

S. Potthast
A.-C. Schulte
G. M. Bongartz
R. Hügli
M. Aschwanden
D. Bilecen

Low-dose intra-arterial contrast-enhanced MR aortography in patients based on a theoretically derived injection protocol

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S. Potthast · G. M. Bongartz · R. Hügli ·
D. Bilecen (✉)
Department of Diagnostic Radiology,
University Hospital of Basel,
Petersgraben 4,
4031 Basel, Switzerland
e-mail: dbilecen@uhbs.ch
Tel.: +41-61-2654249
Fax: +41-61-2655351

A.-C. Schulte
Biocenter, University of Basel,
Klingelbergstrasse 50/70,
4056 Basel, Switzerland

M. Aschwanden
Department of Angiology,
University of Basel,
Petersgraben 4,
4031 Basel, Switzerland

Abstract Multiple intra-arterial contrast agent injections are necessary during MR-guided endovascular interventions. In respect to the approved limits of maximum daily gadolinium dose, a low-dose injection protocol is mandatory. The objective of this study was to derive and apply a low-dose injection protocol for intra-arterial 3D contrast-enhanced MR aortography in patients. Injection rate (Q_{inj}), concentration of injected gadolinium $[Gd]_{inj}$ and aortal blood flow rate (Q_{blood}) were included for the theoretical evaluation of signal intensity (SI) of the arterial lumen. SI simulations were carried out at $Q_{inj}=2$ versus 4 ml/s in the $[Gd]_{inj}$ range between 0–500 mM. Q_{inj} and $[Gd]_{inj}$ with SI above the 75% threshold of the maximal SI were regarded as optimal injection parameters. $[Gd]_{inj}=50$ mM and $Q_{inj}=4$ ml/s were considered as optimal and were administered in five patients for 3D MR aortography. All images revealed clear delineation of the abdominal aorta and its major branches. Mean±

SD of contrast-to-noise ratios of the abdominal aorta, common iliac and renal artery were 70.2 ± 15.2 , 58.6 ± 12.3 and 67.4 ± 12.3 . Approximately seven intra-aortal injections would be permissible in patients during MR-guided interventions without exceeding the maximal dose of gadolinium.

Keywords Gadolinium · Intra-arterial · DSA · MR aortography

Introduction

Atherosclerosis is the leading cause of morbidity and mortality in the Western world. It is a non-inflammatory disease of the vessel wall leading to thickening and loss of the vessel wall's elasticity. Its clinical presentations include stroke, coronary heart disease, and peripheral arterial occlusive disease (PAOD), which predominantly arise from complications of vessel stenoses, occlusions, aneurysms,

or dissections. X-ray digital subtraction angiography (DSA) is regarded as the standard of reference in the diagnosis of arterial lesions. DSA-guidance is also used for endovascular therapies like percutaneous transluminal angioplasty (PTA) or stent placement. In the past decade, intravenous contrast-enhanced MR angiography (CE-MRA) has gained broad acceptance among clinicians and has become a valuable diagnostic tool in the clinical routine [1–7]. The advantages of CE-MRA are well documented and

include the lack of X-ray exposure of the patient and examiner, use of minor nephrotoxic contrast agent with low allergic potential, excellent soft-tissue contrast, and three-dimensional (3D) arterial visualization.

In the face of the fast-growing MR technology, several investigators have made efforts to extend the field of MR angiography towards MR-guided endovascular interventions [8–18]. One of the primary goals of these efforts is to obtain high-spatial-resolution intra-arterial 3D CE-MR angiograms. Adequate arterial enhancement is required by low-dose intra-arterial contrast agent injection through the arterial access provided by the interventional procedure. High contrast-to-noise ratios (CNR) of the vessel lumen are an important precondition for the localization of stenoses and occlusions. This is mandatory to assess precise tracking of endovascular devices like guide wires and catheters.

