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# Accuracy and Repeatability of Automated Injector Versus Manual Administration of an MRI Contrast Agent—Results of a Laboratory Study

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**Objective:** The aim of this study was to compare flow rates over time and the deviations from the target flow rate of a magnetic resonance imaging contrast agent achieved by an automated injector versus manual injection.

**Materials and Methods:** In this laboratory study, the magnetic resonance contrast agent gadobutrol was repeatedly injected by an injector and by 10 experienced technologists. Six scenarios with 2 different target flow rates (1 and 5 mL/s), 2 different contrast volumes (10 and 20 mL), and 2 different intravenous (IV) catheters (22 gauge and 20 gauge) were tested. The flow rates over time were recorded. The target variable was the average absolute deviation and average absolute percentage deviation from the target flow rate.

**Results:** The flow rates over time achieved by an injector were almost identical. Slight deviations from the target flow rate occurred during ramp-up and ramp-down only. Those of manual injection showed high variability over the whole course of the injection. In the 1 mL/s scenarios, the injector deviated from the target flow rate by 0.06 mL/s or less ( $\leq 6\%$ ) and in the 5 mL/s scenarios by 1.02 mL/s or less ( $< 20\%$ ). For the manual injections at the same flow rates, these figures were 0.35 mL/s or less ( $\leq 35\%$ ) and 3.1 mL/s or less ( $\leq 62\%$ ).

**Conclusions:** Injector administration of a magnetic resonance contrast agent minimally deviated from the target flow rate, whereas manual injection varied widely. Injector administration is more accurate and repeatable.

**Key Words:** injector administration, manual administration, target flow rates, MR contrast agents

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All contrast-enhanced magnetic resonance imaging (MRI) procedures should include accurate and repeatable contrast agent administration. An accurate flow rate is most important for first-pass imaging such as MR angiography (MRA) and time-resolved imaging such as hepatic arterial phase measurements. These procedures require a precise synchronization of contrast agent arrival in the target region and the MRI acquisition. This is especially relevant for low-dose contrast agent

injection procedures; particularly, the flow rate should be well defined and standardized.

Magnetic resonance contrast agents can be injected manually or by using an automated injection system. Depending on the patient's characteristics, the indication for the imaging and the contrast agent, different contrast volumes are to be injected at different injection rates using needles or catheters with different diameters.<sup>1</sup> To achieve reproducible, high-quality imaging data, accurate and reproducible flow rates, and a short interval between contrast injection and saline chaser should be a goal.<sup>2,3</sup> To the best of our knowledge, a thorough head-to-head comparison of injection parameters of injector versus manual administration of an MRI contrast agent has not been performed so far.

The primary goal of this study was to record flow rates of an MRI contrast agent achieved by use of an automated injection system versus manual administration over time and to calculate the deviations from the target flow rate.

## MATERIALS AND METHODS

### Study Setup

The experimental setup is shown on Figure 1. It allowed measurement of the flow rate and the total volume injected over time for both contrast and saline. Data for both parameters were recorded electronically. Contrast and saline were injected through different lines, consisting of catheters and a swabable valve transfer set, mimicking the vein, into separate bags placed on a scale so they could be recycled for repeated use without contamination or dilution. The scale was protected from external influences by a built-in wind shield.

### Injector and Manual Administration

The setup for injector and manual injection was identical using the same 2 separated fluid paths for contrast and saline. Either injector or hand syringes were connected to the stopcocks (Fig. 1).

Injector administration was performed with the injection system MRXperion (Bayer AG). The maximum pressure limit was set to the default of 325 psi (2240 kPa). The flow rates were set to be that of the injection targets for the test series, 5 mL/s and 1 mL/s, respectively. The injector was operated by an experienced Bayer scientist/technician (N.U.).

