

Four-dimensional flow cardiovascular magnetic resonance in aortic dissection: Assessment in an ex vivo model and preliminary clinical experience

Hector W. de Beaufort, MD,^{a,b} Dipan J. Shah, MD,^a Avni P. Patel, MSc,^a Matthew S. Jackson, MSc,^a Domenico Spinelli, MD,^b Eric Y. Yang, MD,^a Mohamad G. Ghosn, PhD,^a Kyle Autry, RT(R),^a Stephen R. Igo, BSc,^a Alan B. Lumsden, MD,^a Stephen H. Little, MD,^a Santi Trimarchi, MD, PhD,^{b,c} and Jean Bismuth, MD^a

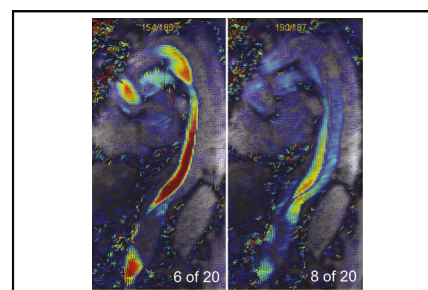
ABSTRACT

Objective: Four-dimensional flow cardiovascular magnetic resonance may improve assessment of hemodynamics in patients with aortic dissection. The purpose of this study was to evaluate the feasibility and accuracy of 4-dimensional flow cardiovascular magnetic resonance assessment of true and false lumens flow.

Methods: Thirteen ex vivo porcine aortic dissection models were mounted to a flow loop. Four-dimensional flow cardiovascular magnetic resonance and 2-dimensional phase-contrast cardiovascular magnetic resonance measurements were performed, assessed for intraobserver and interobserver variability, and compared with a reference standard of sonotransducer flow volume measurements. Intraobserver and interobserver variability of 4-dimensional flow cardiovascular magnetic resonance were also assessed in 14 patients with aortic dissection and compared with 2-dimensional phase-contrast cardiovascular magnetic resonance.

Results: In the ex vivo model, the intraobserver and interobserver measurements had Lin's correlation coefficients of 0.98 and 0.96 and mean differences of 0.17 (± 3.65) mL/beat and -0.59 (± 5.33) mL/beat, respectively; 4-dimensional and sonotransducer measurements had a Lin's concordance correlation coefficient of 0.95 with a mean difference of 0.35 (± 4.92) mL/beat, respectively. In patients with aortic dissection, the intraobserver and interobserver measurements had Lin's concordance correlation coefficients of 0.98 and 0.97 and mean differences of -0.95 (± 8.24) mL/beat and 0.62 (± 10.05) mL/beat, respectively; 4-dimensional and 2-dimensional flow had a Lin's concordance correlation coefficient of 0.91 with a mean difference of -9.27 (± 17.79) mL/beat because of consistently higher flow measured with 4-dimensional flow cardiovascular magnetic resonance in the ascending aorta.

Conclusions: Four-dimensional flow cardiovascular magnetic resonance is feasible in patients with aortic dissection and can reliably assess flow in the true and false lumens of the aorta. This promotes potential future work on functional assessment of aortic dissection hemodynamics. (J Thorac Cardiovasc Surg 2018; ■:1-10)



False lumen filling in early systole and early diastole seen on 4D-flow CMR.

Central Message

4D-flow CMR is feasible in patients with aortic dissection and can reliably assess flow in the true and false lumens of the aorta.

Perspective

4D-flow CMR allows assessment of hemodynamic parameters in patients with aortic dissection. This can help to locate entry and reentry tears or to determine chronicity of the dissection or extent of false lumen thrombosis in patients. Moreover, false lumen flow patterns might be correlated with long-term, dissection-related clinical outcomes.

See Editorial Commentary page ■

From the ^aHouston Methodist DeBakey Heart & Vascular Center, Houston, Tex; ^bThoracic Aortic Research Center, IRCCS Policlinico San Donato, San Donato Milanese, Italy; and ^cDepartment of Scienze Biomediche per la Salute, University of Milan, Milan, Italy.

Funded by the Pumps & Pipes Organization and ExxonMobil Upstream Research Company, WL Gore & Associates.

Received for publication March 8, 2018; revisions received May 24, 2018; accepted for publication June 3, 2018.

Address for reprints: Jean Bismuth, MD, Houston Methodist Hospital, DeBakey Heart & Vascular Center, 6550 Fannin St, Smith Tower, Ste 1401, Houston, TX 77030 (E-mail: JBismuth@houstonmethodist.org).

0022-5223/\$36.00

Copyright © 2018 by The American Association for Thoracic Surgery
<https://doi.org/10.1016/j.jtcvs.2018.06.022>

Abbreviations and Acronyms

4D-flow CMR	= 4-dimensional flow cardiomagnetic resonance
CFD	= computational fluid dynamics
LCCC	= Lin's concordance correlation coefficient
2D PC-CMR	= 2-dimensional phase-contrast cardiomagnetic resonance



Scanning this QR code will
take you to a supplemental
video and tables for the article.

DeBakey type III aortic dissection is uncommon but life threatening when it leads to complications such as malperfusion syndrome, aneurysmal degeneration, and aortic rupture. Endovascular intervention is first-line therapy in the presence of such complications, whereas medical therapy is the recommended treatment for patients with dissection without complications.^{1,2} However, there is currently equipoise regarding the optimal management of uncomplicated aortic dissection.³ A study from the International Registry of Acute Aortic Dissections reports that approximately three quarters of patients with initially uncomplicated dissection eventually develop aneurysms over time, increasing their risk of mortality at 5-year follow-up compared with patients treated with early endovascular repair (29.0% vs 15.5%).⁴ Identifying suitable candidates for early intervention is expected to improve outcomes of patients with dissection, and adverse hemodynamic and biomechanical conditions have been identified as potential predictors of aneurysmal changes and dissection-related morbidity and mortality.^{5,6} However, strong functional imaging data of such hemodynamic factors are lacking, which has been recognized as a major gap in evidence in both American Heart Association and European Society of Cardiology guidelines on aortic disease.^{1,2}

Four-dimensional flow cardiovascular magnetic resonance (4D-flow CMR) of blood flow provides full volumetric spatial and velocity encoded data, which are collected during several minutes but represented as 1 average heartbeat. 4D-flow CMR is promising as a method for functional assessment of blood flow dynamics, but there are few reports validating it with other imaging modalities,⁷⁻⁹ and none specifically in the setting of aortic dissection. Therefore, the purpose of this study was to evaluate the feasibility and accuracy of 4D-flow CMR

assessment of true and false lumens flow volume compared with a sonotransducer reference standard. In addition, we aimed to describe preliminary application of the technique in a clinical setting.

MATERIALS AND METHODS**Creation of an Ex Vivo Porcine DeBakey Type III Aortic Dissection Model**

No live animals were engaged for this research. Aortas of healthy domestic swine, age 6 to 9 months, weighing 150 kg or less, were purchased from a certified, commercial third-party (Animal Technologies, Tyler, Tex). The aorta was initially trimmed of excess tissue and separated from the heart at the aortic root just distal to the coronary arteries and subsequently trimmed up to the level of the renal arteries. Intercostal branches were ligated using silk suture and sealed using biocompatible cyanoacrylate (ETHICON OMNEX Surgical Sealant, Somerville, NJ) to prevent leaking during subsequent hydrodynamic testing. The aortic dissection model was created according to a fixed number of steps (Figure 1).

