Comparison of Prospective and Retrospective Gated 4D Flow Cardiac MR Image Acquisitions in the Carotid Bifurcation

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Abstract

Purpose—To evaluate the agreement of 4D flow cMRI-derived bulk flow features and fluid (blood) velocities in the carotid bifurcation using prospective and retrospective gating techniques.

Methods—Prospective and retrospective ECG-gated three-dimensional (3D) cine phase-contrast cardiac MRI with three-direction velocity encoding (i.e., 4D flow cMRI) data were acquired in ten carotid bifurcations from men (n = 3) and women (n = 2) that were cardiovascular disease-free. MRI sequence parameters were held constant across all scans except temporal resolution values differed. Velocity data were extracted from the fluid domain and evaluated across the entire volume or at defined anatomic planes (common, internal, external carotid arteries). Qualitative agreement between gating techniques was performed by visualizing flow streamlines and topographical images, and statistical comparisons between gating techniques were performed across the fluid volume and defined anatomic regions.

Results—Agreement in the kinematic data (e.g., bulk flow features and velocity data) were observed in the prospectively and retrospectively gated acquisitions. Voxel differences in time-averaged, peak systolic, and diastolic-averaged velocity magnitudes between gating techniques across all volunteers were 2.7%, 1.2%, and 6.4%, respectively. No significant differences in velocity magnitudes or components (vr, vh, vz) were observed. Importantly, retrospective acquisitions captured increased retrograde flow in the internal carotid artery (i.e., carotid sinus) compared to prospective acquisitions (10.4 ± 6.3% vs. 4.6 ± 5.3%; p < 0.05).

Conclusion—Prospective and retrospective ECG-gated 4D flow cMRI acquisitions provide comparable evaluations of fluid velocities, including velocity vector components, in the carotid bifurcation. However, the increased temporal coverage of retrospective acquisitions depicts increased retrograde flow patterns (i.e., disturbed flow) not captured by the prospective gating technique.

Keywords—Biomechanics, Cardiac MRI, Hemodynamics, Phase contrast magnetic resonance imaging, Triggering.

INTRODUCTION

Four-dimensional flow cardiac magnetic resonance imaging (4D flow cMRI) provides a non-invasive, non-ionizing radiation-based diagnostic and prognostic tool to interrogate the in vivo hemodynamic environment. Clinical studies have demonstrated the diagnostic and prognostic benefit of 4D flow cMRI in patients with cardiac and vascular diseases, including aortopathies, diseases of the cardiac valves, and congenital heart diseases.4,11,31 Since the introduction of 4D flow cMRI in the early 2000s, significant efforts have been directed at sequence optimization, such as acceleration techniques, dual velocity encoding (VENC), and pre-and post-processing of image data.16,23,24,29 Yet, there remains a need for continued advancements to enable broader clinical use of 4D flow cMRI and demonstrate its clinical benefit.

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Depending on the cardiovascular territory and hemodynamic metric(s) of interest, there are distinct advantages in acquiring 4D flow cMRI data with retrospective instead of prospective ECG-gating techniques. Indeed, prospective gating has the benefit of knowing exactly where all data were acquired within the cardiac cycle relative to the trigger signal; however, the limited temporal coverage can lead to inaccuracies in analyses that involve integration over the complete cardiac cycle due to missing data. On the other hand, retrospective gating has superior temporal resolution and covers the entire cardiac cycle without a gap for the trigger signal, but issues can arise with increased noise in the image due to temporal smoothing. Thus, the selection of gating technique is a compromise between temporal coverage and image quality that should be carefully considered depending on the clinical application.

In the setting of vascular hemodynamics of the large arteries, complex flow patterns have been spatially correlated with atherosclerotic lesion formation in the carotid arteries, aorta, and coronaries. For example, specific to the carotid bifurcation, the geometric expansion in the bulb region leads to flow separation, strong secondary flows, and recirculation zones that occur in late systole and throughout diastole that promote a pro-atherogenic blood flow environment. In this application, ECG-gated 4D flow cMRI acquired with retrospective gating provides a more comprehensive evaluation of the complex flow patterns in the anatomic region that may advance the clinical management of stroke. However, a direct comparison on the agreement between prospective and retrospective gating techniques, and the potential advantages of one technique over the other, has not been established. Therefore, the purpose of this study was to quantitatively compare 4D flow cMRI-derived fluid velocities in the carotid bifurcation between prospective and retrospective gated acquisitions.

