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Topology of blood transport in the human left ventricle by novel processing of Doppler echocardiography

Sahar Hendabadi¹, Javier Bermejo², Yolanda Benito², Raquel Yotti², Francisco Fernández-Avilés², Juan C. del Álamo³, and Shawn C. Shadden^{*,1}

¹Mechanical, Materials and Aerospace Engineering, Illinois Institute of Technology, Chicago, IL, United States

²Department of Cardiology, Hospital General Universitario Gregorio Marañón, and Instituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain

³Mechanical and Aerospace Engineering, Institute for Engineering in Medicine, University of California San Diego, La Jolla, CA, United States

Abstract

Novel processing of Doppler-echocardiography data was used to study blood transport in the left ventricle (LV) of 6 patients with dilated cardiomyopathy and 6 healthy volunteers. Bi-directional velocity field maps in the apical long axis of the LV were reconstructed from color-Doppler echocardiography. Resulting velocity field data were used to perform trajectory-based computation of Lagrangian coherent structures (LCS). LCS were shown to reveal the boundaries of blood injected and ejected from the heart over multiple beats. This enabled qualitative and quantitative assessments of blood transport patterns and residence times in the LV. Quantitative assessments of stasis in the LV are reported, as well as characterization of LV vortex formations from *E-wave* and *A-wave* filling.

Keywords

cardiomyopathy; intracardiac blood flow; Lagrangian coherent structures; velocimetry

1 Introduction

A number of complex flow phenomena take place in the left ventricle every cardiac beat. Due to the chiral nature of the human heart, unsteady flow follows complex three dimensional trajectories. Furthermore, because the ventricle is not completely emptied during ejection, blood entering through the mitral valve interacts with residual flow from preceding cycles. The clinical and physiological consequences of these fluid dynamics remain poorly understood. Simulation and imaging studies have suggested that intraventricular flow dynamics could have a potential role in overall chamber properties, by facilitating filling, increasing ejection efficiency, and avoiding blood stasis inside the ventricular chamber [13, 36, 34, 35, 24, 17]. These three aspects may be of key importance in patients with dilated cardiomyopathy (DCM). Typical findings of this condition, namely chamber dilatation and depressed systolic function, are known to be related to impaired filling, reduced ejection efficiency, and increased risk of intraventricular thrombosis [19, 22,

*Address correspondence to Shawn C. Shadden, Mechanical, Materials and Aerospace Engineering, Illinois Institute of Technology, Chicago, IL, USA. Phone: 312-567-5126. Fax: 312-567-7230. sshadden@gmail.com.

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33, 9]. The difficulties in obtaining high-resolution measurements of intracardiac flow in patients have traditionally limited clinical research in this field [18].

Ultrasound is currently the most versatile tool for cardiovascular imaging. Although phase contrast magnetic resonance imaging (PCMRI) is capable of measuring the full 3-directional velocity field inside the human LV, major drawbacks are cost, time, availability and poor temporal resolution. In comparison, ultrasound is rapid, widely-accessible, inexpensive and capable of high temporal resolution measurement. Conventional color-Doppler provides measurements of a single flow velocity component that is aligned with the ultrasound beam over a planar section. To solve this limitation, recent methods have been developed to estimate the full two-dimensional map of intracardiac flow using ultrasound. Echo-particle image velocimetry has shown to be accurate [16], but requires intravenous administration of contrast agents and is limited to low temporal resolution or small scanning sectors. Garcia, *et al.* [10] recently developed a technique to construct bi-directional, time-resolved (2D+t) LV velocity field data from conventional transthoracic color-Doppler and LV wall measurements. This digital processing of conventional color-Doppler echocardiograms is fully noninvasive and can obtain high temporal and spatial resolutions of flow inside the full LV chamber. It was demonstrated that, in the apical long-axis view, the errors due to the non-planar nature of the flow are minimized by requiring the estimated flow velocities to be parallel to both the posterior and anteroseptal LV walls. Head-to-head comparison of 2D+t Doppler and PCMRI data indicates that 2D+t Doppler accurately quantifies the main diastolic LV flow patterns in healthy volunteers and patients with DCM [2].

Despite these advances in the measurement of blood flow velocity maps, characterization of flow properties inside the LV chamber remains a challenge. Due to the risk of intraventricular thrombosis in the presence of abnormal geometries and impaired ventricular function, a comprehensive understanding of flow topology inside the LV chamber is particularly relevant in patients with ischemic and nonischemic DCM. Previous analyses of flow topology in the human LV have primarily been based on Eulerian descriptions, including streamlines [24] or vortical motions [12, 7]. Because of the unsteady nature of blood flow through the LV, these descriptions can be insufficient to properly assess transport topology [4].