Due to the paramagnetic properties of gadolinium (Gd)-based contrast agents, the blood concentration of gadolinium ($[Gd]_{\text{blood}}$) must meet a target range during MRA data acquisition. $[Gd]_{\text{blood}}$ values below this range will result in a signal loss because of insufficient T_1 shortening, while $[Gd]_{\text{blood}}$ values above this range will cause rapid spin-dephasing leading to a T_2/T_2^* -dependent reduction of the MR signal. The optimal concentration of gadolinium in blood depends on several factors including the blood flow rate (Q_{blood}), injection rate (Q_{inj}), and concentration of injected gadolinium ($[Gd]_{\text{inj}}$). A theoretical model has been introduced to determine the target range of optimal gadolinium concentration in blood $[Gd]_{\text{blood}}$ [9–17,19]. Based on this model, a low-dose injection protocol for intra-arterial 3D CE-MRA of the infrainguinal arteries has been derived and was successfully validated for the visualization of thigh and calf arteries in PAOD patients [8].

In contrast to the infrainguinal arteries, endovascular interventional procedures in the abdominal aorta are less common. Nevertheless, good luminal signal enhancement of the abdominal aorta during an interventional procedure is required for the retrograde tracking and positioning of guide wires and catheters to sound major branching arteries, the coeliac trunk, the superior mesenteric, the inferior mesenteric, and the renal artery. Until now, no low-dose intra-arterial injection protocol for MR aortography in humans has been proposed or investigated in patients. A theoretical model can be adapted to the flow conditions of the human aorta. However, the range of aortal flow rates is rather large compared to the range of blood flow rates in the lower extremities.

The purpose of this study was to simulate a low-dose intra-arterial injection protocol for optimal signal enhancement of the human aorta. The derived injection protocol was applied in patients to assess the value of low-dose intra-arterial 3D CE-MR aortography for the depiction of the aorta and its major arterial branches.

Materials and methods

Simulations

For particular T1-weighted imaging sequences and given acquisition parameters (repetition time: 2.73 ms; echo time: 0.89 ms and acquisition time: 20.3 s), the contrast agent concentration in blood determines T1 shortening and therefore a signal intensity (SI) of the blood. The contrast agent concentration (relaxivities of R1 and R2) in blood depends on several parameters such as the arterial Q_{blood} , Q_{inj} , and $[Gd]_{\text{inj}}$. (equation 3 in the appendix). When complete mixing of contrast agent with native blood is assumed, an appropriate low-dose intra-arterial injection protocol can be derived. In our study we are focused on the flow condition of the human abdominal aorta with flow blood rates ≤ 30 ml/s. In the appendix the expressions relating the signal intensity (SI) of a spoiled gradient-echo sequence to the parameters Q_{blood} , Q_{inj} , and $[Gd]_{\text{inj}}$ via $[Gd]_{\text{blood}}$ are described in detail. Using these equations we theoretically calculated the SI as a function of the injection parameters, $[Gd]_{\text{inj}}$ and Q_{inj} , regarding aortal flow conditions for the acquisition parameters applied.

Considering the intraindividual variation of the aortal blood flow rates in patients, simulations were performed for Q_{blood} ranging from 0 to 30 ml/s, which was increased in intervals of 10 ml/s. Further, the effect of two injection rates, $Q_{\text{inj}}=2$ ml/s and 4 ml/s, of SI was considered. For these parameters the SI in the aortal lumen as a function of $[Gd]_{\text{inj}}$ from 0 up to 500 mM was simulated. In our patient study we used commercially available Gd-DTPA (Magnevist, Schering, Berlin, Germany) as contrast agent distributed with a full-strength concentration of 500 mM, containing 78.63 mg gadolinium. This stock solution of Gd-DTPA was diluted with physiological saline to obtain a gadolinium concentration of 50 mM. From these simulations a low-dose intra-arterial injection protocol for optimal signal enhancement of the aortal lumen in humans has been derived.

The lowest injected gadolinium concentration providing a SI above 75% of the SI maximum for all aortal blood flow rates and its corresponding injection rate were regarded as optimal. This optimal low-dose injection protocol was applied in patients for intra-arterial 3D CE-MR aortography. All simulations were performed within the Matlab programming environment (Mathworks, MA, USA).