Manual injection was performed by 10 technologists (a–j) with at least 5 years of experience in clinical practice. Each technologist performed a total of 13 manual injections. On each test day, 2 or 3, technologists performed those 13 injections. The first manual injection was performed as a training exercise to familiarize them with the test setup. The technologists were asked to inject as they normally do in their clinical routine. Then they did 12 injections each, 2 for each of 6 scenarios with different IV catheters, different contrast volumes, and different injection speeds (see below). Mimicking their daily routine, 8 technologists exchanged the contrast syringe with a saline syringe to administer the flush, and 2 used the stopcock to switch from contrast to

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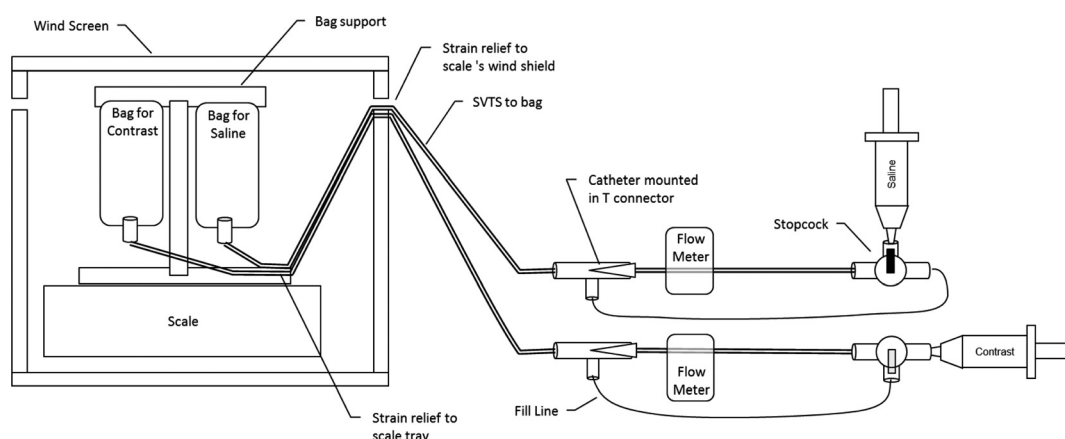
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**FIGURE 1.** Experimental setup. For hand syringe tests, the two stopcocks were mounted one on top of the other to simulate the turning or insertion motion that the technologists use to flush. To mount on the injector, the two stopcocks were separated and mounted on the corresponding injector syringes.

saline. All were blinded to their injection performance to avoid a learning effect. In addition, the staff working with the technologists did not see the flow rate over time curve displayed on the measurement system control panel during the test to avoid accidental feedback by body language. To avoid fatigue, injections were performed on a rotating basis. A technologist performed a given injection followed by the other members of that group so that no technologist performed 2 consecutive manual injections. Each participant on a given day performed a total of 12 manual injections, 2 per scenario for the 6 scenarios. On the days where there were just 2 technologists, one of the Bayer observers took a turn so that the rest time was approximately the same for all test groups.

Six scenarios with 2 different IV catheters (22 gauge and 20 gauge), 2 different contrast volumes (10 and 20 mL) and 2 different injection speeds (1 and 5 mL/s) were tested. The injector and each technologist performed each scenario twice (Table 1).

### Target Parameters

For all 6 scenarios, the flow rates over time were continuously recorded for injector and manual administration. The primary target variable was defined as the average absolute and average absolute percentage deviation from the target flow rate. The deviations were added without considering the direction of deviation. Thus, the term *absolute* refers to the fact that deviations in flow rates above (positive), and below (negative), the target were summed as to their absolute numerical deviation without regard to the  $\pm$  sign, so positive and negative deviations did not average out.

**TABLE 1.** Test Scenarios for Injector and Manual Administrations

Scenario	Target Flow Rate	CM Volume	IV Gauge	MRXperion No. Tests	10 Technologists (a–j) No. Tests
1	5 mL/s	10 mL	22	2	20
2	5 mL/s	20 mL	22	2	20
3	1 mL/s	10 mL	20	2	19
4	1 mL/s	20 mL	20	2	20
5	5 mL/s	20 mL	20	2	20
6	5 mL/s	10 mL	20	2	20
				$\Sigma 12$	$\Sigma 119$

### Statistics

Because this was a pilot study, no statistical hypothesis could be stated. All results are reported descriptively.