METHODS

Five volunteers (men: \( n = 3 \); women: \( n = 2 \); ages: 22–47 years) free of cardiovascular disease (no history of clinical atherosclerosis, elevated blood pressure, or stroke) were recruited for the study. Informed written consent was obtained from all volunteers under protocols approved by the Institutional Review Boards at the University of Utah and Emory University.

Data Acquisition

Data were acquired on a 3T MRI scanner (MA-GENTOM Prisma, Siemens, Erlangen, Germany) using a dedicated 9-channel (U. Utah—custom coil) or 4-channel (Emory Univ.—Machnet BV) neck coil in combination with a 20-channel head/neck coil. For each volunteer, a localizer scan was initially performed to identify the imaging volume that encompassed the vascular territory near the carotid bifurcation. Single-slice (2D), prospectively ECG-triggered, and free-breathing navigator phase contrast MR images were acquired in the common carotid artery (− 3 cm proximal to the bifurcation) to identify a VENC value, which would remain constant for all subsequent scans within a given volunteer. ECG-gated three-dimensional (3D) cine phase-contrast cardiac MRI with three-directional velocity encoding (i.e., 4D flow cMRI) data were acquired over the imaging volume using prospective and retrospective gating techniques. Image slices were oriented perpendicular to the central axis of the common carotid artery. Respiratory gating was required for the 4D flow cMRI sequence, however, no data were rejected due to the lack of respiratory-induced rigid body motions of the carotid arteries. Table 1 summarizes the MR scan sequence parameters. Note that parameter ranges were a result of differences in volunteer physiology and scanning across Institutions; however, parameters were held constant for all scans in a volunteer. Data were corrected for eddy currents and Maxwell terms utilizing standard correction schemes within the commercial MR system. One prospective and one retrospective scan was performed for all volunteers to acquire the right and left carotid bifurcations. Independent scans were performed to acquire the right and left side (i.e., 20 image volumes were acquired in total across the 5 volunteers). To ensure consistency in image acquisition across institutions and volunteers, an imaging protocol was established with the gated sequences occurring systematically in the same order. In addition, repeat prospective and retrospective scans for each carotid bifurcation were performed in three of the five volunteers (i.e., 6 imaging volumes had two retrospectively and two prospectively gated acquisitions). Scans were performed during a single scan session for all volunteers. The temporal coverage was 81 ± 8% (mean ± standard deviation) and 100% for the prospective and retrospective triggered acquisitions, respectively, across the five volunteers.

Data Post-Processing: Visualization and Quantification

Image data were post-processed to aid qualitative and quantitative comparisons of the 4D flow cMRI derived velocity values between the gated acquisitions (Fig. 1). For all scans, the fluid (blood) volume was semi-automatically segmented from magnitude image data at each time point using the Seg3D open-source software.
software suite. In brief, an intensity threshold was automatically applied to the magnitude images via Seg3D and segmentations were manually checked and adjusted, by a single expert reviewer, as needed. A custom Matlab subroutine (MathWorks, Natick, MA) was developed to convert extracted voxel phase values to velocities using the patient-specific defined VENC, and data were converted into a .vtk file format. For flow visualizations, data were imported into the open-source visualization platform ParaView, which included the OSPRay ray tracing framework plugin for high-quality renderings, and processed to create flow streamlines encoded with velocity magnitude.\textsuperscript{1,12,37} In addition, a medial axis thinning algorithm was applied to the segmented fluid volume (i.e., the fluid volume was skeletonized) to define vessel centerlines, and