Patients

The study protocol was approved by our institutional review board. Written informed consent was obtained from all patients prior to inclusion. Within a period of 6 months, five patients (four men, one woman, 56–67 years) were

enrolled in this study. Four of the patients suffered from symptomatic PAOD and were treated with PTA and/or stent placement under DSA-guidance immediately before MR aortography. One patient was a living kidney donor. After X-ray guided angiography (and angioplasty), intra-aortal 3D CE-MRA was performed. Exclusion criteria of this study included all generally accepted contraindications for MRI, e.g., pacemakers, implantable cardioverter defibrillators, and claustrophobia.

Retrograde percutaneous puncture of the common femoral artery was performed under X-ray fluoroscopy. For reference purpose, diagnostic X-ray angiograms were carried out in anterior-posterior (a.-p.) projections. To delineate the abdominal aorta and its run-off, 20 ml of non-ionic contrast agent (Ultravist 300, Schering, Berlin, Germany) was automatically injected at an injection rate of 18 ml/s (Angiomat-6000 Liebel-Flarsheim, Tyco Healthcare/Mallinckrodt, St. Louis, MO, USA). After conventional angiography and/or angioplasty, an MR-compatible 4F or 6F introducer sheath remained in the common femoral artery. X-ray fluoroscopic guidance was used to place the tip of an Omniflush-catheter (AngioDynamics, Queensbury, NY) in the suprarenal position. A permanent saline flush ensured the patency of the device during patient transport from the angio-suite to the MR-scanner.

MR imaging

All MR imaging was performed on a clinical 1.5-T MR-Scanner (Avanto, Siemens Medical Solutions, Erlangen, Germany). For signal detection a phased array surface coil was used. Patients were examined in the supine position with feet first in the MR scanner. Contrast-enhanced data sets of the abdominal aorta, its major branches and the common iliac artery were acquired in the coronal plane with a 3D fast low angle shot (FLASH) gradient-echo sequence with fat suppression using the following acquisition parameters: repetition time, 2.73 ms; echo time, 0.89 ms; flip angle, 25°; field-of-view, 420×378 mm²; matrix: 320×220; one slab of 60 partitions interpolated by zero filling to 80 (slab thickness: 96 mm, slice thickness: 1.6 mm interpolated by zero-filling to 1.2 mm). Seventy-five percent partial Fourier was applied in both phase-encoding directions to reduce the acquisition time to 20.3 s. Asymmetric k-space sampling was performed. The center of the k-space was acquired after 6.6 s.

Commercially available Gd-DTPA (Magnevist, Schering, Berlin) distributed with a full-strength concentration of 500 mM was used as contrast agent. The stock solution of Gd-DTPA was diluted with physiological saline to obtain a gadolinium concentration of 50 mM. The injection rate was 4 ml/s for a duration of 15 s. This corresponds to a total dose of 3.0 mmol gadolinium (50 mM×4 ml/s×15 s). The injection length of 15 s ensures coverage of 75% of the k-space including the center of the

k-space during arterial enhancement. The injection was carried out automatically using a power injector (Spectris, Medrad Indianola, PA, USA). Intra-aortal gadolinium injection and MRA data acquisition were started simultaneously. Prior to gadolinium administration, a native image was acquired to allow digital mask subtraction. Anterior-posterior maximum intensity projections (MIPs) were reconstructed from the intra-arterial 3D CE-MR aortographies.

For quantitative assessment, CNR of the infrarenal abdominal aorta, the common iliac, and the renal artery was determined. The SI of the unsubtracted source images was measured in the regions of interest (ROI). The size of the ROI was approximately 1.2 cm². CNR values of the aortal lumen were calculated according to $CNR = (SI_{\text{blood}} - SI_{\text{tissue}}) / SD_{\text{air}}$, where SI_{blood} and SI_{tissue} refer to the SI of the vessel lumen and the adjacent musculature, respectively. SD_{air} refers to the standard deviation of SI measured in a ROI outside the body.