Physiologic Flow Model

The descending portion of the dissection model was pulled taut and cut to 19.5 cm length, corresponding to the length of the test construct. The aortic root, distal aorta, and arch vessels were cannulated and mounted to the test fixture using custom hose barb fittings. Silicon O-rings sealed the inner and outer surfaces of the fixture to allow complete submerging of the aorta, thereby increasing the total signal of the construct within the magnetic resonance imaging (MRI) magnet. The inflow and outflow hose barb fittings of the test construct were coupled to an MRI-compatible mock circulation loop¹⁰ for testing and imaging under set flow conditions (Figure 2). The system was filled with 4.5 L of blood analog consisting of a 30/70% glycerin/water solution to permit appropriate viscous properties. The MRI-compatible HeartBeat Simulator, which creates controlled filling and ejection of the left ventricular component, was set to a beat rate of 70 beats/min for all models. Stroke volumes were set individually for each aorta, ranging from 30 to 72 mL/beat. Flow transducers (Transonic Systems, Ithaca, NY) with a reported accuracy of $\pm 4\%$ were used to measure aortic inflow and outflow. Thirteen dissection models were created and tested using this method.

Ex Vivo Cardiac Magnetic Resonance Scan Acquisition and Analysis

Each ex vivo model was evaluated using 2-dimensional phase-contrast cardiomagnetic resonance (2D PC-CMR) and 4D-flow CMR techniques within a 1.5T MRI scanner (Magnetom Avanto, Siemens Healthineer, Erlangen, Germany) to assess dissection anatomy and luminal flow (Figure 2). 2D PC-CMR images were acquired at the inlet of the model, arch vessels, proximal descending aorta, mid-descending aorta, and outlet of the model. 2D PC-CMR imaging parameters consisted of the following: slice thickness 4 to 6 mm, bandwidth 445 Hz/px, spatial resolution 173×230 to 300×300 , temporal resolution 41.2 to 58.6 ms, flip angle 20° , and velocity encoding threshold 150 to 225 cm/s. Acquired 2D PC-CMR Digital Imaging and Communications in Medicine datasets were evaluated independently by 2 observers (Argus Flow, Siemens, Germany). 4D-flow CMR imaging parameters consisted of the following: slice thickness 4 mm, bandwidth 490 Hz/px, spatial resolution 320×554 , temporal resolution 44.32 ms, and velocity encoding threshold 185 to 225 cm/s. 4D-flow CMR datasets were evaluated by 2 observers independently (GT flow, GyroTools, Winterthur, Switzerland). To study the same anatomic regions as were studied with 2D PC-CMR (aortic inlet, arch vessels, proximal descending aorta, mid-descending aorta, and aortic outlet), these planes of interest were manually identified using anatomic landmarks from the

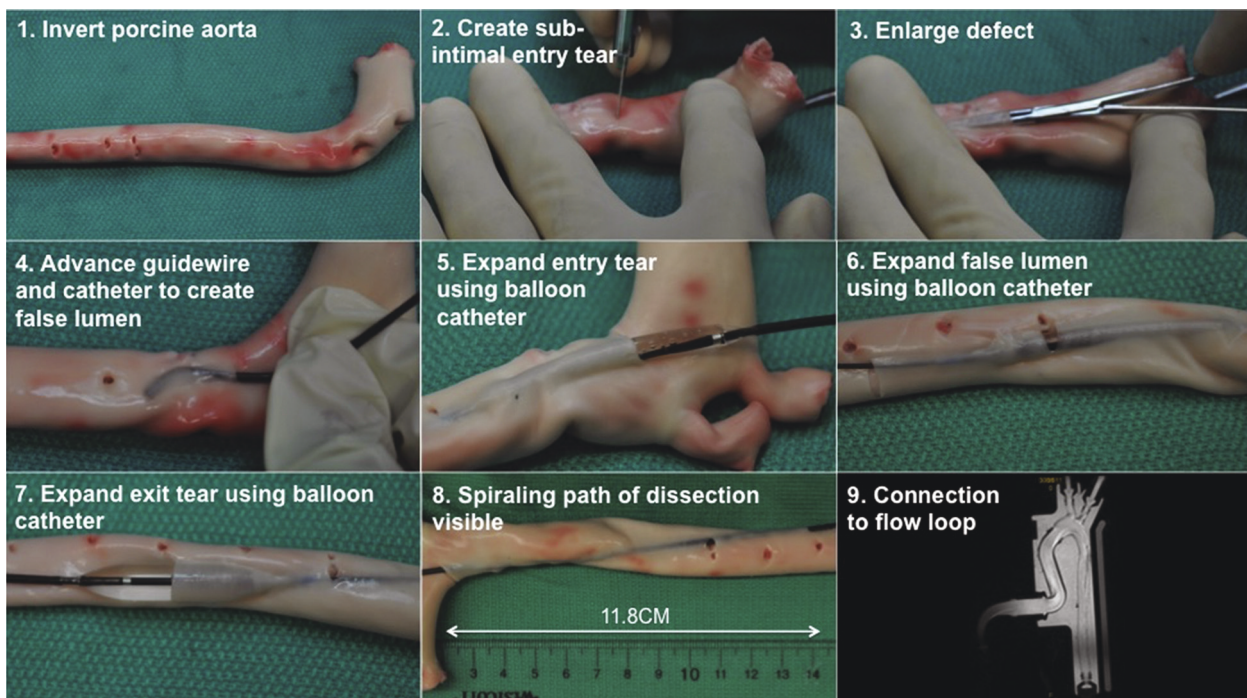


FIGURE 1. Creation of porcine ex vivo dissection model. First, the aorta was inverted (1) and an intimal defect (0.5-1 cm wide) was made distal to the left subclavian artery (2) and enlarged 1 to 2 cm using a hemostat (3), thereby establishing the proximal entry tear. A hydrophilic guidewire was then advanced into a guide catheter and inserted through the entry tear to induce separation of the intimal and adventitial layers through the media (4). The tip of the guidewire was advanced along the length of the descending aorta to yield a spiral dissection; percutaneous transluminal angioplasty catheters were advanced and inflated to enlarge the newly created entry tear (5) and false lumen (6). A secondary incision was made to permit the guidewire to exit, thereby establishing a distal reentry tear (7), once the guidewire had traversed a length of 12 cm from the entry tear (8). Finally, the model was mounted to the pulsatile flow loop (9).

magnitude data of the 4D-flow CMR datasets. The means of the flow values measured by the 2 observers were used to compare 4D-Flow CMR and 2D PC-CMR with each other and with a reference standard of sonotransducer flow measurements.