While mixing and flow unsteadiness in the LV make direct characterization difficult, the computation of Lagrangian coherent structures (LCS) offers a framework to understand complex flow topologies (see [26] for a review). LCS can reveal vortex boundaries, interaction and transport mechanisms, and have been previously utilized to simplify hemodynamics analysis [31, 39, 38, 27, 32, 3, 37, 41]. In this paper we analyze the transport topology in the human LV from 2D+t Doppler echocardiography data in patients with DCM and compare their findings with normal subjects. Clinical LV velocity data derived from the imaging modality in [10] is used to compute LCS in the LV of 6 volunteers and 6 patients with DCM using methods described in §2. We demonstrate unique ability to identify and track the regions of ejected and injected blood in the LV respectively, providing qualitative and quantitative assessments of intraventricular blood transport. Furthermore, the importance of LCS for enabling the analysis of vortex formation and stasis is emphasized.

2 Methods

2.1 Study population

The present study is based on the analysis of data from 6 patients with DCM and 6 healthy volunteers without known cardiovascular risk factors, randomly selected from a large database of two-dimensional velocity maps recruited at our institutions. The study protocol was approved by the local institutional review committee, and all subjects provided written

informed consent for this study. Clinical and ventricular volume data are summarized in Tab. 1. Patients with DCM showed a wide range of LV volumes and ejection fractions.

2.2 Image acquisition

Image acquisition protocols are similar to Garcia, *et al.* [10]. A comprehensive conventional transthoracic Doppler-echocardiogram was performed in all subjects. Special care was taken to accurately record transmitral inflow and outflow tract velocities using pulsed-wave Doppler for the purpose of identifying event times of the cardiac cycle, Fig. 1. The timestamp for different cardiac events was used to identify the times of interest for analyzing results. Key event times were aortic valve opening (AVO) and closing (AVC), and the mitral valve opening (MVO) and closing (MVC). Full sector color-Doppler two-dimensional sequences were obtained from the apical long-axis for 6 to 12 beats during a patient's apnea using a Vivid 7 ultrasound scanner and a broadband 1.9–4.0 MHz transducer (GE Healthcare). Special care was taken to ensure the full LV was enclosed in the Doppler sector. The Doppler (velocity) and harmonic B-Mode (tissue-intensity) images were carefully recorded consecutively without moving or tilting the probe at frame rates of approximately 20 and 100 Hz, respectively.

2.3 Velocity field reconstruction

Two-dimensional, bi-directional, time-resolved (2D+t) velocity maps in the apical long-axis view of the LV were reconstructed from the color-Doppler echocardiography data. Fig. 2 shows representative 2D+t velocity maps superimposed over the B-mode ultrasound images of the LV. This modality was introduced and described in detail by Garcia *et al.* [10]. Briefly, we adopted a polar coordinate system (r, θ) centered at the head of the ultrasound probe, so that the Doppler signal provides the radial component of blood velocity over the LV [15], v_r . Azimuthal velocities, v_θ , which cannot be directly measured since they are perpendicular to the ultrasound beams, were recovered using the continuity equation under an assumption of planar flow,

$$\partial_\theta v_\theta(r, \theta) = -r \partial_r v_r(r, \theta) - v_r(r, \theta). \quad (1)$$

For each instant in time and each radial arc, the continuity equation is integrated using a velocity boundary condition (v_r, v_θ) that, by construction, is parallel to the LV wall. For this purpose, the LV wall was tracked using a commercially available speckle-tracking algorithm (EchoPAC, General Electric Healthcare, Horten, Norway) applied to the B-mode data. Overall, this approach is similar to the vector flow mapping method proposed by Uejima *et al.*, [14] although that method was restricted to the case in which vortices are bilaterally symmetric. This restriction is not applied in our method.

