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ORIGINAL ARTICLE

Accurate measurement of pulsatile flow velocity in a small tube phantom: comparison of phase-contrast cine magnetic resonance imaging and intraluminal Doppler guidewire

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Abstract
Purpose. We compared the accuracy of magnetic resonance imaging (MRI) measurements of pulsatile flow velocity in a small tube phantom using different spatial factors versus those obtained by intraluminal Doppler guidewire examination (as reference).
Materials and methods. We generated pulsatile flow velocities averaging about 20–290 cm/sec in a tube of 4 mm diameter; we performed phase-contrast cine MRI on pixels measuring 1.00^2–2.50^2 mm^2. We quantified spatial peak flow velocities of a single pixel and a cluster of five pixels and spatial mean velocities within regions of interest enclosing the entire lumen in the phantom's cross-section. Finally, we compared the measurements of temporally mean and maximum flow velocity with the Doppler measurements.
Results. Linear correlation was excellent between both measurements of spatial peak flow velocities in one pixel. The highest spatial resolution using spatial peak flow velocities of a single pixel allowed the most accurate MRI measurements of both temporally mean and maximum pulsatile flow velocity (r = 0.97 and 0.99, respectively: MRI measurement = 0.95x + 8.9 and 0.88x + 24.0 cm/s, respectively). Otherwise, MRI measurements were significantly underestimated at lower spatial resolutions.
Conclusion. High spatial resolution allowed accurate MRI measurement of temporally mean and maximum pulsatile flow velocity at spatial peak velocities of one pixel.

Key words Intraluminal Doppler guidewire · Phantom experiment · Phase-contrast cine magnetic resonance imaging · Pulsatile flow velocity quantification

Introduction

A pressure-monitoring guidewire has been used widely to measure myocardial fractional flow reserve (FFR) for evaluating the functional severity of coronary artery stenoses independent of changes in systemic blood pressure and heart rate; its use is unaffected by conditions known to increase baseline myocardial flow.[1] However, FFR may not be a reliable gauge of coronary lesion severity and may underestimate it in patients with marked microvascular dysfunction.[2] On the other hand, intraluminal Doppler guidewire examination has also been widely used to measure coronary flow velocity and flow velocity reserve, the ratio of maximum hyperemic to baseline coronary flow velocity for assessing both the functional severity of coronary artery stenoses and deranged coronary microcirculation in patients with a transplanted heart or hypertrophic or dilated cardiomyopathy.[3–14] Critical issues include the guidewire's invasiveness and

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its exposure of the patient to radiation and nephrotoxic contrast medium.

Several recent studies[5–22] have validated the use of cardiac-gated, segmented k-space, phase-contrast (PC) cine magnetic resonance imaging (MRI)—a noninvasive alternative to Doppler guidewire examination—for quantifying coronary flow velocity and flow velocity reserve. Because coronary arteries are small and subject to cardiac and respiratory motion, various issues affecting temporal or spatial factors on MRI measurements can produce discrepant absolute coronary flow velocity measurements obtained by either method. Especially, spatial offsets (e.g., suboptimal spatial resolution, intravoxel phase dispersion, intervoxel averaging) and a methodological discrepancy between measurements by the two methods—the Doppler guidewire technique generally detects the peak of the flow velocity spectrum in laminar flow, and PC cine MRI provides averaged flow velocity within the region of interest (ROI)—can cause underestimation of coronary flow velocity measurements by MRI imaging compared with the Doppler guidewire method.

Previously, measurements of constant flow velocity in a small tube phantom by PC cine MRI were compared with those obtained by the intraluminal Doppler guidewire technique as a reference. Relatively high spatial resolution allowed accurate MRI measurement using spatial peak velocities of one pixel within the ROI enclosing the entire lumen of the tube cross section.[23] However, spatial factors affecting the accurate MRI measurement of pulsatile flow velocity, a more complex and physiological state, have not been thoroughly investigated.

In this study, using a small tube phantom, we compared measurements of temporally average and maximum pulsatile flow velocity by segmented k-space PC cine MRI versus those obtained by the intraluminal Doppler guidewire technique as a reference. We then estimated the impact of systemic spatial factors on the accuracy of the MRI quantifications.