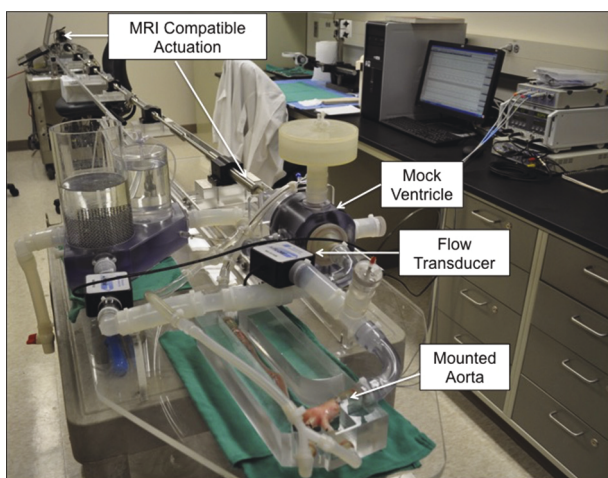


FIGURE 2. Experimental setup with ex vivo porcine aorta connected to the flow loop with MRI-compatible HeartBeat Simulator. MRI, Magnetic resonance imaging.

In Vivo Human Cardiac Magnetic Resonance Scan Selection, Acquisition, and Analysis

Our experience with 4D-flow CMR scanning of patients with aortic dissection started in 2011. At the time, scan acquisition times were still approximately 40 minutes. This has decreased to approximately 7 to 12 minutes in 2016, when the last patient was included. Imaging parameters were slice thickness 2 to 3 mm, bandwidth 445 to 789 Hz/px, spatial resolution 2.3×3.8 mm to 3.4×5.0 mm, temporal resolution 38 to 47 ms, flip angle 7° to 15° , and velocity encoding threshold 150 to 200 cm/s. The institutional database of CMR images was reviewed retrospectively for 4D-flow CMR datasets acquired in patients with aortic dissection from January 2011 to December 2016. The study was approved by the institutional review board at Houston Methodist Hospital. Datasets that were incomplete or acquired after endovascular treatment were excluded. Included datasets were evaluated by 2 observers independently at several standardized planes of interest (ascending aorta, proximal descending aorta, mid-descending aorta, distal descending aorta), which were assigned manually and identified on the basis of relation to the pulmonary artery bifurcation (ascending aorta, proximal, and mid-descending aorta) and celiac trunk (distal descending aorta). Furthermore, ascending and descending aortic flow visible on standard 2D PC-CMR acquisitions of the ascending aorta were compared with matched locations in the 4D-flow CMR flow measurements. This was done visually by selecting a plane in the 3D volume that was perpendicular to the aorta in all directions (x,y,z), corresponding to the 2D flow plane. GTflow software (GyroTools, Winterthur, Switzerland) creates the transversal image belonging to this plane, which was compared with the magnitude image of the 2D data as a double check. The parameters of these 2D PC-CMR acquisitions in the ascending aorta were slice

thickness 6 to 7 mm, bandwidth 606 to 704 Hz/px, spatial resolution 263×400 to 367×470 , temporal resolution 38 to 47 ms, flip angle 30° , and velocity encoding threshold 150 to 200 cm/s.

Statistical Analysis

The intraobserver and interobserver correlation of 4D-flow CMR flow assessment and correlation to other modalities was tested with Lin's concordance correlation coefficient (LCCC). An LCCC of greater than 0.95 was considered as good agreement, 0.90 to 0.95 was considered as reasonable agreement, and less than 0.90 was considered as poor agreement between measurements. The difference between measurements was assessed with Bland–Altman analysis. Other correlations were tested with Spearman's rank correlation.

RESULTS

Ex Vivo Flow Assessment

Figure 3, shows intraobserver and interobserver variability of 4D-flow CMR flow measurements, which had LCCCs of 0.98 (0.97–0.99) and 0.96 (0.94–0.97), and mean differences of $0.17 (\pm 3.65)$ mL/beat and $-0.59 (\pm 5.33)$ mL/beat, respectively. Figure 4 shows the comparisons among sonotransducer, 2D, and 4D-low CMR flow measurements. The agreement between 4D and 2D flow measurements had an LCCC of 0.97 (0.95–0.98), and the mean difference was $-0.60 (\pm 4.81)$ mL/beat. The agreement between 4D-flow CMR and sonotransducer measurements had an LCCC of 0.95 (0.92–0.97), and the mean difference was $0.35 (\pm 4.92)$ mL/beat. The agreement between sonotransducer and 2D flow measurements had an LCCC of 0.97 (0.94–0.98), and the mean difference was

$0.84 (\pm 3.56)$ mL/beat. The results of 4D-flow CMR flow measurements ex vivo are shown in Table E1.

In Vivo Human Flow Assessment

Thirty-six patients with aortic dissection with available 4D-flow CMR scans were identified. Ten patients were excluded because the scan had been performed after endovascular repair, and a further 12 patients from the start of our experience were excluded because the Digital Imaging and Communications in Medicine datasets were incomplete or contained errors, such as incorrect spatial resolution, too few phases per cardiac cycle, aliasing, or scans that were aborted in the middle of acquisition, leaving 14 patients with 4D-flow CMR scans for analysis. For the included patients, 4D-flow acquisition duration was 15 ± 7 minutes. Seven of these patients had a DeBakey type I aortic dissection, and 7 patients had a DeBakey type III aortic dissection. More details on patient characteristics are shown in Table 1.

Figure 5, A and B, show the intraobserver and interobserver variability of 4D-flow CMR flow measurements in vivo. The intraobserver and interobserver agreement between measurements had an LCCC of 0.98 (0.97–0.99) and 0.97 (0.96–0.98), and mean differences were $-0.95 (\pm 8.24)$ mL/beat and $0.62 (\pm 10.05)$ mL/beat, respectively. Figure 5, C, shows the comparison of 2D and 4D-flow CMR flow measurements in vivo. The agreement between 4D and 2D flow measurements had an LCCC of 0.91 (0.84–0.95), and the mean difference was $-9.27 (\pm 17.79)$ mL/beat,