One can use the boundary value of (v_r, v_θ) measured at the posterior wall and integrate from left to right in Fig. 2 or, alternatively, use the boundary value at the anteroseptal wall and integrate from right to left. In practice, these two independent boundary conditions generally produce distinct solutions. A final solution can be constructed as a weighted sum where respective weightings of each solution range from 1 to 0 depending on the azimuthal distance from the respective LV wall. We employed the same weight function as [10], which cancels the error due to the planar flow approximation when this error is proportional to the signal in the continuity equation, v_θ . The error of 2D+t Doppler velocimetry has been characterized in two previous studies. Garcia *et al.* [10] found the accuracy of this modality to be robust with respect to variations in the location of the transducer and the imaged long-axis plane. In a more recent clinical study, Alhama *et al.* [2] compared 2D+t Doppler velocimetry with PCMRI on 17 human volunteers, concluding that 2D+t Doppler velocimetry accurately quantifies the flow patterns in the LV. In particular, Alhama *et al.*

showed that the LV vortex position correlated well between techniques (intra-class correlation coefficient $R_{ic} = 0.66$), and the agreement for vortex circulation and energy was excellent, without significant bias ($R_{ic} = 0.83$ and 0.77 ; error = $3 \pm 47\%$ and $6 \pm 57\%$, respectively). The radial and azimuthal resolutions of the velocity data used in this study were approximately 5.4×10^{-1} mm and 2.3×10^{-2} radians. The equivalent length range in the azimuthal direction ranged from roughly >0.5 mm to <3 mm over the length of the LV. The temporal resolution of the data ranged between 5.2 to 7.5 ms from the retrospective frame-interleaving algorithm that merged data from consecutive beats taken during the acquisition. It should be noted that this procedure only requires acquiring ≈ 10 consecutive beats and, thus, it can be performed in our method without increasing the image acquisition time.

2.4 Unstructured moving mesh generation

The computation of LCS described in §2.5 below requires the integration of dense sets of particle trajectories over the LV. The polar representation of the velocity data inherent to ultrasound measurement creates a “staircase boundary” of velocity nodes near the LV wall. This has at least two disadvantages for trajectory computations: (1) an inaccurate representation of the LV boundary, and (2) difficulty imposing the no penetration condition at the LV wall. The second disadvantage is the most important. The advection of particle trajectories using structured empirical data, from ultrasound or MR, leads to significant leakage of particles through the LV boundary into regions where the velocity field is ill-defined, cf. Fig 3. This leakage results in significant errors in trajectory computation that pollute Lagrangian statistics derived from the trajectory information. Therefore, to ensure accurate flow structure analysis, we interpolate the polar grid data to an unstructured mesh that (1) is defined only over the LV interior, and (2) deforms consistently with the LV wall motion recovered from B-mode ultrasound.