Results

Simulations

Figure 1a shows the results of the simulation of the model function for $Q_{\text{inj}}=2$ ml/ and Fig. 1b for $Q_{\text{inj}}=4$ ml/s. The horizontal lines indicate the 75% threshold of maximum SI used for the determination of optimal injection parameters. The theoretically predicted SI as a function of $[Gd]_{\text{inj}}$ displays a steep increase until a rather broad maximum is attained. Following the maximum, a relatively slow decrease of the SI is observed. Rather low SI values are found for the highest $[Gd]_{\text{inj}}=500$ mM. A general finding for paramagnetic compounds is that the given signal gain is based on a T1 shortening, but is in competition with the signal loss due to the T2* effect, which is becoming superior to the T1 effect. The decline of the SI curve after peaking has to be attributed to the increase of T2* signal loss due to spin-dephasing.

Generally, at a fixed injection rate, lower $[Gd]_{\text{inj}}$ is needed for slower blood flow rates in order to reach the maximum SI and vice versa. On the other hand, for a particular blood flow rate lower $[Gd]_{\text{inj}}$ is required at higher injection rates and vice versa. For example, for $Q_{\text{inj}}=2$ ml/s and $Q_{\text{blood}}=10$ ml/s, a $[Gd]_{\text{inj}}$ of at least 38.3 mM is needed to surpass the 75% threshold. Contrarily, for $Q_{\text{inj}}=4$ ml/s and $Q_{\text{blood}}=10$ ml/s, a $[Gd]_{\text{inj}}$ of only 22.3 mM/s is required.

Explicitly, for $Q_{\text{inj}}=2$ ml/s, optimal $[Gd]_{\text{inj}}$ was found at 6.4 mM for $Q_{\text{blood}}=0$ ml/s, at 38.3 mM for $Q_{\text{blood}}=10$ ml/s, at 70.1 mM for $Q_{\text{blood}}=20$ ml/s, and finally at 102.0 mM for $Q_{\text{blood}}=30$ ml/s. For $Q_{\text{inj}}=4$ ml/s, optimal $[Gd]_{\text{inj}}$ was found at 6.4 mM for $Q_{\text{blood}}=0$ ml/s, at 22.3 mM for $Q_{\text{blood}}=10$ ml/s, at 38.3 mM for $Q_{\text{blood}}=20$ ml/s, and at 54.2 mM for $Q_{\text{blood}}=30$ ml/s.

