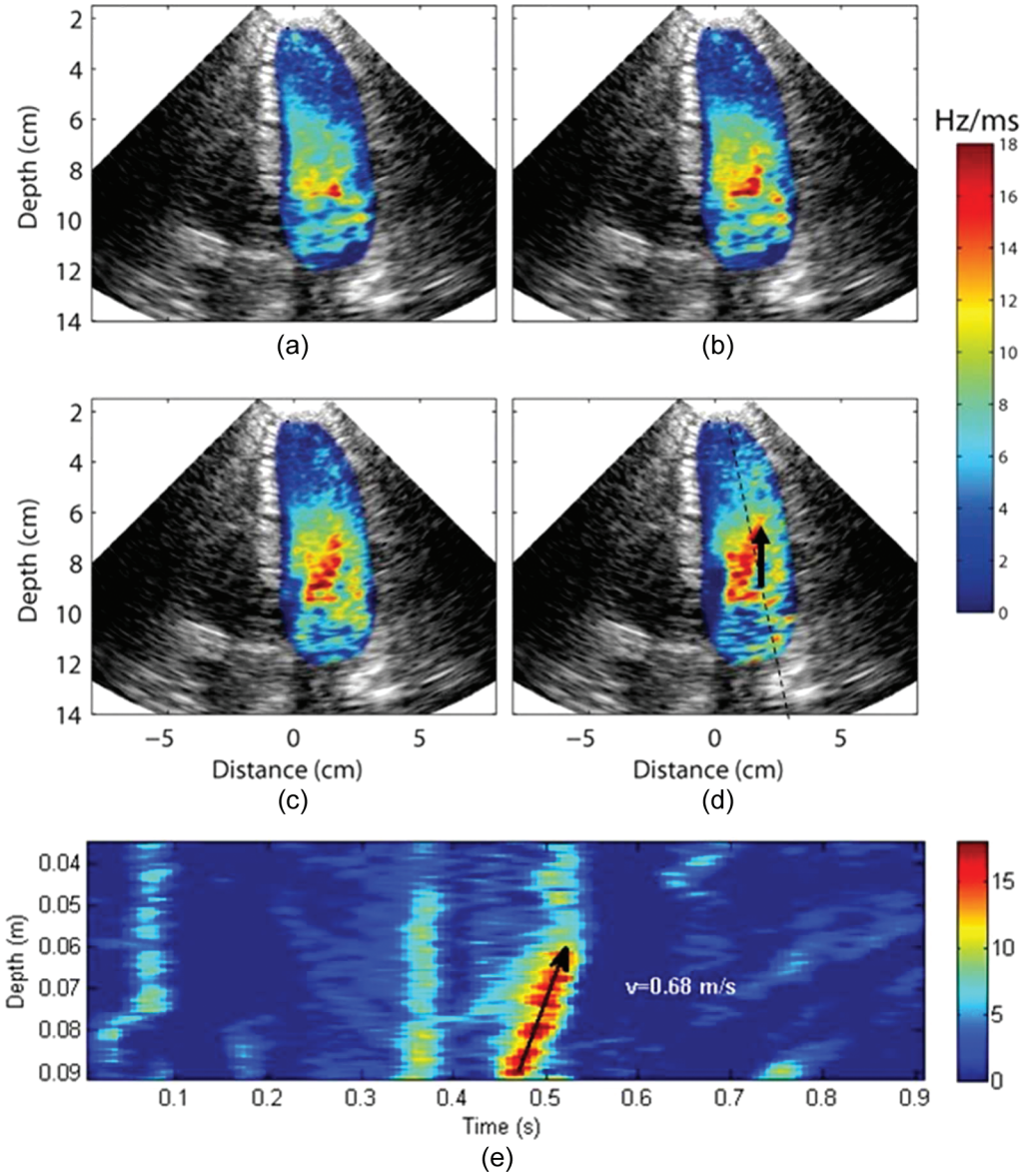

Fig. 4. Progression of local acceleration during early filling. (a)–(d) show the acceleration maps at 13 ms intervals. The black arrow shows the direction of the maximal propagation speed, which is not exactly aligned to the scan line that would be performed in M-mode. (e) Spatio-temporal analysis of the acceleration peak progression and flow propagation velocity.

tissue and blood velocity maps simultaneously within a single cardiac cycle, as shown by Osmanski *et al.* [33].

One limitation of the ultrafast imaging sequence used in this study is the low contrast of the B-mode image. This low contrast is due to choice of a single cylindrical wave transmit to limit aliasing and reach the maximum frame rate. Ejection and filling peak velocities can reach several meters per second, which requires the highest frame rate possible. In other cardiac phases with lower blood velocities, the frame rate could be decreased and the contrast increased by adding more cylindrical waves, as described by Papadacci *et al.* [24]. Another limitation of this study is that only axial velocities were computed in 2-D, which represents only a small part of the complex 3-D blood flow distribution in the ventricle. Finally, like PW Doppler, UFD is sensitive to aliasing. For measuring flow with a magnitude over 1 m/s in the left ventricular outflow track, for example, continuous wave Doppler should be used.

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David Maresca was born in June 1983 in Paris, France. He received a Magistere degree in fundamental physics and an M.S. degree in acoustics from Paris Diderot University in 2007. He was appointed for a year as research scientist at the Philips High Tech Campus, Eindhoven, the Netherlands, working on acoustic fluid lenses for ultrasound imaging. In October 2008, he joined the Thorax Centre, Department of Biomedical Engineering, of Erasmus University Medical Centre, Rotterdam, the Netherlands, to carry out a Ph.D. study in contrast-enhanced intravascular ultrasound imaging under the supervision of Nico de Jong and Antonius F. W. van der Steen. In August 2013, he began a postdoctoral fellowship in ultrafast echocardiography at the Langevin Institute in Paris, France. His research interests include ultrafast Doppler and contrast-enhanced imaging of the cardiovascular system, as well as the sociology of innovation in biomedical technology. He is the recipient of the 2013 Young Investigator Award of European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB).

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Horton, etc., and classic peripheral arterial diseases). He is involved in multiple clinical studies on new drugs in thrombosis (rivaroxaban, innohep, UFH) and registers clinical rare vascular diseases (Reference center in France). He also developed vascular application of new ultrasound tools for vascular wall properties evaluation (elastography by ultrafast echo). His department is one of the leaders in this field in France. At the same time, he continues to conduct his 10 years of research experience (2 years at Harvard Medical School, Boston) on valve diseases (Mechanism and new treatments: percutaneous approaches) for which he received multiple NIH grants (CoPI, collaboration with Robert A. Levine, MGH, Boston, MA) and patents (working with the world leader in this field Pr. A. Carpentier) on mitral regurgitation after myocardial infarction and device for percutaneous mitral valve repair.

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