The coordinates of the LV wall from the EchoPAC tracking algorithm used in deriving the velocity field data were used at an arbitrarily chosen time as boundary nodes to generate an unstructured (triangular) grid over the interior of the domain using the DISTMESH package [21]. To avoid topological changes in the mesh over time, the connectivity was maintained by allowing this initial mesh to deform according to the LV wall motion as described next. Let $\mathbf{v}(\mathbf{x}_b, t)$ denote the velocity of the LV wall at the arbitrary boundary point $\mathbf{x}_b$ and time t . A fixed reference point $\mathbf{x}_f$ was chosen arbitrarily near the center of the LV. Each node in the unstructured grid was updated as follows:

```

for each velocity time frame  $k$ , except last do
  for each node  $n$  in the unstructured grid do
    Compute vector from the reference point to node  $n$ :  $\mathbf{x}_{fn} = \mathbf{x}_n - \mathbf{x}_f$ 
    Determine boundary segment  $\mathbf{s}_k = \mathbf{x}_{b_{k-1}} - \mathbf{x}_{b_k}$  intersected by the
    ray along  $\mathbf{x}_{fn}$ 
    Compute intersection point  $\mathbf{i}_k$  between ray along  $\mathbf{x}_{fn}$  and vector  $\mathbf{s}_k$ 
    Interpolate wall velocity  $\mathbf{v}(\mathbf{i}_k)$  using boundary velocities  $\mathbf{v}(\mathbf{x}_{b_{k-1}})$ 
    and  $\mathbf{v}(\mathbf{x}_{b_k})$ 

    Compute mesh displacement velocity  $\mathbf{v}(\mathbf{x}_n) = \mathbf{v}(\mathbf{i}_k) \frac{d_n}{d_b}$ , where  $d_n$ 
    =  $\mathbf{x}_n - \mathbf{x}_f$  and  $d_b = \mathbf{i}_k - \mathbf{x}_f$ 
    Update  $\mathbf{x}_n(t_{k+1}) = \mathbf{v}(\mathbf{x}_n) \times (t_{k+1} - t_k)$ 
  end for

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end for

Velocities from the polar grid can then be transferred to the moving unstructured grid via space-time interpolation. While the above choice for deforming interior nodes is ad hoc, this has little consequence if the unstructured elements remain commensurate in size (or smaller) to the elements of the polar grid. Under these circumstances, there is generally no loss of information in interpolating the polar grid onto the unstructured grid. A maximum edge size of 1 mm was used for the unstructured grid generation and the temporal resolution of the interpolated data was around 12 ms to match the wall tracking data. The resulting velocity data was post-processed to obtain finite-time Lyapunov exponent (FTLE) fields for LCS identification as described below. It was verified that further refinement in the spatial resolution of the unstructured velocity grid resulted in negligible change to the results.

2.5 LCS identification

The computation of LCS has become a standard tool for advective transport analysis. LCS are typically defined as locally the most strongly attracting or repelling material surfaces and help reveal the structures organizing fluid transport and mixing, see [26] and references therein. A common method to identify LCS is by plotting the spatial distribution of the FTLE and identifying LCS as curves that locally maximize the FTLE measure, see [30].

The basic strategy of computing the FTLE field is straightforward. A grid of particles is seeded over the fluid domain and advected from t_0 to $t_0 + T$, which provides the flow map $\mathbf{F}_{t_0}^t: \mathbf{x}(t_0) \mapsto \mathbf{x}(t_0 + T)$ for each particle. This enables the right Cauchy-Green deformation tensor,

$$\mathbf{C}(\mathbf{x}_0, t_0, t) = \nabla \mathbf{F}_{t_0}^t(\mathbf{x}_0)^T \cdot \nabla \mathbf{F}_{t_0}^t(\mathbf{x}_0), \quad (2)$$

to be evaluated at the initial locations $\mathbf{x}_0 = \mathbf{x}(t_0)$. The FTLE, Λ , is computed from the largest eigenvalue of $\mathbf{C}$ as

$$\Lambda(\mathbf{x}_0, t_0, t) = \frac{1}{|T|} \ln \sqrt{\lambda(\mathbf{x}_0, t_0, t)}. \quad (3)$$

Computing the backward time flow map ($T < 0$) is used to identify *attracting* LCS and the forward time flow map is used to identify *repelling* LCS. For unsteady flow, the above procedure is repeated for a range of times t_0 to provide a time-series of FTLE fields, and thus a time history of the LCS movements. For the results herein, the forward, and backward, FTLE field was computed at 30 time points in the cardiac cycle for each subject. Each of these FTLE fields was computed using a 2 beats forward, or 2 beats backward, integration length. Tracers leaving through open boundaries (valves) were continued with their exit velocity until the integration length. The methods for particle tracking and FTLE computation on unstructured, moving grids was described in [5].

2.6 Residence time mapping

As shown in the results below, the identified LCS enable tracking of regions of injected and ejected blood to and from the LV. With this information residence time maps for blood inside the LV can be generated. LCS were manually extracted for this purpose as piecewise linear curves to delineate regions of injected or ejected flow. The LCS region analysis was performed by incorporating the time-events of the cardiac cycle measured offline, as well as the EKG signal, to enable tracking of the transport topology at common instants of the cardiac cycle.