### Materials

This study used the following materials: injector, MRXperion (VV1010 with a valid calibration sticker); contrast, 1 M gadobutrol (Gadovist; Bayer AG, Leverkusen, Germany)<sup>4,5</sup>; computer, Lenovo G40 equipped with Windows XP (National Instruments Labview 2013 service pack 1, M62x651571); program, Mettler Balance and flow meter (ver04\_john.vi saved on May 24, 2013, 12:18 PM), NI cDAQ-9147 support frame, NI 9215 input module for flow meter; transonic flow meters, ME2PX11019 Medrad Calibration 13405–1 and ME2PX11018 Medrad Calibration 13405–2 (Rev Filter on 40 Hz, measuring 20 data points per second [1 data point each 0.05 second]); scale, Mettler Toledo, PR 2003 Delta Range (control number 13347 Rev.—PR2003 DR SNR 1125360581 TDNR 26473122–0; last calibrated, December 2014); Stopcock 565311, IV catheters (20 gauge, BD Ref 381134 and 22 gauge: BD Ref 381123); SVTS (swabable valve transfer set); Halkey Roberts swabable valve 245204024, 13-in length of MR 65/115 VS tubing (0.075-in ID, 0.125-in OD).

### RESULTS

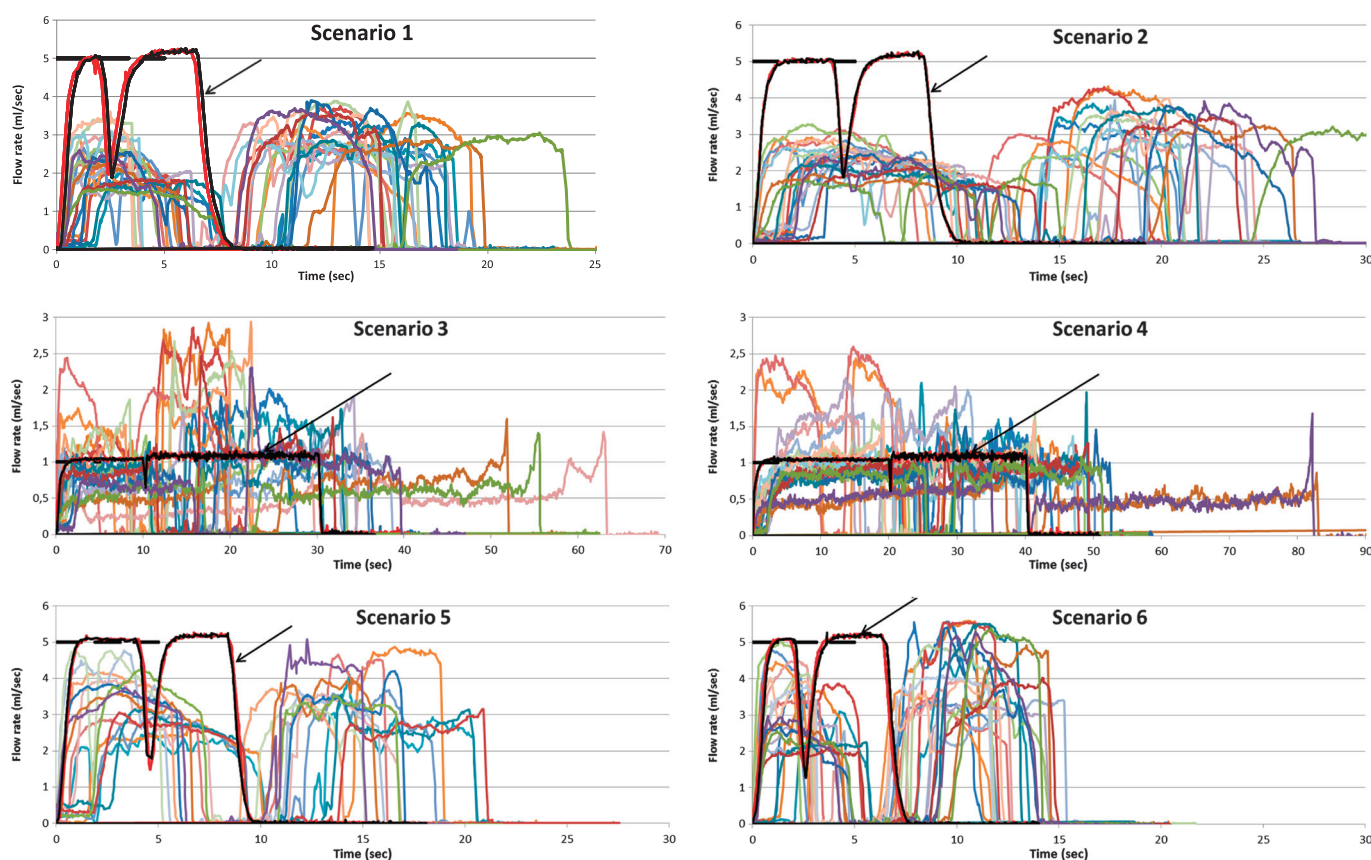
The flow rates over time for all 6 scenarios are shown in Figure 2.