**TABLE 1. MRI sequence parameters.**

| Parameter                                      | 4D Flow cMRI               |
|------------------------------------------------|-----------------------------|
| Field of view [mm$^3$]                        | $200 \times 160–162.5 \times 21–28$ |
| Spatial resolution [mm$^3$]                    | $1.25–1.56 \times 1.25–1.56 \times 1.75–2.00$ |
| Temporal resolution [ms]                      | $28.5–55.0^\dagger$         |
| Echo time, TE [ms]                            | $2.9–4.0$                   |
| Repetition time, TR [ms]                      | $5.4–6.8$                   |
| Velocity encoding value [cm/s]                | $70–100$                    |
| Flip angle [degrees]                          | $7–15$                      |
| Phase lines/cardiac cycle (segments)          | $2$                         |
| Frames/cardiac cycle                          | $11–21$ (prospective); 19–24 (retrospective) |

Data ranges reported across the 5 volunteers. While ranges are reported across patients, parameter values were held constant across all scans for a given volunteer unless explicitly noted. Ranges were a result of differences in volunteer physiology and scanning across Institutions.\textsuperscript{1} no statistical difference between prospective and retrospective values.
velocity data were visualized as 2D topographic images at cross-sections perpendicular to these centerlines at locations $\pm 3.5$ mm from the carotid bifurcation in the common carotid (CCA), internal carotid (ICA), and external carotid (ECA) arteries (Fig. 1).

For quantitative analysis, velocity data were evaluated over the entire blood volume and at the extracted cross-sections in the CCA, ICA, and ECA. For each volunteer, the volumetric coverage and slice thickness were held constant for the prospective and retrospective scans which ensured the data (i.e., imaging slabs) were spatially co-registered. In addition, the retrospective data were truncated in time such that data from the same period of the cardiac cycle were compared between the gating techniques. Velocity data were transformed into cylindrical coordinates [i.e., radial ($v_r$), circumferential ($v_\theta$), axial components ($v_z$)] to aid evaluation of through-plane ($v_z$) and in-plane ($v_r$, $v_\theta$) velocity fields. To understand the relative contribution of each component to the overall velocity vector, components were normalized by the sum of the individual component magnitudes (e.g., $v_r\text{normalized} = v_r/(v_r + v_\theta + v_z)$). Through-plane velocities (i.e., $v_z$) were used to evaluate retrograde flow (i.e., reverse flow), which was defined as $v_z < -2$ cm/s. This threshold was identified by calculating the absolute value of the time-averaged velocity magnitude in static tissue regions outside the fluid domain across all volunteers. To demonstrate potential benefit of the increased temporal coverage with retrospective gating, the percentage of voxels that exhibited retrograde flow over a spatial domain (e.g., cross-section) were quantified across the cardiac cycle.

**Statistical Analysis**

Velocity data were evaluated across the complete cardiac cycle (i.e., time-averaged), at peak systole, and across diastole (i.e., diastolic-averaged), which was defined from the volumetric flow waveform as the period from the dicrotic notch to the end of the cardiac cycle (Fig. 1). Interscan (i.e., prospective vs. retrospective) and intrascan (i.e., scan reproducibility) agreement were evaluated by calculating the concordance correlation coefficient (CCC) and Bland-Altman analysis. Due to differences in cardiac temporal coverage between prospective and retrospective gating, only data across the same time periods were compared unless directly indicated. Continuous data are reported as mean ± standard deviation. Statistical differences between groups were determined using a Mann–Whitney U test with $p < 0.05$ considered statistically significant. Statistical analyses were performed using Prism 9 (GraphPad Software, Inc., San Diego, CA).