Residence times (τ) were determined from the regions enclosed by the LCS and quantified in number of cardiac cycles. The ± 2 cardiac cycle integration time used for FTLE computations enabled regions with the following residence times to be quantified: flow injected and ejected in the same beat ($\tau = 0$, also referred as direct flow [4]), flow residing for a complete beat ($\tau = 1$), and flow residing for two complete beats ($\tau = 2$). Additionally, if blood regions that do not enter or leave the ventricle over ± 1 beats are also considered, regions of $\tau = 2, 3, 4$ can be identified (cf. Fig. 8 and accompanying table).

In order to illustrate the inherent Lagrangian nature of the transport processes dictating LV stasis, we compare τ obtained from analysis of LCS with two complementary Eulerian residence times obtained directly from time averages of the velocity field,

$$\tau_1 = \frac{T \sqrt{S}}{\| \int_0^T \mathbf{v}(\mathbf{x}, t) dt \|} \quad \text{and} \quad \tau_2 = \frac{T \sqrt{S}}{\left[\int_0^T \| \mathbf{v}(\mathbf{x}, t) \|^2 dt \right]^{1/2}}, \quad (4)$$

where T is the period of the cardiac cycle and S is the area of the imaged LV section. In Eq. (4), τ_1 and τ_2 are non-dimensionalized so that they measure residence time in whole beats, thereby enabling direct comparison with τ coming from LCS analysis. Note also that τ_1 quantifies the stasis from the time-averaged velocity field while τ_2 quantifies the time-averaged stasis from the velocity magnitude.

3 Results

3.1 Transport topology

Figure 4 displays snapshots of the backward FTLE field for a representative subject (Patient 1) over the LV filling phase. There are distinct curves of high FTLE that identify attracting LCS resulting from blood injection from the left atrium. These structures are generated from *E-wave* and *A-wave* filling. Notably, the *E-wave* LCS denotes the propagating boundary of early diastolic filling (top row). This volume of injected blood rolls up into a vortex ring and the *E-wave* LCS becomes the leading edge of the vortex. Subsequent filling due to atrial contraction produces an *A-wave* LCS that reveals the propagating boundary of the blood volume from end-diastolic filling (middle row). This injected blood creates separate swirling motion leading to an entrained vortex; the *E-wave* LCS becomes the leading edge of this second vortical structure. The bottom row displays these regions combining and beginning to eject from the LV during early to mid systole.

Figures 5 and 6 display, respectively, the evolution of the forward time and backward time FTLE fields at different instances of the cardiac cycle in a second representative subject (Patient 2). The nature by which the identified attracting and repelling LCS reveal the transport template of injected and ejected blood to and from the LV for this subject is indicative of the LCS computations for the other 11 subjects analyzed. Snapshots of forward FTLE at 8 times in the cardiac cycle are displayed in Fig. 5 starting and ending with AVO, which is the onset of blood ejection from the LV. Because the FTLE is computed from a 2 beat integration, the LCS reveal the regions of blood that will be ejected from the LV over the current and subsequent beats and these regions have been shaded. The red region is blood ejected during the cycle displayed and the green region is the blood ejected during the subsequent heart beat. Comparing panels (a) and (h), the green region replaces the red region after one cycle, and the yellow region (shown only for the last panel) replaces the green region.

The snapshots of backward time FTLE at 8 times in the cardiac cycle for the same subject (Patient 2) are shown in Fig. 6. These fields span one cardiac cycle starting and ending at

MVO, which is the onset of injection into the LV. The curves of high backward FTLE identify attracting LCS that reveal the boundaries of injected blood to the LV from the left atrium, as described for Fig. 4. The LCS bounding the region shaded in red reveals the boundary of injected blood into the LV during the cardiac cycle displayed, and the region shaded green reveals the blood injected to the LV from the previous cycle. The yellow region (shown only for the first panel) is the region of blood injected from 2 cycles prior the cycle shown. Comparing panels (a) and (h), the red region replaces the green region, and the green region replaces the yellow region after one cycle. Note that the identified regions are those enclosed by the *E-wave* LCS since these regions generally enclose blood from *A-wave* filling as well.

3.2 Quantifying LV stasis

Figure 7 displays superposition of forward and backward FTLE fields for all subjects, immediately following mitral valve closing (MVC). The shaded regions enclosed by the LCS delineate the blood being ejected/injected during the same cardiac cycle. Overlap of the injected flow that is ejected in the same cycle is defined as *direct flow*, which has been shaded green. The region shaded red is the blood injected from the left atrium that remains in the LV at the end of systole and is often termed the *retained inflow*. The portion of the blood being ejected through the aortic valve that originated in the LV itself at the start of the cycle (i.e. not originating from the left atrium in the same cycle) is defined as *delayed ejection flow*. To compare with a recent study of LV transport [4], *direct flow* was calculated for each subject, and results are presented in Tab. 2 and Tab. 3. The values listed in Tab. 2 are the ratio of the direct flow area to the area of the LV at MVC for each subject, and the ones presented in Tab. 3 are the ratio of the direct flow area to the area of the total inflow at the end of diastolic phase.