While the flow rates over time of the 2 injector administrations in each scenario were almost identical, those for the intraindividual and interindividual manual injections varied widely.

Contrast injections were followed by a saline flush. The time interval between the administration of contrast and saline was clearly visible as a trough in the flow rate curves between these 2 injection phases. This was best shown in the 5 mL/s scenarios (scenarios 1, 2, 5, and 6) performed by the injector.

The target flow rate of 5 mL/s in scenarios 1, 2, 5, and 6 was quickly reached by the injector with some slight deviation during ramp-up and ramp-down, whereas the flow rate of 5 mL/s was reached only in rare cases by manual injection. The target flow rate of 1 mL/s (scenarios 3 and 4) was precisely reached by the injector with almost no gap between the contrast and saline phase, whereas the flow rates over time for manual injections varied up to 3.1 mL/s.

The total injection duration depends on the contrast volume and the injection speed. In the 1 mL/s scenarios (scenarios 3 and 4), the injector precisely injected the contrast within 10 and 20 seconds, respectively. In the 5 mL/s scenarios, the injection duration with the injector



**FIGURE 2.** Injection profiles of 2 injector administrations (arrows) in comparison to a series of manual administrations by multiple technologists. The dip indicates the switch from contrast to saline.

was slightly longer as calculated to achieve the total flow due to the controlled ramp-up and ramp-down. Manual injections always took significantly longer than injector administrations.

There was a remarkable difference between the hand injections with the smaller 22-gauge catheter and the larger 20-gauge catheter (compare scenario 1 with 6 and 2 with 5; see Fig. 2). This was not observed for the injector administrations.

Figure 3 and Table 2 show the average absolute and average absolute percentage deviations from the target flow rate for all 10 technicians (a–j) and the injector administrations.

In the 1 mL/s scenarios, the injector deviated from the target flow rate by 0.06 mL/s or less ( $\leq 6\%$ ) and in the 5 mL/s scenarios by 1.02 mL/s or less ( $< 20\%$ ). For the manual injection, these figures were 0.35 mL/s or less ( $\leq 35\%$ ) and 3.1 mL/s or less ( $\leq 62\%$ ), respectively. The flow rates of the saline flush are shown in Table 2. The applied contrast agent volume of 10 or 20 mL does not systematically affect the accuracy of the flow rate.

Two of the technologists used stopcocks for switching from contrast to saline, 8 exchanged the syringes. The mean switching time for all 10 technicians varied between 1 and 6 seconds. The injector injected saline immediately after the contrast (Fig. 4).