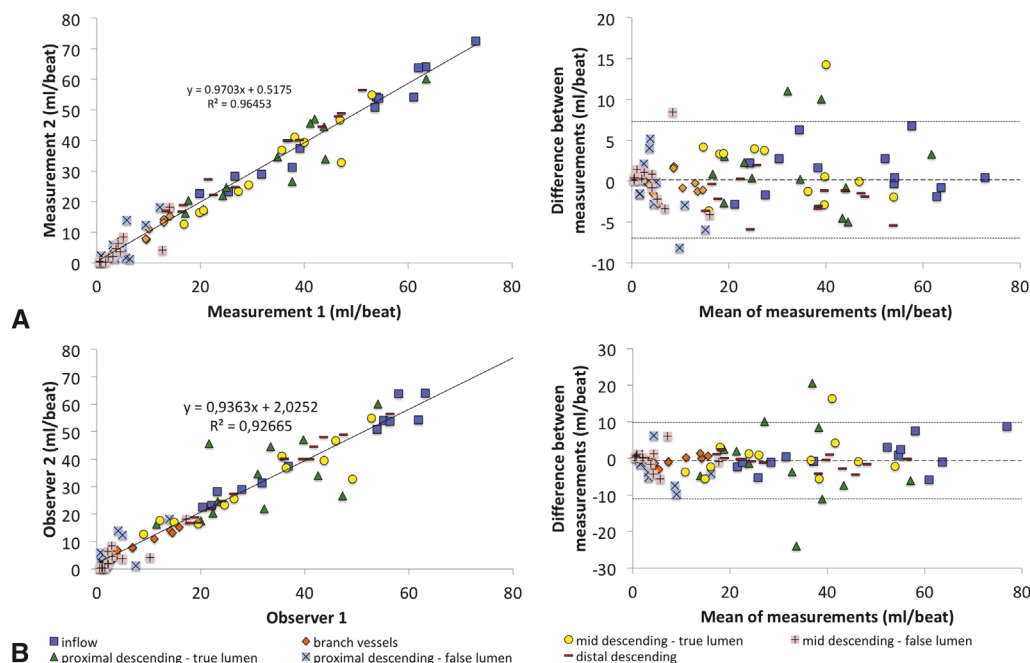


FIGURE 3. Correlation and Bland–Altman plots of 4D-flow CMR flow volume measurements in the ex vivo porcine aortic dissection model. A, Intraobserver variability. B, Interobserver variability.

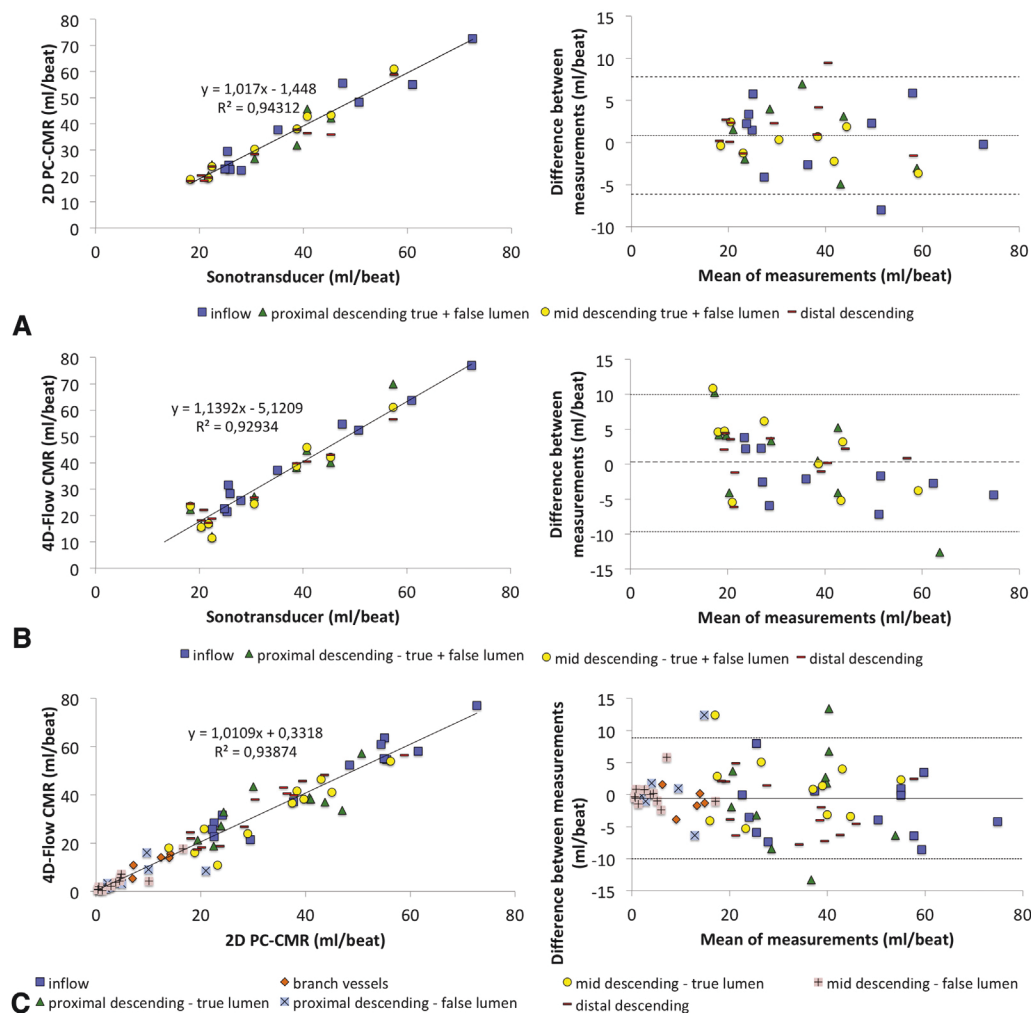


FIGURE 4. Correlation and Bland–Altman plots of sonotransducer, 2D phase contrast, and 4D-flow PC-CMR flow volume measurements in the ex vivo porcine aortic dissection model. A, Sonotransducer versus 2D PC-CMR. B, Sonotransducer versus 4D-flow CMR. C, 2D versus 4D-flow CMR. 2D PC-CMR, 2-Dimensional phase-contrast cardiomagnetic resonance; 4D-flow CMR, 4-dimensional flow cardiomagnetic resonance.

with ascending aortic flow especially showing consistently higher flow volumes on 4D-flow CMR (mean difference -23.76 ± 11.03 mL/beat). The discrepancy between 2D and 4D ascending aortic flow was greater in patients with (repaired) DeBakey type I versus type III aortic dissection: $-28.77 (\pm 10.34)$ versus $-18.91 (\pm 9.37)$ mL/beat ($P = .07$). Baseline correction of flow measured with 2D PC-CMR did not improve the correlation with 4D-flow CMR flow. Various other potential causes for the offset between 2D and 4D in the ascending aorta were investigated, but no significant correlation was found for maximum diameter of the aortic root, maximum diameter of the ascending aorta, previous aortic valve replacement, or tortuosity index of the ascending aorta. We also checked which of the 2 methods had closer correlation with the stroke volume as measured on cine-MRI sequences, but both had only a weak correlation (2D: Spearman's rho: 0.31, $P = .33$; 4D: 0.35, $P = .26$).

In vivo measurements of flow using 4D-flow CMR are shown in Figure 6 and Table E2. Mean forward flow was larger in the true lumen than the false lumen, whereas more reverse flow was measured in the false lumen. For example, in the mid-descending aorta, forward flow was $29.4 (\pm 26.1)$ mL/beat higher in the true lumen, whereas reverse flow was $6.78 (\pm 7.3)$ mL/beat higher in the false lumen. Examples of some of the qualitative information that can be obtained with 4D-flow CMR in the setting of aortic dissection are shown in Figure 7 and Videos 1 and 2.