Materials and methods

Flow phantom

We used an original flow phantom that consisted of a straight cylindrical acryl tube 4 mm across and 5 cm long and a computer-controlled flow pump (Alpha Flow SV Pro1; Fuyo, Tokyo, Japan). We submerged the tube entirely in degassed water that filled a plastic chamber placed on the MRI scanner bed in front of the gantry and placed the pump outside the examination room to avoid difficulties related to the magnetic field.

We circulated blood-mimicking fluid for Doppler ultrasonography (US) (model 707 test fluid; ATS Laboratories, Bridgeport, CT, USA) (fluid density 1.04 g/cm^3; viscosity 1.69 g/cm·s) in the phantom. The pump generated a pulsatile flow at various velocities within the tube that was directed parallel to the magnet bore. We made all measurements in the study utilizing an electrocardiographic (ECG) pattern simulated by the pump's computer of a heart rate of 60 beats/min.

Intraluminal Doppler guidewire technique

For the intraluminal Doppler guidewire technique, we first predetermined pulsatile flow velocities ranging from approximately 20 to 290 cm/s using the time average of the instantaneous spectral peak velocity (APV), which was measured by a 0.014-inch, 175 cm long intracoronary Doppler guidewire with a 12-MHz piezoelectric US transducer integrated onto its tip (FloWire System; Volcano Therapeutics, Rancho Cordova, CA, USA). A fast online Fourier frequency analysis (more than 100 spectra/s) provided the basis for continuous tracking of the upper edge of the frequency spectrum, which corresponded to the instantaneous peak velocity. APV was automatically computed based on segments consisting of the envelope of the phasic velocity spectrum during two cardiac cycles. Specifically, at each measurement of flow velocity, the guidewire was introduced into the phantom tube via a side port of the proximal hose and connected to the real-time, gray-scale spectral analyzer (FloMap System; Volcano Therapeutics) outside the examination room. The guidewire was rotated to optimize the audio signal. The flow spectrum and APV were instantaneously displayed on the spectral analyzer and confirmed to be constant when minimal or no fluctuation was apparent for 1 min.

We confirmed the constancy of the Doppler measurements of flow spectrum, APV, and the maximum value of instantaneous spectral peak velocity (MPV) and recorded the measurements for later review on a computer connected online to the spectral analyzer, with ECG gating from the pump's triggering signal for 3 min. The MPV was also automatically computed based on segments consisting of the envelope of the phasic velocity spectrum during 2 cardiac cycles. The Doppler guidewire was left in place in the phantom tube during subsequent MRI measurements of the same flow velocity under the same flow conditions.

Finally, following each MRI measurement, we reconfirmed the flow spectrum and APV instantaneously displayed on the spectral analyzer to be unchanged for 1 min from those obtained before the measurement. We repeated the aforementioned procedures to measure

different velocities. The recorded adequate APV and MPV measurements were temporally averaged for 3 min. The results of the APV measurements were defined as temporally mean flow velocities and those of the MPV measurements as temporally maximum flow velocities obtained by the Doppler guidewire technique. Thus, we compared the former results with the temporally mean flow velocities and the latter results with the temporally maximum flow velocities obtained with MRI.

Phase-contrast cine MRI

We obtained all MRI data utilizing a 1.5-tesla (T) superconducting system (MAGNETOM Avanto; Siemens Medical Systems, Erlangen, Germany). The phantom on the scanner bed was moved into the gantry horizontally at a constant height and positioned centrally within the transmit-receive, eight-channel, phased array pelvic coil covering the anterior aspect of the chamber and the spine coil covering the posterior aspect of the chamber, with ECG gating from the pump's triggering signal. We used localizer images for accurate selection of a plane perpendicular to the direction of the flow phantom. We acquired retrospective ECG-gated, segmented k-space, PC cine MRI scans of the cross section of the phantom lumen as near as possible to the indwelling guidewire tip to avoid susceptibility artifact from the guidewire [field of view (FOV), 32 × 32 cm; section thickness 6 mm; repetition time/echo time (TR/TE) 50/5.6 ms; flip angle 15°; three segments; bandwidth 710 Hz/pixel; 20 frames per R-R interval). Following quantification by the Doppler guidewire technique, we measured each flow velocity in the phantom using reconstructed magnitude and phase images for five in-plane pixel dimensions—1.00, 1.25, 1.67, and 2.50 mm^2 with no parallel imaging and 2.40 × 1.67 mm with GRAPPA (generalized autocalibrating partially parallel acquisition)—with a reduction factor of 2. The most clinically available sequence is the last one during which patients can generally hold their breath (Table 1). Velocity-encoding (VENC) gradients were applied along only the section-selection direction that coincided with flow direction. To avoid aliasing, we determined VENC at a level 50% higher than each MPV measured by the Doppler guidewire method.