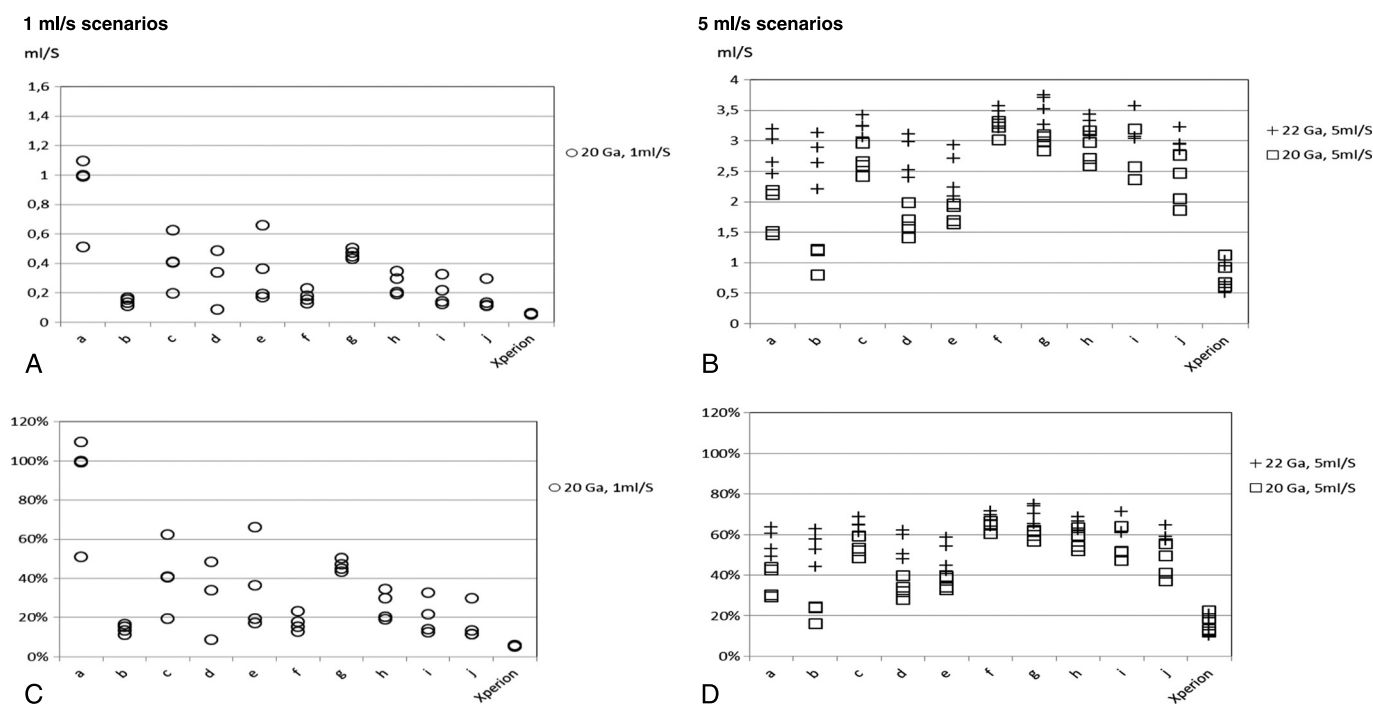
## DISCUSSION

In this laboratory study, we measured flow rates of an MRI contrast agent and saline chaser achieved by injector versus manual administration over time. As primary target parameters, we calculated the average absolute deviation and average absolute percentage deviations from the target flow rate. To the best of our knowledge, a direct comparison of manual versus injector flow rates has not been published so far.

The data from this study showed that flow rates over time of the 2 injector-based contrast agent administrations in each scenario were almost identical, whereas those for the manual injections showed wide intraindividual and interindividual variations. This evidence substantiates the accuracy and repeatability of the injector administrations. In particular, the target flow rate of 5 mL/s was consistently achieved by the injector and rarely via the manual method. This may be of clinical importance for dynamic imaging procedures to evaluate perfusion (dynamic susceptibility contrast imaging and dynamic contrast-enhanced [DCE] Imaging), which require a high injection rate, for example, for cardiac perfusion imaging<sup>6</sup> or perfusion imaging in acute ischemic stroke.<sup>7</sup> Here, a short compact contrast agent bolus shape with a high bolus peak and consequently an increased signal-to-noise ratio are key.<sup>8</sup>

Also, low injection rates such as 1 mL/s are highly time-critical, for example, in MRA of run-offs and liver imaging. Here, highly precise synchronization of contrast delivery and image acquisition is necessary. The basis for this synchronization is a well-controlled contrast injection procedure that provides accurate and repeatable bolus timing. Our data show that this is achievable with injector-based administration but not with manual administration, which is highly operator dependent.