A more complete view of stasis is offered in Fig. 8. This figure shows compartmentalization of LV based on the blood residence time, measured in whole beats, for Patient 2. The most lightly shaded region corresponds to the direct flow region highlighted in Fig. 7. The ± 2 beats integration lengths used to compute FTLE enables tracking of blood injected from the current beat and proceeding beat, as well as tracking of blood ejected during the current beat and subsequent beat. This leads to 9 distinct blood transit scenarios described in the inset table of Fig. 8; these scenarios lead to 6 correspondingly unique residence time descriptions as shown. Comparison of the residence time mappings for all 12 subjects is presented in Fig. 9.

Fig. 10 displays τ_1 and τ_2 for two representative examples of healthy and dilated LVs, revealing that the Eulerian residence times underestimate stasis, and do not reproduce the intricate compartmentalization of the ventricular chamber in terms of residence time.

To investigate the reproducibility of LCS extraction and consequently transport template detection using color Doppler images, two image sequences blindly obtained and processed by two different observers from a healthy volunteer were used for LCS computations. Fig. 11 shows the overlap of attracting and repelling LCS immediately after MVC, as used to quantify direct flow. Analysis of the data obtained by the first observer produced a direct flow value of 49.7% while analysis of the data from the second observer resulted in a value of 47.0%.

4 Discussion

A novel method to non-invasively quantify the transport topology and stasis inside the human LV from echocardiography has been presented. This is achieved by recent developments in digital processing of color-Doppler echocardiography, as well as recent

developments in fluid transport analysis through LCS identification. The significance of this work is to enable characterization of the *in vivo* transport topology inside the human LV. This information provides novel physical insights into the fluid dynamical processes that could be useful for clinically evaluating LV function, such as filling, ejection, vortex mechanics and stasis. Specifically, we combine the computation of attracting and repelling LCS in the human LV from *in vivo* measurements to quantify injection and ejection properties. We also report clear delineation of the propagating vortex boundaries associated with *E-wave* and *A-wave* filling. Quantification of these vortices could potentially provide physiological information on the impact of different diseases and therapeutic interventions on global chamber function.

This study employs high-resolution 2D+t velocity maps obtained from echocardiography in the apical long-axis view of the LV [10]. This modality has been validated *in vitro* against particle image velocimetry and *in vivo* against PCMRI for healthy volunteers and patients with DCM [2]. The velocity field reconstruction computations, and subsequent FTLE field computations, can be achieved relatively rapidly once appropriate data is available and parameters are determined. While this is currently time-intensive, much of this process can be automated through improved algorithmic and software design. Under these conditions, each FTLE field can be computed on the order of minutes from raw echocardiography data using a standard desktop computer. The most time-intensive aspect of this post-processing is LCS extraction for quantitative assessment. This was done manually for the study herein. Inter-observer variability in this manual extraction resulted in uncertainty in LCS location up to ± 2 mm, which was less than 1% of the short axis width of the LV, manifesting in nearly indistinguishable change in LCS locations when viewed at the scale of the LV. However automated techniques for LCS extraction would be needed for high throughput clinical applications. These methods are currently being developed [20].

In all healthy and DCM subjects, prominent LCS were observed that revealed the time-varying boundary of injected and ejected blood. Increasing the integration time span of FTLE computation enabled regions injected from previous cycles or ejected from subsequent cycles to be identified. We note however, that as the integration time increases, the folding and mixing of these regions becomes more complex and less clearly recognizable from visual inspection or amenable to algorithmic extraction. Furthermore, subharmonic (e.g. breathing) modulations in the flow velocity maps were neglected by acquiring the echocardiographic while breath holding and merging the data into a single periodic heart beat. For these reasons, we limited our integration times to ± 2 beats for FTLE computations.