Aided by a magnitude image, we placed circular ROIs manually within the cross section of the phantom lumen to enclose the entire lumen and then measured the spatial peak and average velocities in the ROI on the corresponding phase image. We repeated both measurements for all cardiac phases with the same ROI for each frame to depict the phasic time–velocity curves throughout the ECG-gated R-R interval, carefully checked the phase images and phasic time–velocity curves for aliasing and measurement fluctuation, and confirmed the adequacy of each measurement.

We analyzed data using a commercially available software package (ARGUS; Siemens Medical Systems, Erlangen, Germany). We defined the spatial peak velocity of one pixel (V_{max1}) as its maximum velocity measurement and the spatial peak velocity of five pixels (V_{max5}) as the average of the maximum velocity measurements of a central pixel and the four pixels above, below, and to the right and left within the ROIs placed as described earlier. In addition, the spatial mean velocities (V_{mean}) were defined as the average velocity measurements of all pixels within the ROIs. We obtained both temporally mean and maximum flow velocities for each V_{max1}, V_{max5}, and V_{mean}.

Thereafter, we moved the phantom on the scanner bed horizontally from the gantry and repositioned it at the same site used for the Doppler measurement, adjusted the pump to obtain different flow velocities for the following measurement, and repeated the Doppler guidewire and PC cine MRI measurement procedures.

Statistical analysis

We compared measurements of both temporally mean and maximum flow velocity by MR imaging (V_{max1}, V_{max5}, V_{mean}) and by the Doppler guidewire technique using linear regression analysis and tested the correlation coefficient for significant difference. Furthermore, we used the Bland and Altman analysis to determine the 95% limits of agreement, equivalent to ± 2 SD.[24] We

Table 1. Magnetic resonance scan profiles by in-plane pixel dimensions

In-plane pixel dimension (mm)	Matrix	Average	PAT mode	Scan time
1.00 × 1.00	320 × 320	3	None	6′ 55″
1.25 × 1.25	256 × 256	3	None	4′ 22″
1.67 × 1.67	192 × 192	3	None	3′ 14″
2.50 × 2.50	128 × 128	3	None	2′ 11″
2.40 × 1.67	134 × 192	1	GRAPPA 2	25″

PAT, parallel acquisition technique; GRAPPA 2, generalized autocalibrating partially parallel acquisition, reduction factor 2

determined the mean proportional difference for this analysis using the absolute difference of both measurements divided by the average of both measurements and assessed this significant difference from zero using the Wilcoxon signed-ranks test. $P < 0.05$ was regarded as statistically significant.

Results

We found good to excellent linear correlations between PC cine MRI and Doppler guidewire measurements of both temporally mean ($r \geq 0.90$) and maximum pulsatile flow velocity ($r \geq 0.86$) (Fig. 1); all P values were <0.05. MRI measurements of flow velocity were likely to decrease according to a decline in spatial resolution and, at the same spatial resolution, in the order V_{max1}, V_{max5}, and V_{mean}. The highest spatial resolution using V_{max1} allowed the most accurate MRI measurements of both temporally mean ($r = 0.97$: MRI flow velocity for a pixel 1.00 $mm^2 = 0.95x + 8.9$ cm/s) and temporally maximum pulsatile flow velocity ($r = 0.99$: MRI flow velocity for a pixel 1.00 $mm^2 = 0.88x + 24.0$ cm/s). Furthermore, higher spatial resolution tended to result in more accurate MRI measurements, in the order V_{max1}, V_{max5}, and V_{mean}.