**RESULTS**

Examination of the fluid kinematic data demonstrated agreement between bulk flow features and velocity data acquired with either prospectively or retrospectively gated acquisitions. Flow streamlines encoded with time-averaged velocity magnitude revealed distinct similarities in flow characteristics between the gating techniques within a volunteer and general similarities across the entire volunteer cohort (e.g., unidirectional flow in the CCA and multidirec-
tional flow in the carotid bulb; Fig. 2). For example, complex flow patterns were observed in the proximal carotid bulb of volunteer 2 derived from image data acquired with either gated acquisition (Fig. 2, black arrows). More specifically, in this anatomic region flow velocities were low in magnitude and the velocity field was rotational and separated from the main flow field. Comparing velocity magnitudes across the entire imaging volume (i.e., all voxels) demonstrated quantitative agreement across the gating techniques. Whether evaluating across all volunteers or an individual volunteer, no significant differences were observed in time-averaged, peak systolic, and diastolic-averaged velocity magnitudes (Fig. 3). For example, voxel differences in time-averaged, peak systolic, and diastolic-averaged velocity magnitudes between gating techniques across all volunteers were 2.7%, 1.2%, and 6.4%, respectively. It should be highlighted that peak systolic values had the largest difference in velocity values between the gating techniques across each volunteer.

Comparison of velocity data between the gating techniques at defined anatomic planes in the carotid bifurcation (CCA, ICA, and ECA) further confirmed agreement between gating techniques. Across all volunteers, a voxel-by-voxel comparison of velocity magnitude values within these cross-sections demonstrated no statistical difference in time-averaged, peak systolic, and diastolic-averaged velocity magnitudes (Fig. 3). For example, voxel differences in time-averaged, peak systolic, and diastolic-averaged velocity magnitudes between gating techniques across all volunteers were 2.7%, 1.2%, and 6.4%, respectively. It should be highlighted that peak systolic values had the largest difference in velocity values between the gating techniques across each volunteer.

Comparison of velocity magnitude values across entire imaging volume (i.e., all voxels) between gating techniques. (a) All volunteer data. (b) Individual volunteer data (includes the number of voxels within imaging volume). Data are reported as mean ± standard deviation. $|\mathbf{v}|$: velocity vector magnitude, TA time-averaged, PS peak systolic, DA diastolic-averaged.
In the CCA region across all volunteers, $v_z$ accounted for approximately 87% and 88% of the velocity vector magnitude in the prospective and retrospective gated data, respectively, whereas $v_r$ and $v_h$ values were each approximately 6% of the total velocity vector (Table 3). In contrast, in-plane components ($v_r, v_h$) had 2- to 3-fold higher contributions to the velocity vector in the ICA and ECA (ranging from 15 to 20%); however, $v_z$ was still the primary velocity component. No significant differences were observed in normalized time-averaged velocity vector components between the gating techniques. Evaluation of the flow field in volunteer 4, who exhibited a large recirculation zone in the ICA (Fig. 2), demonstrated the transition from primarily unidirectional flow in the CCA to a multidirectional flow in the ICA (Fig. 6). More specifically, $v_z$ comprised nearly 80% of the component resolved time-averaged velocity vector in the CCA, whereas in the ICA, it comprised $<60$% and $v_r$ and $v_h$ accounted for 20–30% of the vector, respectively.

Retrograde flow was captured with both gating techniques, however, evaluating this flow feature with retrospective gating resulted in significantly higher values than prospective gating (Fig. 7a). Across all patients, retrograde flow was observed in 10.4 ± 6.3% and 4.6 ± 5.3% ($p < 0.05$) of the ICA cross-sections across the cardiac cycle with retrospective and prospective acquisitions, respectively, with the greatest difference observed in volunteer 3 (retrospective—10.8%, prospective—1.6%). Examining a representative temporal distribution of retrograde flow (volunteer 2) indicated that minimum retrograde flow occurred during systole, when the flow is accelerating, whereas maximum retrograde flow was evident at late systole and into diastole when blood flow was decelerating (Figs. 7b and 7c). Spatial analysis demonstrated that the flow reversal occurred in the carotid sinus region (Fig. 7d), where there is flow separation from the main flow stream (Fig. 2, black arrows), and further highlighted the agreement between the gating techniques.