Evolution of identified LCS indicated swirling motion of the fluid, both while entering the LV in the diastolic phase and exiting the LV in systolic phase. From previous isolated vortex formation studies [28, 29], it was shown that hyperbolic trajectories at the leading and trailing edge of a vortex ring produce dominant attracting and repelling LCS that together form the vortex boundary and describe entrainment and detrainment. In the recent study of [37], *E-wave* filling boundaries were observed from PCMRI LV data. We likewise observed leading edge attracting LCS associated with vortex formation from *E-wave* filling, but also identified an *A-wave* filling vortex boundary, as shown in Fig. 4. The trailing edge of these vortices could be identified from the repelling LCS, although usually less well defined. Because the focus here was on filling and ejection patterns, especially in relation to stasis, the complete vortex boundaries from the attracting and repelling LCS were not highlighted.

Although the *E-wave* vortex carrying injected blood from the left atrium reached the LV apex in most cases (especially in healthy cases), regions near the apex and posterior walls of the LV are generally not flushed during the same cardiac cycle. The direct flow regions of

injected blood that is immediately ejected in a single beat were uncovered by superimposing forward and backward FTLE. Direct flow percentage of end diastolic volume and total inflow volume are presented in Tab. 2 and Tab. 3. A previous LV transport study using 3D PCMRI data reported values of direct flow as low as 11%, and $44\pm 11\%$, of total inflow in DCM, and healthy volunteers, respectively [4], which was accomplished by direct tracking of numerically integrated trajectories. We reported values of direct flow percentage of total inflow to be $71\pm 9\%$ in healthy volunteers and $47\pm 17\%$ in DCM patients. Similarly, the values of direct flow percentage of end diastolic volume were $27\pm 13\%$ for DCM cases, and $43\pm 11\%$ for healthy volunteers, compared to 4%, and $21\pm 6\%$, for DCM, and healthy, cases in the Bolger, et al., study [4]. We hypothesize that the larger direct flow measures observed in this study are the result of limiting analysis to the apical long axis view, which is the most direct path of blood to and from the LV. While our average value of direct flow for DCM patients was significantly lower than for healthy subjects, the direct flow average was not as low as reported for the single DCM subject in [4]. We noticed wide variation in direct flow values for healthy and DCM cases, resulting in partial overlap in the ranges from both populations. This overlap between populations could be related to the wide range of LV volumes and ejection fractions from the group with DCM.

Direct flow regions could be obtained by tracking particles forward and backward in time, tagging particles that pass through the aortic or mitral valve during the same beat, and mapping them back to their starting locations, as done previously [4, 6]. However, one advantage of the approach presented here is that LCS depict the time-dependent flow topology, in addition to providing a means to quantify these measures. Thereby this framework enables both qualitative and quantitative assessment of LV flow, which is not as readily accessible from particle tracking alone. Furthermore, more fundamental insight into fluid mechanic structures, such as the *A-wave* boundary, the trailing vortex boundary, or fluid entrainment and detrainment mechanisms (all of which have not been previously reported on) are not readily accessible from particle tracking statistics or visualization.

By analysis of LCS, this study has provided quantitative maps of blood residence time in the LV. While blood flow stasis is a widely recognized risk factor for thrombosis [1], so far its assessment remains relatively qualitative and is often based on flow visualization or surrogate Eulerian metrics [23]. This limitation is particularly challenging in the LV because flow in the heart is highly unsteady compared to most other vessels. Furthermore, since the ventricular chambers are not tubes, low wall-shear stress cannot be employed to identify regions of recirculation and stasis in the LV. Our results suggest that Eulerian estimation of residence time based on the magnitude of the velocity tends to underestimate stasis, and fails to capture the accuracy and complexity of transport patterns in the LV.

Intracardiac LCS computations based on static grid measurements are especially susceptible to particle flux, which may lead to erroneous flow structures. We interpolated the original static polar grid data from ultrasound to a deformable unstructured mesh that matched precisely to the LV wall motion recovered from B-mode ultrasound. This enabled explicit representation of the LV boundary, and the ability to impose the no penetration condition at the wall when computing trajectory-based FTLE fields. Spurious LCS that we had encountered previously [25, 11] were removed by this processing, which could potentially explain why we observed more robust and better-defined coherent structures than in intracardiac FTLE computations presented in the recently published PCMRI study [37].

The velocity reconstruction domain was automatically truncated to exclude radial stations intersecting the base of the LV, which allowed us to minimize the error associated to planar flow as outlined above (see Garcia *et al.* [10] for further details on the reconstruction algorithm). Due to careful alignment of the ultrasound probe, this led to a small excluded