There were systemic underestimations of MRI measurements of the temporally mean flow velocity relative to Doppler guidewire measurements using V_{max1} with pixels 2.50 mm^2, V_{max5} with pixels 1.25–2.50 mm^2, and V_{mean} with all pixel dimensions, according to the Bland and Altman analysis and the proportional differences of flow velocity measurements by both modalities (Table

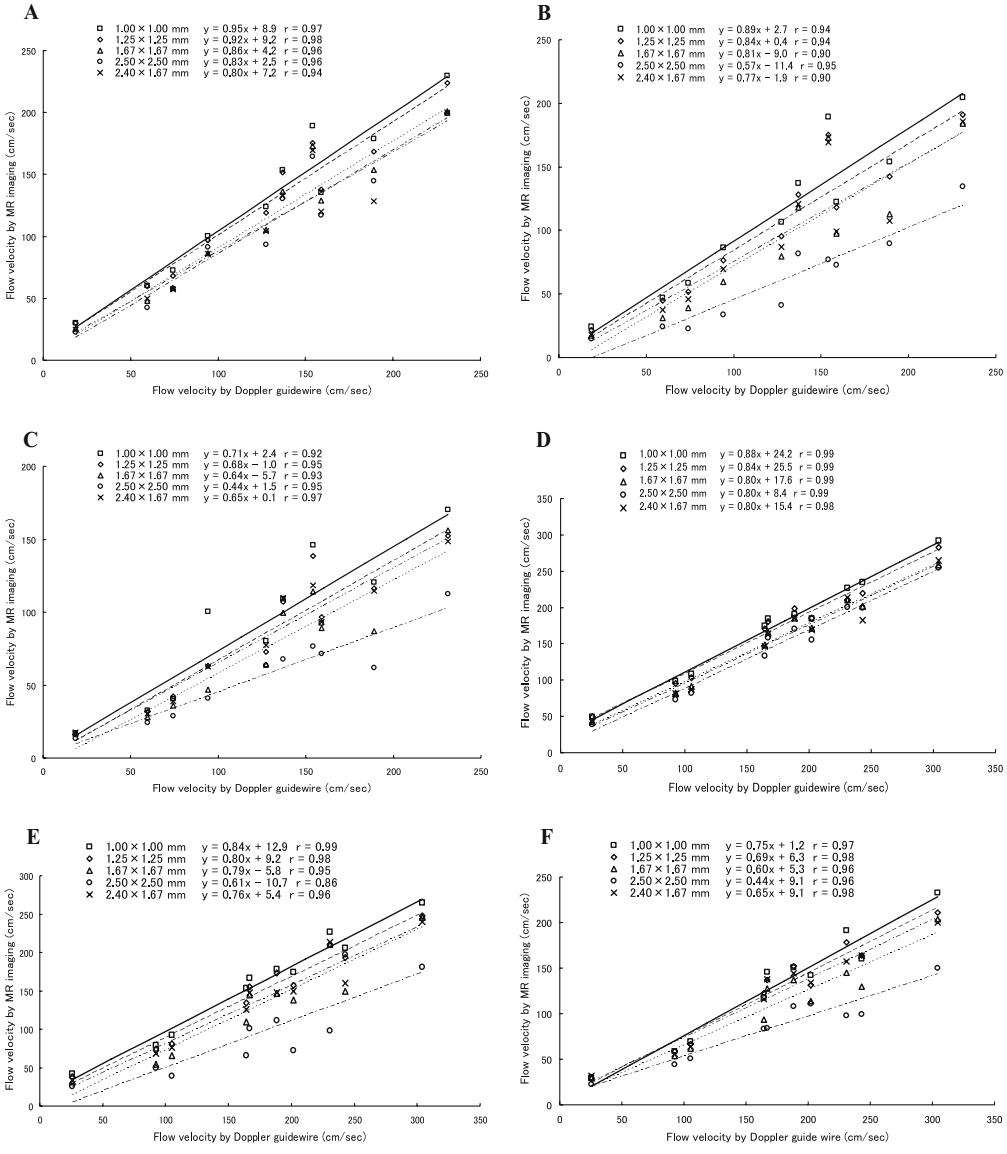

Fig. 1. Linear regression analysis of in vitro temporally mean (**A–C**) and maximum (**D–F**) pulsatile flow velocity measurements by intraluminal Doppler guidewire examination (x-axis) and phase-contrast cine magnetic resonance imaging (MRI) (y-axis). The data markers represent the flow velocity measurements using the spatial peak velocities of a single pixel (**A**, **D**) and five pixels (**B**, **E**) and the spatial mean velocities (**C**, **F**) in the regions of interest on pixel dimensions of 1.00, 1.25, 1.67, and 2.50 mm^2 and 2.40 × 1.67 mm. Regression lines, equations, and correlation coefficients are shown