Wall Shear Stress

The data on wall shear stress in the false lumen, generated with GT flow software, were evaluated for all 14 patients. Average wall shear stress magnitude in the proximal, mid-, and distal descending aorta was 0.10 ± 0.05 , 0.12 ± 0.06 , and 0.14 ± 0.08 N/m², respectively. Peak wall shear stress magnitude in the proximal,

TABLE 1. Characteristics of patients with aortic dissection with 4-dimensional flow cardiovascular magnetic resonance included in the study

	N = 14
Age, y (\pm SD)	60.2 (\pm 12.8)
Male, n (%)	8 (57)
Body surface area	2.0 (\pm 0.3)
Systolic blood pressure, mm Hg (\pm SD)	124.2 (\pm 22.5)
Diastolic blood pressure, mm Hg (\pm SD)	67.5 (\pm 11.5)
Heart rate, beats/min (\pm SD)	66.0 (\pm 12.0)
Stroke volume, mL (\pm SD)	99.7 (\pm 25.5)
Cardiac output, L/min (\pm SD)	6.2 (2.1)
Dissection type, n (%)	
DeBakey Type I	2 (14)
DeBakey Type I after graft replacement of the ascending aorta	5 (36)
DeBakey Type III	7 (50)
Dissection phase, n (%)	
Acute	3 (21)
Subacute	2 (14)
Chronic	7 (50)
Unknown	2 (14)
Maximum diameter, mm (\pm SD)	
Ascending aorta	41.0 (\pm 16.0)
Descending aorta	41.8 (\pm 7.8)
Abdominal aorta	33.9 (\pm 12.7)
No. of vessels from false lumen, median (range)	1 (0-2.5)
Presence of branch vessel obstruction, n (%)	
Dynamic	1 (7)
Static	2 (14)
False lumen thrombosis, n (%)	
No	8 (57)
Partial	6 (43)
Complete	0

SD, Standard deviation.

mid-, and distal descending aorta was 0.22 ± 0.11 , 0.23 ± 0.09 , and 0.29 ± 0.14 N/m², respectively. The extent of the dissection (DeBakey type I vs III) showed a significant correlation with average wall shear stress in the mid and distal descending aorta (Spearman's rho: -0.55 , $P = .04$ and -0.48 , $P = .08$), and with peak wall shear stress in the mid- and distal descending aorta (Spearman's rho: -0.48 , $P = .08$ and -0.59 , $P = .03$). No significant correlations were found for false lumen wall shear stress and maximum diameter of the descending aorta, chronicity of the dissection, or partial false lumen thrombosis.

DISCUSSION

4D-flow CMR is a promising imaging technique for the study of aortic hemodynamics, but has had limited clinical use so far, mainly because of long scan acquisition times in

the past. Other obstacles are the availability of postprocessing software and the additional cost of a research tool that may or may not be covered by insurance until its clinical relevance is firmly established. Today, scan acquisition durations are reduced to 7 to 12 minutes, paving the way for clinical application of 4D-flow CMR in acute disorders, including acute aortic dissection. However, to have full confidence in the assessment of flow in the true and false lumens by 4D-flow CMR, a physical model that permits the controlled creation of dissection geometry and that can subsequently be tested under known, controllable flow conditions is essential. By using such an ex vivo experimental set-up, 4D-flow CMR proved to correlate well with transducer measurements of luminal flow across all evaluated areas, without consistent overestimation or underestimation of true or false lumen flow. Moreover, the intraobserver and interobserver variability of 4D-flow CMR flow assessment in vivo proved to be small, confirming the reliability of the technique for clinical use.

An advantage of 4D compared with 2D flow techniques is the ability to assess the entire flow field of the aorta, instead of only a few select planes, allowing "off-line" assessment of regions of interest that at the moment of scanning may not have seemed relevant. Our study has not demonstrated any clinical implications, yet in the setting of aortic dissection, the ability to assess the flow field within the true and false lumens may be useful in identifying specific parameters such as retrograde filling, oscillatory flow, wall shear stress, false lumen stroke volume, helical flow patterns, and entry tear position. Some of these parameters have been correlated to disease progression in other studies, with small patient samples.^{11,12} Moreover, the detailed flow information that 4D-flow CMR can offer may be used to improve the quality of simulations of aortic hemodynamics with computational fluid dynamics (CFD).^{13,14} The reliability of CFD simulations depends on the set boundary conditions,¹⁵ which is notoriously difficult in aortic dissection, and 4D-flow CMR may help to set these detailed flow and velocity profiles. An advantage of 4D-flow CMR is that it is not as time-consuming and does not carry the high computational costs of CFD.

We noted consistently higher flow values in the ascending aorta but not the descending aorta with 4D-flow CMR compared with 2D PC-CMR. Previous studies comparing 2D- and 4D-flow assessment in the ascending aorta, in healthy volunteers, found that flow volume is equal or lower and peak velocity is higher when estimated with 4D-flow techniques compared with 2D measurements.¹⁶ This causes some uncertainty about which measurement depicts the actual flow volume most accurately. Of note, 2D PC-CMR has been shown to lead to a consistent underestimation of ascending aortic flow volume compared with left ventricular systolic volume measured on cine sequences, with more eccentric flow patterns causing a larger