region in close proximity to the mitral and aortic valves. This typically excludes roughly 2.5% of the apical long axis LV area. For example, the evolution of repelling LCS in some DCM cases seemed to indicate that the volume of the incoming blood to the LV increased slightly after mitral valve closing. This appeared to occur when portions of the injected (or ejected) blood may have been out of the field of view during MVC and later came into the field of view. We are working to adapt our velocity reconstruction algorithm so that reliable velocity field data in proximity to the valve can be obtained. It should also be noted that the wall tracking algorithm used here tracked the mid-myocardial movement, not endocardium. This led to errors in velocity field measurement close to the LV wall in some cases, which resulted in apparent stagnation in some near-wall regions. This did not affect the LCS boundaries described above, but could have led to apparent reduction in reported direct flow values since the LV volume is being over estimated. We are developing methods to track the endocardium to prevent this from occurring.

It is recognized that the flow topology in the LV is three-dimensional. Thus, tracking LCS in two-dimensions constitutes a potential limitation of this study, and the present results can at most be interpreted as 2D samplings of the 3D transport templates in the LV. Alternatively PCMRI can be used to obtain 3D flow fields, but not without limitations. These include reduced temporal and/or spatial resolution, and PCMRI may not satisfy continuity without regularization [8]. While resolution is obviously important when tracking flow trajectories, the flow topology is also very sensitive to the first invariant of the velocity gradient tensor, which is precisely the divergence of the velocity field [40]. The present 2D+t Doppler LCS method is less sensitive to these limitations since 2D+t Doppler provides higher-resolution velocity fields that satisfy mass conservation and the boundary conditions at the LV walls by construction. Nonetheless, a systematic error study of LCS in both PCMRI and Doppler derived intraventricular velocity fields has not been performed yet and should be actively pursued in the future.

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Figure 1.
Cardiac event times.

Figure 2.
Velocity data reconstructed from Doppler-echocardiogram superimposed over the B-mode ultrasound image.

Figure 3.

Ultrasound's polar grid is not well suited for trajectory computations. Interpolation of the polar velocity data (dashed cell) immediately inside (“+” marker) or outside (“x” marker) the domain leads to erroneous use of data outside the blood flow domain. This leads to spurious particle flux that in turn pollutes LCS computation. Interpolating the velocity field to a moving unstructured grid helps prevent this problem.

Figure 4.

The backward time FTLE field reveals two well-defined LCS that enable qualitative and quantitative assessment of the *E-wave* and *A-wave* filling topology into the LV.

Figure 5.

The forward time FTLE field reveals a repelling LCS that bounds the region of blood that will be ejected from the LV, as shown in this time series. FTLE snapshots start and end with AVO for DCM Patient 2. ■ Ejected during current heart beat. ■ Ejected during next heart beat.

Figure 6.

The backward time FTLE field reveals an attracting LCS that bounds the region of blood that is injected from the right atrium, as shown in this time series. FTLE snapshots start and end with MVO for DCM Patient 2. ■ Injected during current heart beat. ■ Injected from previous heart beat.

Figure 7.
Superposition of backward and forward FTLE fields immediately following MVC for all 12 healthy and DCM patients. ■ Retained inflow. ■ Direct flow. ■ Delayed ejection flow.

Figure 8.
LV compartmentalization based on the residence time () considering a ± 2 beat horizon at MVC for DCM Patient 2.

Figure 9.
Residence time mapping for all 12 healthy and DCM subjects

Figure 10.

Comparison between residence times obtained from analysis of LCS (, left panels) and the Eulerian estimations of residence time defined in Eq. (4) (τ_1 , center panels, and τ_2 , right panels).

Figure 11.
Comparison of filling and ejection patterns following MVC from analysis of data obtained by two different observers for the same patient.

Table 1

Clinical data for cases under study.

ID	Age (yrs)	Gender	Ethiology	Regional Wall Motion	Heart Rate (bpm)	EDV (ml)	ESV (ml)	EF (%)
Healthy								
1	56	F	-	Normal	55	91	27	70
2	56	F	-	Normal	58	75	33	56
3	66	F	-	Normal	64	68	24	65
4	68	F	-	Normal	68	79	29	63
5	55	F	-	Normal	74	63	27	57
6	61	M	-	Normal	59	78	26	67
DCM								
1	78	M	Isch	Anterior & Apical Akinesis	52	140	91	35
2	36	M	Non Isch	Global Hypokinesis	86	164	119	27
3	63	M	Isch	Inferior & Apical Akinesis	57	170	110	35
4	70	M	Non Isch	Global Hypokinesis	62	91	48	47
5	41	F	Non Isch	Global Hypokinesis	62	135	89	34
6	75	F	Non Isch	Global Hypokinesis	53	102	79	23

Abbreviations: End Diastolic Volume (EDV), End Systolic Volume (ESV), Ejection Fraction (EF), Ischemic (Isch), Non Ischemic (Non Isch).

Table 2

Direct flow percentage of the end diastolic volume for healthy and DCM subjects.

Subject Number	Healthy	DCM
1	42%	27%
2	29%	4%
3	37%	24%
4	43%	35%
5	49%	41%
6	61%	32%
Mean±SD	43±11%	27±13%

Table 3

Direct flow percentage of the total diastolic inflow volume for healthy and DCM subjects.

Subject Number	Healthy	DCM
1	74%	45%
2	58%	17%
3	72%	37%
4	67%	62%
5	68%	58%
6	87%	60%
Mean±SD	71±9%	47±17%