Table 2. Proportional differences of in vitro temporally mean and maximum flow velocity measurements between phase-contrast cine-MRI and Doppler guidewire examination

	In-plane pixel dimensions (mm)				
MRI measurements	1.00 × 1.00	1.25 × 1.25	1.67 × 1.67	2.50 × 2.50	2.40 × 1.67
Mean flow velocity					
V_{max1}[a]	6.0 ± 35.3	2.9 ± 36.1	–8.6 ± 35.8	–14.2 ± 36.3[d]	–11.9 ± 38.6
V_{max5}[b]	–8.4 ± 37.1	–16.9 ± 36.4[d]	–34.5 ± 50.1[d]	–72.7 ± 51.0[d]	–28.8 ± 43.0[d]
V_{mean}[c]	–31.9 ± 46.9[d]	–39.5 ± 35.5[d]	–51.7 ± 43.8[d]	–73.1 ± 36.3[d]	–41.3 ± 37.1[d]
Maximum flow velocity					
V_{max1}[a]	7.1 ± 41.1	4.6 ± 43.6	–4.7 ± 41.3	–11.9 ± 40.5	–6.4 ± 42.2
V_{max5}[b]	–4.1 ± 37.9	–12.2 ± 38.4	–27.2 ± 44.9[d]	–58.7 ± 62.3[d]	–20.2 ± 37.4[d]
V_{mean}[c]	–26.0 ± 35.0[d]	–28.8 ± 34.9[d]	–40.8 ± 44.4[d]	–62.9 ± 39.5[d]	–31.6 ± 41.7[d]

Values are expressed as mean proportional difference ± 95% limit of agreement (2 SD) (proportional difference in % = absolute difference of the two measurements/average of the two measurements)
[a] Spatial peak velocity of one pixel
[b] Spatial peak velocity of five pixels
[c] Spatial mean velocity
[d] Magnetic resonance imaging (MRI) measurements are significantly underestimated compared with Doppler measurements ($P < 0.05$)

2). In addition, there were systemic underestimations of the MRI temporally maximum flow velocity measurements relative to Doppler guidewire measurements using V_{max5} with pixels of 1.67–2.50 mm^2 and V_{mean} with all pixel dimensions (Table 2).

Discussion

We compared both temporally mean and maximum pulsatile flow velocity measurements obtained using segmented k-space PC cine MRI in a small tube phantom with those obtained by the intraluminal Doppler guidewire method as a reference modality and estimated the impact of systemic spatial factors on the accuracy of the MRI quantification. Our results indicated good to excellent linear correlations between the two measurements; especially, sufficiently high spatial resolution allowed the most accurate MRI measurements of the pulsatile flow velocity using V_{max1}. In contrast, MRI measurements of the pulsatile flow velocity using V_{max5} and V_{mean} in relatively low spatial resolutions tended to be less accurate and to reveal systemic underestimations.

The laminar flow velocity usually encountered in clinical settings is highest at the vessel center and lowest at the vessel margin, in a parabolic manner. Most clinical studies using PC cine MRI to measure velocity have provided the spatial mean velocity within the ROI, but the Doppler guidewire technique generally detects the spatial peak velocity spectrum in the laminar flow. Because pixels of lower velocities nearer the vessel boundary are included within the ROI with MRI, intervoxel averaging results in an underestimation of measurements of flow velocity by MRI compared with those by the Doppler guidewire method.[20,25–28] This averaging can be significant for small vessels, such as the coronary arteries. Applying small ROIs with local flow velocities in a phantom tube, Matre and colleagues showed a better comparison between the MRI and Doppler measurements.[26] However, reproducible selection of those small ROIs was difficult, especially in both a small tube and the coronary artery. Instead of using small ROIs, we manually determined ROIs that would enclose the entire lumen within the cross section of the phantom lumen on magnitude images because this is the most clinically available method to reduce such user-dependent technical error. The commercially available data analysis software we used can also measure spatial peak velocity of a single pixel, which approximates measurements with small ROIs and can be useful for accurately measuring MRI flow velocity other than spatial mean velocity, which is usually available in clinical settings. Furthermore, different velocities are found, even within a single pixel; and inclusion of lower velocities nearer the vessel boundary for MRI measurements of flow velocity leads to an underestimation of this measurement as intravoxel phase dispersion. In addition, the spatial peak velocity of a single pixel can still be underestimated because re–placing the pixel displaying the velocity measurement exactly in the center of the cross section of the lumen on MRI imaging is almost impossible. Only improved spatial resolution can reduce these underestimations.[25] Even the current in-plane pixel dimension of MRI (approximately 1 mm^2) may be insufficient to quantify coronary flow velocity accurately.[19,29] Nevertheless, measurements of constant flow velocity in a small tube phantom obtained using segmented k-space PC cine MRI were previously compared with those obtained