**DISCUSSION**

In ten carotid bifurcations from a cohort of five volunteers free from cardiovascular disease, our results demonstrate agreement in 4D flow cMRI-derived bulk flow features and velocity magnitude values between prospectively and retrospectively gated acquisitions in the carotid bifurcation. Furthermore, this study shows agreement in resolved velocity component data (i.e., $v_r$, $v_h$, $v_z$) between the gating techniques and highlights the advantage of retrospectively gated acquisitions in
capturing retrograde flows that occur in late systole and throughout diastole. These data suggest that 4D flow cMRI data acquired with retrospective ECG-gating offer an advantage over prospective acquisitions in capturing complex and pro-atherogenic flow patterns in the carotid bifurcation, and potentially other elastic arteries, and may provide diagnostic and prognostic value in the clinical management of stroke.

The introduction of ECG-gating proved fundamental for the advancement of cardiac MRI by synchronizing image acquisition with the phases of the cardiac cycle, and thus reducing motion artifacts and improving image quality. The introduction of retrospectively ECG-gated 4D flow cMRI offers an advantage over prospective acquisitions in capturing complex and pro-atherogenic flow patterns in the carotid bifurcation, and potentially other elastic arteries, and may provide diagnostic and prognostic value in the clinical management of stroke.

### TABLE 2. Interscan and intrascan agreement in velocity magnitudes across periods in cardiac cycle at defined anatomic planes (CCA, ICA, and ECA).

| Parameter                                      | Comparisons                  | Time-averaged | Peak systolic | Diastolic-averaged |
|------------------------------------------------|------------------------------|---------------|---------------|--------------------|
| **Concordance correlation coefficient (CCC)** | Pro., A1 vs. Retro., A1      | 0.89          | 0.84          | 0.88               |
|                                                | Pro., A1 vs. Pro., A2        | 0.67          | 0.72          | 0.65               |
|                                                | Retro., A1 vs. Retro., A2    | 0.70          | 0.72          | 0.69               |
| **Bias (95% CI), [cm/s]**                      | Pro., A1 vs. Retro., A1      | 0.37 (8.36)   | -2.63 (22.52) | -0.06 (7.31)       |
|                                                | Pro., A1 vs. Pro., A2        | 2.20 (15.71)  | 5.73 (28.32)  | 1.71 (12.68)       |
|                                                | Retro., A1 vs. Retro., A2    | 1.12 (15.00)  | 0.76 (34.10)  | 1.23 (12.35)       |
| **p-value (Mann-Whitney U test)**              | Pro., A1 vs. Retro., A1      | <0.01         | <0.01         | <0.01              |
|                                                | Pro., A1 vs. Pro., A2        | <0.01         | <0.01         | <0.01              |
|                                                | Retro., A1 vs. Retro., A2    | <0.01         | 0.13          | <0.01              |

Pro prospective, Retro retrospective, A1 acquisition 1, A2 acquisition 2.

Sample sizes: Prospective A1—4,197; Retrospective A1—4,197; Prospective A2—2,259; Retrospective A2—2,259.

### FIGURE 5. Interscan agreement in velocity magnitude data at defined anatomic planes (CCA, ICA, and ECA) across all patients between gating techniques. Linear regression plots for (a) time-averaged, (b) peak systolic, and (c) diastolic-averaged velocity magnitude data (solid line: regression line, dotted line: $y = x$), Bland-Altman plots for (d) time-averaged, (e) peak systolic, and (f) diastolic-averaged velocity magnitude data. CCC concordance correlation coefficient, CI confidence interval, A1 1st scan acquisition.
sively collected over multiple cardiac cycles using $k$-space segmentation techniques. Prospective and retrospective gating techniques each require a physiologic trigger (e.g., R-wave in ECG tracing). While prospective gating utilizes the trigger to initiate data acquisition over a finite window that is paused before the end of the cardiac cycle to compensate for physiologic variation across cycles (i.e., the cardiac cycle is truncated), retrospective gating collects data continuously and fills $k$-space according to the phase of the cardiac cycle that is determined from the ECG recording during image acquisition.22 As we observed in our study, prospective gating only covered $-81\%$ of the cardiac cycle on average across the five volunteers, with one volunteer only having $52\%$ coverage. Previous cardiac studies comparing these ECG-gating techniques in mice have shown comparable image quality and agreement in functional heart parameters (e.g., end-diastolic volume, ejection fraction).9,14 In the application of phase-contrast CMR, an in vitro (pulsatile flow through Plexiglass tube) and in vivo (flow in the human abdominal aorta) study performed a comparison between 2D PCMR (through-plane) velocities acquired with prospective and retrospective ECG-gating techniques and found agreement between peak velocities and volumetric flow rates.9 More recently, studies examining the agreement in PCMR-derived through-plane velocities acquired with (free-breathing) prospective and retrospective cardiac triggering in human common carotid arteries, ascending aorta, and pulmonary trunk, all of which were free from vascular disease, showed no statistical differences in maximum and mean blood flow velocities and volumetric flow rates.32 Data from our study extend these observations, as well as present the agreement of velocity vector components, to 4D flow cMRI. With the advantage of increased temporal coverage, 4D flow cMRI acquisitions with retrospective ECG-gating provide a more comprehensive examination of the hemodynamic environment in most vascular applications, where complex flow patterns extend into diastole. Indeed, a 2015 consensus statement indicated retrospective ECG-gating as the ideal gating technique for 4D flow CMR acquisition.7