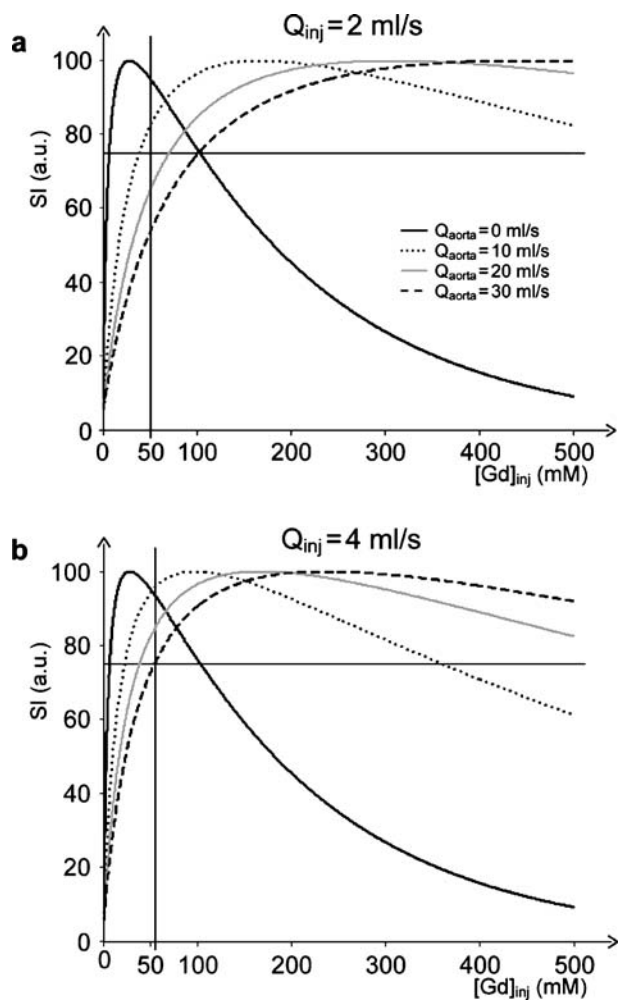


Fig. 1 **a** Quantitative results obtained from the simulation with $Q_{inj}=2$ ml/s for four aortal blood flow rates: $Q_{blood}=0, 10, 20,$ and 30 ml/s. The horizontal line indicates 75% of the corresponding maximum of SI. A vertical line indicates the simulated SI for $[Gd]_{inj}=50$ mM. **b** Quantitative results obtained from the simulation with $Q_{inj}=4$ ml/s for four aortal blood flow rates: $Q_{blood}=0, 10, 20,$ and 30 ml/s. The horizontal line indicates 75% of the corresponding maximum of SI. For $[Gd]_{inj}=54.2$ mM, indicated by the vertical line, the simulated signal intensities of all four aortal flow rates lie above the 75% threshold

For $Q_{inj}=2$ ml/s, 102.0 mM is the lowest $[Gd]_{inj}$ providing a SI above the 75% threshold for all four aortal blood flow rates, whereas the lowest optimal $[Gd]_{inj}$ for $Q_{inj}=4$ ml/s is 54.2 mM. Both sets of optimal injection parameters lead to an injected gadolinium dose of approximately 3.1 mmol.

For low-dose intra-arterial 3D MR aortography in patients, we chose the $[Gd]_{inj}$ with the higher injection rate, $[Gd]_{inj}=54.2$ mM and $Q_{inj}=4$ ml/s, since higher injection rates ensure better mixing of gadolinium with blood at the tip of the catheter. However, for practical reasons, we applied 50 mM of $[Gd]_{inj}$, which corresponds to 1:10 of the stock solution of Gd-DTPA.

Patient study

In all patients, low-dose intra-arterial MR aortography was feasible and well tolerated. No side effects occurred. In general, high-spatial-resolution intra-arterial 3D CE-MR aortography demonstrated a clear delineation of the abdominal aorta and its major branching arteries. Disturbing venous overlay or motion artifacts were not observed. Mean $CNR \pm SD$ was 70.2 ± 15.2 for the infrarenal abdominal aorta, 58.6 ± 12.3 for the renal artery, and 67.4 ± 12.3 for the common iliac artery.

MIPs obtained with low-dose intra-arterial 3D CE-MR aortography in patients are presented in the upper row of Fig. 2a–e. For comparison, the corresponding DSA images are illustrated in the lower row. Abdominal aorta, mesenteric, and parts of the iliac arteries are clearly visualized in all MIPs.

The DSA image in Fig. 2a (lower row) acquired before PTA and stenting demonstrates bilateral high-grade stenoses of the common iliac artery. The upper row of Fig. 2a displays the corresponding MR aortogram after bilateral stenting of the common iliac artery. Signal loss is observed within the stent lumen because of shielding artifacts of the metal meshwork [20]. A MIP-reconstructed MR aortogram of a living kidney donor is shown in Fig. 2c (upper row). Two renal arteries are depicted on the right side and one single artery on the left side. The DSA image in Fig. 2d (lower row) displays a short high-grade stenosis of the right common iliac artery. Good signal enhancement of the iliac lumen is observed in intra-arterial MR aortograms acquired after angioplasty. Similar findings are demonstrated in Fig. 2b and e.

Discussion

Adequate signal enhancement of the aortal lumen will be mandatory for MR-guided endovascular interventions. Our study demonstrates that the theoretically derived low-dose intra-arterial injection protocol is feasible and may provide high-spatial-resolution 3D CE-MR aortograms with high CNR of the aorta and its branching arteries. The derived injection protocol accounts for the aortal flow conditions (≤ 30 ml/s), the paramagnetic properties of gadolinium-based contrast agents (R_1, R_2^*), and conventional T1-weighted spoiled gradient-echo sequences. Optimal injection parameters were determined by simulations based on a theoretical model, whose prediction value has been validated in phantom and animals studies [9,10], as well as in a recent patient study [8].