A slight deviation from the target flow rate during injector administrations is recorded as ramp-up and ramp-down. This is caused by a programmed acceleration rate intended to limit the amount of catheter whip and turbulence in the patient's vein and thus increasing the safety of the injection for the patient.<sup>9</sup> In dynamic susceptibility contrast imaging and DCE MRI studies of the brain, a minimum bolus injection rate of 3 mL/s is recommended to allow compact bolus arrival in the cerebral tissue,<sup>10</sup> providing the needed temporal signal intensity change.



**FIGURE 3.** The measured average absolute deviations (mL/s) (A and B) and average percentage deviations (%) (C and D) from target contrast flow rate (1 mL and 5 mL) per technician (a–j) and injector (MRXperion).

Also in cardiac perfusion imaging and for the characterization of tumor microvasculature in prostate cancer, DCE is frequently used.<sup>11</sup> In clinical scenarios such as these, the data from this study indicate that manual administration may be inconsistent and thus suboptimal. In addition, also at 1 mL/s, high accuracy and repeatability are important, for example, for injection protocols for MRA of run-offs and contrast-enhanced liver imaging.

The average absolute deviation and average absolute percentage deviation from the target flow is the key parameter for injection accuracy. We could show that the relative deviations for injector administrations were 6% or less and less than 20% for the 1 mL/s and 5 mL/s

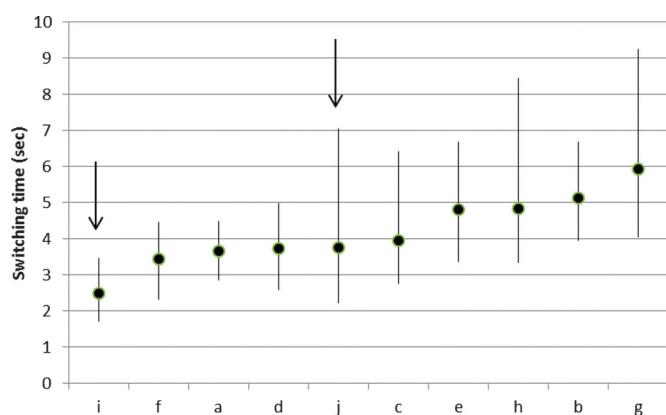
scenarios, respectively. These results are mainly caused by the ramp-up and ramp-down phase. A safety feature in the injector's software limits the acceleration rate to a set value to reduce any jetting effects and vessel wall damage on ramp-up and “water hammer” from hydraulic inertia on the ramp-down phase. For manual administration, the deviation was more than 3-fold higher, that is,  $\leq 35\%$  and  $\leq 62\%$ . These results show that due to intraindividual and interindividual variations accurate and repeatable injection flow rates are unlikely when manually administering intravenous MRI contrast media.

Furthermore, correct total injection duration was only possible with the injector administrations. Manual injections lasted typically

**TABLE 2.** Average Absolute Deviation (mL/s) and Average Absolute Percentage Deviation (%) From Target Flow Rate for Injector vs Manual Administration for Contrast and Saline (20 mL) in each Scenario