Given the extent of data that have convincingly demonstrated an association between hemodynamics and the development of cardiovascular disease, efforts have been directed at establishing clinical techniques that can interrogate the in vivo hemodynamic environment and provide critical physiologic data.17,28,36 Early clinical application of PCMR demonstrated its utility across a range of cardiovascular diseases, including septal defects, valvular disease, and aortic coarctation.15 Integration of PCMR to evaluate complex flow patterns in regions prone to atherosclerosis development highlighted the ability of this imaging technique to capture these hemodynamic environments. For example, initial studies showed the ability of MRI velocimetry to visualize and quantify the non-uniform velocity profiles in an in vitro model of the abdominal aorta, including the presence of retrograde flow on the lateral-posterior wall of the infra-renal aorta.26–28 Importantly, all MR measurements in these early studies were acquired with prospective ECG-gating, so the extent of retrograde flow was likely underestimated. Due to the increased cardiac coverage of retrospective ECG-gating, our data detail the ability of these gated scans to capture significantly greater retrograde flow in the carotid bulb than prospectively gated scans. As illustrated and quantified in Fig. 7, the ability of retrospective gating to capture the full cardiac cycle affords the ability to evaluate late diastolic flow patterns, including the presence of retrograde flow, that are missed with prospective gating techniques. Thus, it is likely that time-averaged WSS values will be lower and have increased spatial oscillation when quantified from retrospective versus prospective 4D flow cMRI data, and potentially provide increased prognostic value for identifying patients at risk for stroke. Albeit in a different cardiovascular pathology, quantification of WSS directly from 4D flow data has shown clinical value in implicating valve-related hemodynamics as a contributing factor in bicuspid aortic valve aortopathy.2,11 Given the caliber of the

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**TABLE 3. Time-averaged normalized velocity components between scan acquisitions across all patients.**

|                  | Prospective acquisition | Retrospective acquisition | $p$-values ($v_r, v_0, v_z$) |
|------------------|-------------------------|---------------------------|----------------------------|
|                  | $v_r$                   | $v_0$                     | $v_z$                      | $v_r$           | $v_0$           | $v_z$           | $p$-values |
| CCA              | 0.06 ± 0.10             | 0.06 ± 0.10               | 0.87 ± 0.18                | 0.06 ± 0.09     | 0.06 ± 0.09     | 0.88 ± 0.17     | 0.94, 0.90, 0.75 |
| ICA              | 0.15 ± 0.16             | 0.17 ± 0.17               | 0.68 ± 0.24                | 0.15 ± 0.17     | 0.20 ± 0.20     | 0.65 ± 0.27     | 0.80, 0.18, 0.28 |
| ECA              | 0.16 ± 0.18             | 0.18 ± 0.20               | 0.65 ± 0.29                | 0.16 ± 0.18     | 0.18 ± 0.19     | 0.67 ± 0.28     | 0.08, 0.55, 0.31 |