Due to the rapid dilution of gadolinium-based contrast agents in circulating blood, repetitive injections during an interventional procedure will be mandatory. However, the total administered dose of gadolinium during an intervention should not exceed the approved limits of the Food and Drug Administration (FDA). The total amount of injected



Fig. 2 Upper row: MIP-reconstructed intra-arterial 3D CE-MR aortograms, lower row: corresponding DSA images in a-p. projection. **a** Fifty-nine-year-old male patient suffering from PAOD with a high-grade stenosis of the left common iliac artery and a mid-grade stenosis of the right common iliac artery. The left and right side were treated with a 10- and 40-mm Smart stent (Cordis, Miami, FL, USA), respectively. Due to shielding effects no signal enhancement can be depicted in the lumen of the stent. However, the run-off in the periphery is excellently visualized. **b** Sixty-seven-year-old male patient suffering from PAOD with multiple atherosclerotic plaques in the infrarenal aorta and the left common artery. **c** Sixty-three-year-old male living renal kidney donor. The abdominal aorta,

inferior mesenteric artery, iliac arteries and some lumbar arteries are clearly visualized. Two renal arteries exist on the right side, while there is only a single renal artery on the left side. Homogenous signal enhancement of the right kidney is observed. The left kidney shows a perfusion deficit in the periphery (*arrow*). **d** Fifty-eight-year-old male patient with a non-Hodgkin's lymphoma suffering from a high-grade stenosis of the common iliac artery on the right side. The patient was treated with PTA. A plaque of the distal aorta is nicely depicted in the DSA image and the intra-arterial MR aortogram. **e** Fifty-six-year-old female patient with multiple atherosclerotic plaques who was treated with PTA of the common iliac arteries on both sides

gadolinium is based on the $[Gd]_{inj}$, Q_{inj} and the injection length, which is 15 s. Therefore, the total injected gadolinium dose amounted to 3 mmol, even if a diluted Gd-DTPA solution of only 50 mM of gadolinium is administered. Assuming an average body weight of 70 kg, a dose of 3 mmol gadolinium corresponds to approximately 14% of the FDA-approved maximum dose. Thus, only seven intra-aortal injections will be permissible for an adult patient of average body weight until the FDA-approved maximum dose is exceeded. However, a complex endovascular intervention might require more than seven intra-aortal injections, which might limit the application of this technique.

According to the theoretical model, the SI for a specific CE-MRA sequence is a function of the $[Gd]_{blood}$. Since the optimal $[Gd]_{blood}$ for a given blood flow rate is approximately proportional to the product of $[Gd]_{inj}$ and Q_{inj} (Eq. 4), different combination of $[Gd]_{inj}$ and Q_{inj} can be used to achieve identical arterial enhancement. Therefore, a lower optimal $[Gd]_{inj}$ of 54.2 mM was found for $Q_{inj}=4$ ml/s in our study, whereas the lower Q_{inj} of 2 ml/s required a correspondingly higher $[Gd]_{inj}$ of 102.0 mM. Since we have optimized the product of $[Gd]_{inj}$ and Q_{inj} regarding 75% of maximum signal enhancement in the aorta, a further reduction of the gadolinium dose can be achieved by a further reduction of injection length. In our

study, the k-space coverage was 75% ($TA=20$ s, injection length=15 s). However, a further reduction down to 50% coverage might be feasible without significant loss of signal-to-noise ratio. This was recently demonstrated in an aortal phantom study [16].

Additionally, a shorter acquisition time might also enable a reduction of the injection length and injected gadolinium dose. Parallel imaging techniques like Sensitivity Encoding (SENSE) [21] or generalized autocalibrating partially parallel acquisition (GRAPPA) [22] permits to speed up MR data acquisition by a factor of two or even higher. A corresponding reduction of injection length and thereby of gadolinium dose of at least 50% might be possible. Nevertheless, further studies are obligatory to evaluate the potential of these techniques to minimize the injected gadolinium dose while preserving the SNR and diagnostic quality of intra-arterial MR angiography.