by the intraluminal Doppler guidewire technique as a reference. It was determined that sufficiently high spatial resolution (lowest pixel dimension 1.00 mm^2) allowed accurate MRI measurement using spatial peak velocities of one pixel within the ROI to overcome the aforementioned spatial offsets.[23]

Whereas the Doppler guidewire technique can continuously record velocity information throughout the cardiac cycle (>100 samples/s), PC cine MRI shows limited temporal resolution (e.g., 20 samples/s in the present study) and can miss temporal peak velocities of pulsatile flow during MRI data acquisition. We first guessed that the lower temporal resolution on PC cine MRI would produce underestimated and inaccurate MRI measurements of both temporally mean and maximum flow velocity compared with those obtained by the Doppler guidewire technique.

However, in the present study, which focused on pulsatile flow velocity measurement in a stationary phantom, we obtained results similar to those in our previous study of constant flow velocity measurement, presumably because the pulsatile flow also showed a laminar flow pattern—fastest at the vessel center and slowest at the vessel margin, in a parabolic manner. Thus, with improved temporal resolution, we can noninvasively quantify accurate flow velocity of the proximal coronary artery in the stationary state by reducing the spatial offsets in PC cine MRI.

Our study has four major limitations. First, we did not pulsate the phantom tube to simulate cardiac motion. The complex in- and through-plane motion of the contracting heart can blur the coronary arteries, thereby causing inaccurate coronary flow velocity measurement by MRI.[29] A method to correct coronary arterial motion may be needed to reduce this offset. As well, better receiver coils, faster gradients, view-sharing reconstruction, and intravascular contrast agents could improve the temporal resolution of PC cine MRI and further enhance its flow velocity measurement capabilities. A second limitation is that we used quantification of flow velocity by the Doppler guidewire technique as a reference method because of its wide use as a clinical standard; however, to our knowledge, its accuracy is uncertain. Third, we neglected respiratory motion. Many institutions use breath-holding techniques to quantify flow velocity using PC cine MRI, so we applied a clinically available sequence with which patients can generally tolerate one breath-hold (at lower spatial resolution with pixels of 2.40×1.67 mm). The use of this sequence was much less accurate than a sequence using pixels of 1.00 mm^2 (scan time of approximately 7 min) because of reduced spatial resolution. By enhancing spatial and temporal resolution to overcome issues regarding respiratory motion, navigator-guided free-breathing is believed useful for MRI flow velocity measurements in coronary arteries.[25] With these improvements, our experimental results will allow accurate noninvasive measurement of coronary flow velocity and flow velocity reserve by MRI in the future. Finally, accurate MRI measurement of the pulsatile flow velocity is difficult in case of turbulent flow, which is sometimes seen in a coronary artery with stenosis or a tortuous artery, although our result shows that high spatial resolution allowed the most accurate MRI measurement using V_{max1}. In addition, MRI measurement of peak flow velocity of a single pixel is susceptible to the effect of turbulent flow. Further study is needed to investigate if our conclusion is true for turbulent flow.

Conclusion

In this experiment, using a small tube phantom to simulate the coronary artery, linear correlation was good to excellent between measurements of temporally mean and maximum pulsatile flow velocity by MRI using a segmented k-space PC cine method and by the intracoronary Doppler guidewire technique. However, inadequate MRI spatial factors caused significantly underestimated measurements. Accurate MRI measurement of flow velocity can benefit from combining high spatial resolution with the spatial peak flow velocity of a single pixel in the ROI enclosing the entire lumen within the cross section of the phantom. Although our MRI technique requires improved spatial and temporal resolution for clinical use, this study supports the development of MRI as an accurate, noninvasive modality for evaluating the functional significance of coronary arterial stenoses.

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