Data are reported as mean ± standard deviation across the 5 volunteers. $p$-values derived from comparing velocity components between gating techniques. CCA common carotid artery, ICA internal carotid artery, ECA external carotid artery, $v_r$, $v_0$, $v_z$: radial, circumferential, and axial velocity components.
carotid vessels as compared to the aorta, we recognize that MR image resolution presents more of a challenge in the carotid bifurcation to calculate WSS. Rigorous investigation examining the impact of image resolution on WSS accuracy derived from proposed techniques are warranted in this vascular territory.\textsuperscript{15,33} The continued integration and clinical application of retrospective ECG-gated 4D flow cMRI may aid in identifying hemodynamic diagnostic and prognostic markers, specifically those that capture the temporal change in the flow direction, that aid the comprehensive evaluation of patients with atherosclerotic diseases.

It is worth noting that the primary reason that no study has directly compared prospective and retrospective ECG-gating techniques for 4D flow cMRI in the clinical setting is the lack of flexibility between gating techniques across a single MR platform. While advances have been made across all commercial platforms, gating techniques, until recent, have remained constant across a given platform. The addition of retrospective ECG-gating to the 4D flow sequence on the Siemens MR platforms provides versatility for the hemodynamic evaluation in the clinical setting; however, the user must be mindful of the limitations of each gating technique to promote image quality and accuracy of derived flow metrics in the vascular territory of interest.

While not detracting from the significance of the presented data, there are limitations in this study that should be noted. First, the volunteers were free of cardiovascular disease, and thus no atherosclerotic lesions were present in the carotid bifurcation. As data indicate that the presence of flow-limiting lesions and turbulent flow could lead to significant MR signal loss, the results presented herein would need additional evaluation before extension into diseases that induce non-periodic fluctuations in the velocity fields.\textsuperscript{31} Second, image data at each institution were collected by a single operator, so intra- and inter-operator variability could not be examined. The quantification of data variability across, for example, operators, MR system manufacturers, and imaging centers must be identified to provide benchmarks for acceptable differences between prospectively and retrospectively acquired 4D cMRI fluid velocities and aid introduction of these techniques to the clinical environment. Likewise, all image segmentation was performed by a single, expert reviewer, and segmentation variability exists with semi-automatic approaches. The high contrast between the blood pool and surrounding tissue, and the lack of cardiac and respiratory motion, provides increases confidence on segmentation accuracy; however, future studies to assess observer variability are warranted. Third, an anisotropic voxel size was utilized in this study, whereby the slice thickness was slightly larger than the in-plane voxel dimensions. While consensus documents recommend an isotropic resolution, suffi-
cient in-plane resolution required a compromise in the slice thickness to minimize noise in the image data and reduce scan time. Finally, the study lacked a gold-standard method and acquisition of 2D PCMR image data, to quantify the velocity field in the volunteers. However, experimental and in vivo studies have validated fluid velocities measured with prospective ECG-gated 4D flow cMRI against gold-standard measurement techniques (e.g., Doppler ultrasound, 2D PCMR).8,10,34

In conclusion, we present an analysis framework that allows for evaluation of 4D flow cMRI data and apply it to examine the agreement between fluid velocities derived from prospective and retrospective ECG-gated acquisitions in the carotid bifurcation. We report qualitative and quantitative agreement in bulk flow features and local fluid velocities derived from either gating technique. Notably, we demonstrate the benefit of retrospectively gated acquisitions in quantifying increased retrograde flow due to complete cardiac cycle coverage. Such findings may have significant implications on advancing diagnostic and prognostic strategies for atherosclerotic diseases, such as stroke, in which the focal hemodynamic environment regulates structural wall remodeling and lesion formation.

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COMPETING INTEREST

The authors have no conflicts of interests or competing interests to declare.
CONSENT TO PARTICIPATE

Informed consent was obtained from all individual participants included in the study.

CONSENT FOR PUBLICATION

The authors affirm that human research participants provided informed consent for the publication of images in Fig. 1.

ETHICAL APPROVAL

Approval was obtained from the Institutional Review Boards at the University of Utah and Emory University. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

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