Scenario	Target Flow Rate	Average Absolute Deviation $\pm$ SD (mL/s)			
		Average Absolute Percentage Deviation $\pm$ SD (%)			
		Injector Administration		Manual Administration	
		Contrast	Saline	Contrast	Saline
1	5 mL/s	0.99 $\pm$ 0.05 20% $\pm$ 1%	1.32 $\pm$ 0.03 26% $\pm$ 1%	3.1 $\pm$ 0.45 62% $\pm$ 9%	2.4 $\pm$ 0.32 49% $\pm$ 6%
2	5 mL/s	0.57 $\pm$ 0.07 11% $\pm$ 1%	1.33 $\pm$ 0.01 27% $\pm$ 0%	3.0 $\pm$ 0.35 60% $\pm$ 7%	2.3 $\pm$ 0.49 46% $\pm$ 10%
3	1 mL/s	0.06 $\pm$ 0.00 6% $\pm$ 0%	0.09 $\pm$ 0.00 9% $\pm$ 0%	0.35 $\pm$ 0.21 35% $\pm$ 21%	0.51 $\pm$ 0.40 51% $\pm$ 40%
4	1 mL/s	0.05 $\pm$ 0.00 5% $\pm$ 0%	0.10 $\pm$ 0.00 10% $\pm$ 0%	0.33 $\pm$ 0.28 33% $\pm$ 28%	0.34 $\pm$ 0.30 34% $\pm$ 30%
5	5 mL/s	0.64 $\pm$ 0.03 13% $\pm$ 1%	0.99 $\pm$ 0.01 20% $\pm$ 0%	2.4 $\pm$ 0.68 48% $\pm$ 14%	1.8 $\pm$ 0.53 36% $\pm$ 11%
6	5 mL/s	1.02 $\pm$ 0.10 20% $\pm$ 2%	1.00 $\pm$ 0.01 20% $\pm$ 0%	2.2 $\pm$ 0.68 45% $\pm$ 14%	1.6 $\pm$ 0.51 33% $\pm$ 10%





**FIGURE 4.** Switching time (maximum, average, minimum) (second) between contrast and saline injection during manual injection per technician (i–g), arrows indicate 2 technicians using stopcocks. Plot is in order of fastest to slowest technologists.

longer than calculated and required (for optimal imaging), which makes estimating the peak enhancement in a certain vascular area a challenge. In particular, for long injection times (>15 seconds), the recirculated contrast agent mix with the injected contrast agent, and thus contributes to the bolus profile. In contrast to CT, the impact on the image quality has not yet systematically been investigated. However, considering the low injection volumes in MRI, the effect of recirculation might be limited.<sup>12</sup>

In addition, the time (gap) between the end of the contrast injection and beginning of the saline flush for all 10 technicians varied between 1 and 6 seconds. Technician “i” was the fastest with 2.5 seconds by using a stopcock. The switching time was independent of the technicians' years of job experience. The gap for the injector was remarkably smaller. Both parameters, the total injection duration as well as the gap between the 2 injection phases have an effect on the accurate timing between contrast agent injection and image acquisition, which is important for all first-pass contrast-enhanced MR techniques in particular 3D-MRA. If the image acquisition and the arterial phase are mistimed, suboptimal arterial enhancement or venous contamination may result in reduced image quality. Technically, synchronization for bolus arrival and image acquisition can be ensured by the use of bolus tracking techniques or prior test bolus measurement.<sup>13–15</sup> However, the latter highly depends on repeatable injection rates. An additional source of variation can be the longer gap between the 2 injection phases, that is, hand switching times. Longer switching times may cause inconsistent bolus spreading in patients because some of the contrast agent bolus may be carried downstream by the more rapid central venous flow and the more peripheral segment of the bolus may be delayed. The direct impact of the injection duration and switching time on the bolus geometry (ie, the bolus width and peak height) has—to the best of our knowledge—not been investigated yet.

Although these bench tests cannot prove or demonstrate a direct clinical impact in humans, they clearly demonstrate the significantly higher capability of an injector-based contrast administration in terms of accuracy and repeatability when compared with a manual injection. The final goal is to show that highly accurate and repeatable injection of the MRI contrast agent results in improved image quality or—in

the best of all scenarios—in improved diagnoses and treatment planning. Therefore, our study program is complemented by a preclinical study in pigs<sup>16</sup> and a clinical study on brain perfusion tests in patients with brain tumors, which is still running. The preclinical study in 6 pigs by Jost et al<sup>16</sup> recently confirmed that injector contrast agent administration results in more standardized bolus shapes and higher vascular contrast in MRA. In addition, they suggested that injector-based contrast administration also results in more robust visualization of target vessels and hence provide potentially higher diagnostic image quality.

## CONCLUSIONS

Injector administration of an MRI contrast agent minimally deviated from the target flow rate, whereas manual injection varied widely. Injector administration is more accurate and repeatable.

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