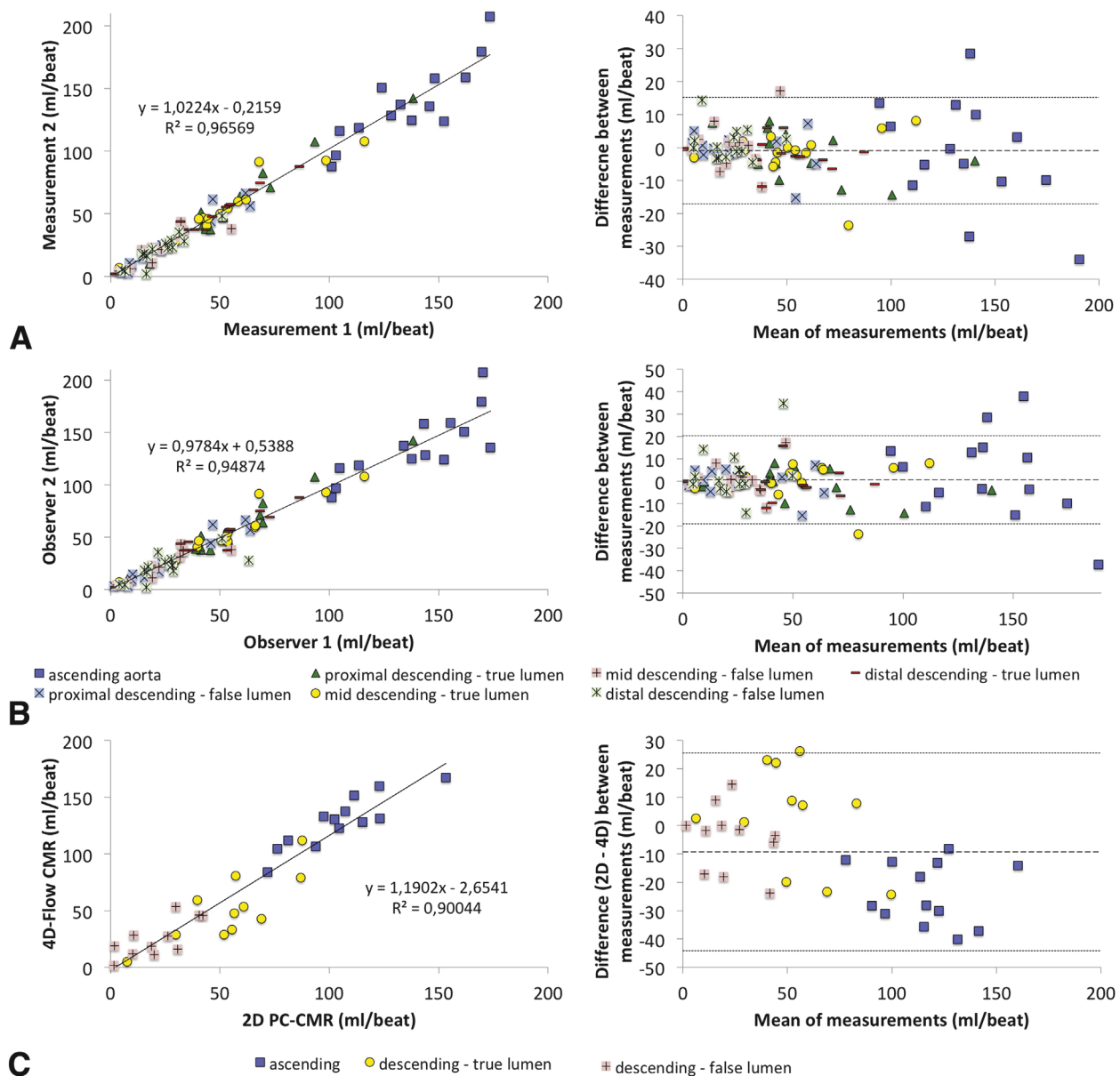


FIGURE 5. Correlation and Bland–Altman plots of 4D-flow CMR flow volume measurements in patients with aortic dissection (N = 14). A, Intraobserver variability. B, Interobserver variability. C, 2D PC versus 4D-flow CMR. 4D-flow CMR, 4-dimensional flow cardiac magnetic resonance.

underestimation.¹⁷ Eccentric or complex aortic flow patterns should not lead to an underestimation with 4D-flow CMR, which can detect voxels in any direction through a 3D volume.¹⁸ In healthy volunteers, in whom flow patterns are laminar, the discrepancy between 2D and 4D-flow CMR is generally small.¹⁸ We did not note a significant discrepancy between 2D and 4D-flow assessment in our ex vivo model or in the descending aorta in vivo. In both situations, flow patterns are more laminar than in the ascending aorta. This suggests that the discrepancy between 2D and 4D measurements in the ascending aorta in vivo may be due to an underestimation of 2D measurements rather than an overestimation of 4D measurements. We noted a greater

discrepancy between 4D and 2D in patients with (repaired) type I aortic dissection than those with type III aortic dissection. Graft repair has been shown to lead to more eccentric flow patterns,^{19,20} which could partly explain the discrepancy between 2D and 4D in our study. Imperfect matching of locations between 2D and 4D dataset, with potentially off-axis measurements, also could have played a role, which is a limitation of this work.

Study Limitations

The most important limitation of this study is the absence of a “gold standard” for assessing human in vivo aortic flow. Nevertheless, the data acquired in the ex vivo model,

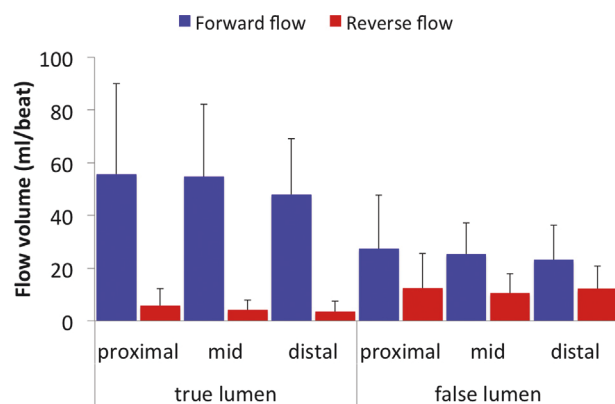


FIGURE 6. Bar graph showing forward and reverse flow as assessed by 4D-flow CMR in the true and false lumens of patients with aortic dissection (N = 14) for different sections of the descending thoracic aorta.

with strong correlations among 4D, 2D, and sonotransducer flow measurements, decrease the degree of uncertainty for the in vivo measurements. Furthermore, the clinical part of the study included scans performed between 2011 and 2016. A number of scans, from the early clinical experience, had to be excluded for technical errors, when scan acquisition times were still approximately 40 minutes, which in practice meant the scan was sometimes aborted before it was completed. The number of aborted scans is lower now that scan acquisition times have been reduced to approximately 10 minutes. A further limitation is that eddy current corrections are not part of the analysis in the software that was used for 4D-flow dataset postprocessing, even though eddy current corrections can lead to differences in flow volume of up to 10 mL/beat.²¹ Finally, the lack of follow-up data and small sample size limit the potential to interpret the clinical impact of the measured flow