Recently, first results of intra-arterial MR angiography in patients have been reported [8, 23, 24]. However, these studies have applied injection protocols, which were either not aimed to minimize the injected gadolinium dose or not optimized for the aortal flow condition. Paetzel et al. [23] showed that intra-arterial MR angiography is feasible by injecting a gadodiamide dose of 5 mmol ($[Gd]_{inj}=83$ mM, $Q_{inj}=3.5$ ml/s, injection length 17 s). For an adult patient

with an average body weight of 70 kg, this protocol would permit only four repetitive injections. The SNR values obtained in their study were referenced to the SI in the left psoas muscle. Therefore, they can not be compared with our values, which were referenced to the standard deviation of SI measured in a ROI outside the body. Bilecen et al. proposed a low-dose intra-arterial injection protocol for 3D CE-MRA of the infrainguinal arteries in PAOD patients. Good image quality and high arterial enhancement of the infrainguinal arteries were achieved with $[Gd]_{inj}=50$ mM, $Q_{inj}=1.0$ ml/s and $TA=20$ s [8]. Although both protocols include the same $[Gd]_{inj}$ the total injected gadolinium in their study amounted to only 1 mmol as the infrainguinal blood flow rate is small with ≤ 5 ml/s. In our study we used extra-cellular gadolinium chelates, Magnevist, as contrast agent. Blood-pool agents provide the opportunity to image during the steady state of contrast agent concentration. The impact of intra-arterial injection of blood-pool agent is not yet known, but might be taken into account to reduce the total amount of injected gadolinium during endovascular interventions [25].

In conclusion, the proposed low-dose injection protocol for intra-arterial high-spatial-resolution 3D CE-MR aortography in patients provided good luminal enhancement of the aorta and its branching arteries. Simulations based on a theoretical model were performed to determine the optimal injection parameters under aortal blood flow conditions. The injected gadolinium dose was 3 mmol permitting approximately seven injections in adult patients of average body weight without exceeding the FDA-approved maximum gadolinium dose. This study is a first step towards low-dose intra-arterial 3D MR aortography in humans. Methodical and technical improvements are necessary to further reduce the injected gadolinium dose in order to enable a sufficient number of repetitive intra-aortal injections during an MR-guided endovascular intervention.

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Appendix

MR angiography with T_1 -shortening contrast agents typically employs spoiled gradient-echo sequences. The SI of a spoiled gradient-echo sequence is given by

$$SI \propto \sin \alpha \cdot e^{-TE/T_2^*} \frac{1 - e^{-TR/T_1}}{1 - e^{-TR/T_1} \cos \alpha}, \quad (1)$$

where TR, TE, and α are the repetition time, echo time, and flip angle, respectively. For CE-MRA, T_1 and T_2^* refer to the relaxation rates of the blood-contrast mixture (T_{1bc} , T_{2bc}^*), which depend on $[Gd]_{blood}$ via

$$\frac{1}{T_{1bc}} = \frac{1}{T_{1b}} + R_1 [Gd]_{blood} \quad \text{and} \quad (2)$$

$$\frac{1}{T_{2bc}^*} = \frac{1}{T_{2b}^*} + R_2 * [Gd]_{blood},$$

with the relaxation rates of blood, T_{1b} and T_{2b}^* , and the relaxivities of gadolinium, $R_1=4.5$ mM⁻¹s⁻¹ and $R_2^*=6.0$ mM⁻¹s⁻¹. Additionally, according to the dilution model [9], $[Gd]_{blood}$ can be expressed as a function of $[Gd]_{inj}$, Q_{inj} , and Q_{blood} of the artery of interest

$$[Gd]_{blood} = [Gd]_{inj} \cdot \frac{Q_{inj}}{Q_{inj} + Q_{blood}}, \quad (3)$$

For $Q_{inj} \leq Q_{blood}$, Eq. (3) reduces to

$$[Gd]_{blood} \approx \frac{[Gd]_{inj} \cdot Q_{inj}}{Q_{blood}}, \quad (4)$$

Inserting T_{1bc} and T_{2bc} from Eq. (2) and $[Gd]_{blood}$ from Eq. (4) in Eq. (1) provide the SI of a particular spoiled gradient-echo sequence with $[Gd]_{inj}$, Q_{blood} , and Q_{inj} .

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