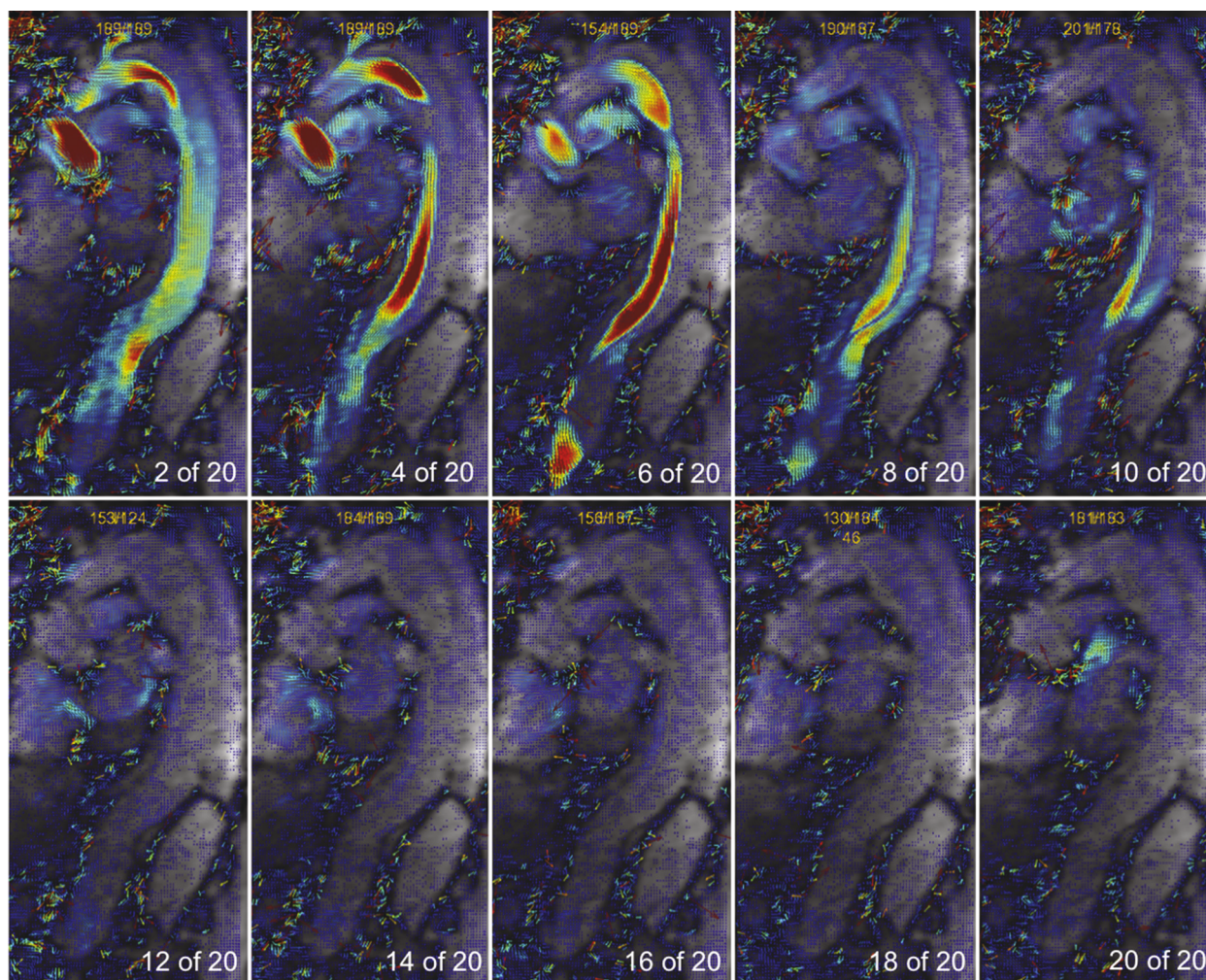
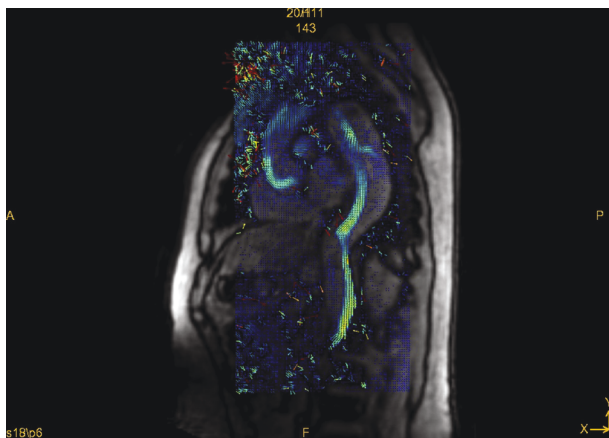


FIGURE 7. Images generated by GTflow (GyroTools, Winterthur, Switzerland) of selected timesteps from 4D-flow CMR in a patient with type III aortic dissection, showing false lumen filling especially during early systole (timestep 2 of 20) and early diastole (timesteps 8 and 10 of 20).

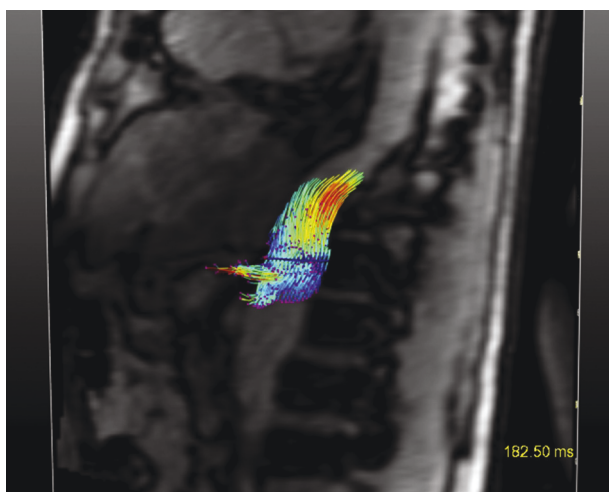


VIDEO 1. Video generated by GTflow (GyroTools, Winterthur, Switzerland) with images of 4D-flow CMR in a patient with type III aortic dissection, revealing a large entry tear in the mid-descending aorta. The video is looped so the same cardiac cycle is seen repeatedly. Video available at: <https://www.jtcvs.org>.

conditions. Future work may be focused on determining the diagnostic and prognostic value of 4D-flow CMR by correlating flow patterns to baseline factors, such as the chronicity of the dissection or the extent of false lumen thrombosis, and to long-term dissection-related outcomes.

CONCLUSIONS

4D-flow CMR is feasible in patients with acute aortic dissection and is a reliable technique to assess flow in the true and false lumens of the aorta. This allows future work on functional assessment of aortic dissection hemodynamics.



VIDEO 2. GTflow-generated video of 4D-flow CMR data, showing pathlines of blood flow in a patient with DeBakey type III dissection during 1 cardiac cycle, revealing normal flow into the celiac artery during systole and retrograde flow into the false lumen during diastole. Video available at: <https://www.jtcvs.org>.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

The authors thank the Pumps & Pipes Organization and Exxon-Mobil Upstream Research Company for the funding, design, and construction of the HeartBeat Simulator hardware and software. The authors also thank WL Gore & Associates for additional funding of the study.

References

- Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE Jr, et al. American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM guidelines for the diagnosis and management of patients with Thoracic Aortic Disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, American College of Radiology, American Stroke Association, Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, Society of Interventional Radiology, Society of Thoracic Surgeons, and Society for Vascular Medicine. *Circulation*. 2010;121:e266-369.
- Erbel R, Aboyans V, Boileau C, Bossone E, Bartolomeo RD, Eggebrecht H, et al. 2014 ESC guidelines on the diagnosis and treatment of aortic diseases: document covering acute and chronic aortic diseases of the thoracic and abdominal aorta of the adult. The task force for the diagnosis and treatment of aortic diseases of the European Society of Cardiology (ESC). *Eur Heart J*. 2014;35:2873-926.
- Mussa FF, Coselli JS, Eagle KA. Feasibility of a proposed randomized trial in patients with uncomplicated descending thoracic aortic dissection: results of worldwide survey. *Am Heart J*. 2016;181:137-44.
- Fattori R, Montgomery D, Lovato L, Kische S, Di Eusanio M, Ince H, et al. Survival after endovascular therapy in patients with type B aortic dissection: a report from the International Registry of Acute Aortic Dissection (IRAD). *JACC Cardiovasc Interv*. 2013;6:876-82.
- Zhang Y, Lu Q, Feng J, Yu P, Zhang S, Teng Z, et al. A pilot study exploring the mechanisms involved in the longitudinal propagation of acute aortic dissection through computational fluid dynamic analysis. *Cardiology*. 2014;128:220-5.
- Nauta FJ, Conti M, Kamman AV, van Bogerijen GH, Tolenaar JL, Auricchio F, et al. Biomechanical changes after thoracic endovascular aortic repair in type B dissection: a systematic review. *J Endovasc Ther*. 2015;22:918-33.
- Frydrychowicz A, Markl M, Hirtler D, Harloff A, Schlensak C, Geiger J, et al. Aortic hemodynamics in patients with and without repair of aortic coarctation: in vivo analysis by 4D flow-sensitive magnetic resonance imaging. *Invest Radiol*. 2011;46:317-25.
- Wehrum T, Kams M, Gunther F, Beryl P, Vach W, Dragonu I, et al. Quantification of retrograde blood flow in the descending aorta using transesophageal echocardiography in comparison to 4D flow MRI. *Cerebrovasc Dis*. 2015;39:287-92.
- Rose MJ, Jarvis K, Chowdhary V, Barker AJ, Allen BD, Robinson JD, et al. Efficient method for volumetric assessment of peak blood flow velocity using 4D flow MRI. *J Magn Reson Imaging*. 2016;44:1673-82.
- Jackson MS, Igo SR, Lindsey TE, Maragiannis D, Chin KE, Autry K, et al. Development of a multi-modality compatible flow loop system for the functional assessment of mitral valve prostheses. *Cardiovasc Eng Technol*. 2014;5:1-12.
- Clough RE, Waltham M, Giese D, Taylor PR, Schaeffer T. A new imaging method for assessment of aortic dissection using four-dimensional phase contrast magnetic resonance imaging. *J Vasc Surg*. 2012;55:914-23.
- Francois CJ, Markl M, Schiebler ML, Niespodzany E, Landgraf BR, Schlensak C, et al. Four-dimensional, flow-sensitive magnetic resonance imaging of blood flow patterns in thoracic aortic dissections. *J Thorac Cardiovasc Surg*. 2013;145:1359-66.
- Karmonik C, Bismuth J, Shah DJ, Davies MG, Purdy D, Lumsden AB. Computational study of haemodynamic effects of entry- and exit-tear coverage in a DeBakey type III aortic dissection: technical report. *Eur J Vasc Endovasc Surg*. 2011;42:172-7.

14. Dillon-Murphy D, Noorani A, Nordsletten D, Figueroa CA. Multi-modality image-based computational analysis of haemodynamics in aortic dissection. *Bio-mech Model Mechanobiol*. 2016;15:857-76.
15. Youssefi P, Gomez A, Arthurs C, Sharma R, Jahangiri M, Alberto Figueroa C. Impact of patient-specific inflow velocity profile on hemodynamics of the thoracic aorta. *J Biomech Eng*. 2018;140: <https://doi.org/10.1115/1.4037857>.
16. Bollache E, van Ooij P, Powell A, Carr J, Markl M, Barker AJ. Comparison of 4D flow and 2D velocity-encoded phase contrast MRI sequences for the evaluation of aortic hemodynamics. *Int J Cardiovasc Imaging*. 2016;32:1529-41.
17. Muzzarelli S, Monney P, O'Brien K, Faletra F, Moccetti T, Vogt P, et al. Quantification of aortic flow by phase-contrast magnetic resonance in patients with bicuspid aortic valve. *Eur Heart J Cardiovasc Imaging*. 2014;15:77-84.
18. Nordmeyer S, Riesenkampff E, Messroghli D, Kropf S, Nordmeyer J, Berger F, et al. Four-dimensional velocity-encoded magnetic resonance imaging improves blood flow quantification in patients with complex accelerated flow. *J Magn Reson Imaging*. 2013;37:208-16.
19. Bogren HG, Buonocore MH, Follette DM. Four-dimensional aortic blood flow patterns in thoracic aortic grafts. *J Cardiovasc Magn Reson*. 2000;2:201-8.
20. Kvitting JP, Ebbens T, Wigstrom L, Engvall J, Olin CL, Bolger AF. Flow patterns in the aortic root and the aorta studied with time-resolved, 3-dimensional, phase-contrast magnetic resonance imaging: implications for aortic valve-sparing surgery. *J Thorac Cardiovasc Surg*. 2004;127:1602-7.
21. Gatehouse PD, Rolf MP, Graves MJ, Hofman MB, Totman J, Werner B, et al. Flow measurement by cardiovascular magnetic resonance: a multi-centre multi-vendor study of background phase offset errors that can compromise the accuracy of derived regurgitant or shunt flow measurements. *J Cardiovasc Magn Reson*. 2010;12:5.

Key Words: aorta, aortic dissection, 4D-flow MRI, ex vivo model

TABLE E1. Flow measurements in the porcine ex vivo aortic dissection model

	4D-flow CMR mL/beat (\pm SD)	2D PC-CMR mL/beat (\pm SD)	Sonotransducer mL/beat (\pm SD)
Ascending aorta/inlet	45.27 (\pm 18.21)	44.21 (\pm 17.69)	39.63 (\pm 17.27)
Arch vessels	7.42 (\pm 4.65)	10.00 (\pm 4.88)	–
Proximal descending			
True lumen	32.16 (\pm 11.99)	34.57 (\pm 10.61)	–
False lumen	4.48 (\pm 4.55)	5.21 (\pm 5.19)	–
Mid-descending			
True lumen	30.62 (\pm 14.12)	32.63 (\pm 13.22)	–
False lumen	4.15 (\pm 4.78)	4.49 (\pm 4.76)	–
Distal descending/outlet	33.80 (\pm 13.12)	32.67 (\pm 12.43)	31.62 (\pm 13.29)

4D-flow CMR, 4-dimensional flow cardiomagnetic resonance; SD, standard deviation; 2D PC-CMR, 2-dimensional phase-contrast cardiomagnetic resonance.

TABLE E2. Four-dimensional flow cardiovascular magnetic resonance measurements in vivo

	Forward flow volume mL/beat (\pm SD)	Reverse flow volume mL/beat (\pm SD)
Ascending aorta*	138.9 (\pm 27.3)	14.4 (\pm 12.9)
Proximal descending		
True lumen	55.7 (\pm 34.3)	5.3 (\pm 6.5)
False lumen	27.4 (\pm 20.5)	13.2 (\pm 12.8)
Mid-descending		
True lumen	54.7 (\pm 27.5)	3.8 (\pm 3.7)
False lumen	25.4 (\pm 11.8)	10.6 (\pm 7.2)
Distal descending		
True lumen	48.0 (\pm 21.1)	3.1 (\pm 2.9)
False lumen	23.2 (\pm 13.1)	12.8 (\pm 8.6)

SD, Standard deviation. *For the 2 patients with type I aortic dissection, the sum of the flow volume in the true and the false lumens and peak velocity in the true lumen were considered.

000 Four-dimensional flow cardiovascular magnetic resonance in aortic dissection: Assessment in an ex vivo model and preliminary clinical experience

Hector W. de Beaufort, MD, Dipan J. Shah, MD, Avni P. Patel, MSc, Matthew S. Jackson, MSc, Domenico Spinelli, MD, Eric Y. Yang, MD, Mohamad G. Ghosn, PhD, Kyle Autry, RT(R), Stephen R. Igo, BSc, Alan B. Lumsden, MD, Stephen H. Little, MD, Santi Trimarchi, MD, PhD, and Jean Bismuth, MD, Houston, Tex, and San Donato Milanese and Milan, Italy

4D-flow CMR is feasible in patients with aortic dissection and can reliably assess flow in the true and false lumens of the aorta.