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Gated thoracic magnetic resonance angiography at 3T: noncontrast versus blood pool contrast

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Abstract

Both noncontrast and contrast-enhanced approaches to gated thoracic magnetic resonance angiography (MRA) for aortic root evaluation have been reported at 3T. We compare qualitative and quantitative image quality measures for the two approaches, and assess the reproducibility of standard aortic measurements. Respiratory and cardiac gated MRA of the chest was performed at 3T in 45 patients: 23 after administration of iron-based blood pool contrast, and 22 without contrast. Image quality was assessed with a 5-point Likert scale, vessel lumen-to-muscle contrast ratios, and vessel wall sharpness. Two reviewers measured the ascending aorta diameter and valve annulus area. Interrater agreement was assessed using Bland–Altman plots and coefficient of variation (CV). Qualitative image quality was better with blood pool contrast in all principal vessels of the chest (mean Likert of 4.20 ± 0.79 vs. 2.60 ± 0.77, $p < 0.001$). Quantitative assessment was also improved with higher contrast ratios in all vessels (5.26 ± 3.3 vs. 1.90 ± 0.53, $p < 0.001$), and greater sharpness of the aortic annulus and ascending aorta (0.70 ± 0.16 vs. 0.56 ± 0.14 mm^{-1}, $p < 0.001$, and 0.87 ± 0.16 vs. 0.62 ± 0.16 mm^{-1}, $p = 0.008$, respectively). Reproducibility of measurement was marginally better for the ascending aorta diameter (CV of 2.80 vs. 3.23%), but substantially increased for the aortic valve annulus area with blood pool contrast (CV of 4.93 vs. 7.32%). The use of a blood pool contrast agent for gated thoracic MRA improves image quality compared to a noncontrast technique, and provides more reproducible measurements of the aortic valve annulus area.

Keywords

Aorta; MRA; TAVR; Contrast; Measurement reproducibility

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Chengcheng Zhu and Henrik Haraldsson have contributed equally to this work.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Introduction

With the emergence of transcatheter aortic valve replacement (TAVR), precise imaging of the aortic root with gated cross-sectional imaging is increasingly needed. Computed tomography angiography (CTA) has become the favored imaging approach for TAVR planning [1]. Compared to valve sizing with echocardiography alone, prosthesis selection based on CTA reduces the occurrence of paravalvular regurgitation, the most common complication of the procedure [2–4]. The iodinated contrast that is required for CTA, however, may increase the risk of renal dysfunction in patients with pre-existing renal dysfunction, which is common in the elderly patients undergoing TAVR [5].

Magnetic resonance angiography (MRA) has been explored as an alternative to CTA for TAVR planning. Conventional contrast-enhanced MRA with gadolinium is not well suited for the respiratory and cardiac gated imaging of the aortic root that is required for TAVR evaluation. The intravascular residence time of gadolinium-based contrast is too short to achieve both the high temporal and spatial resolution imaging needed [6]. Instead, gated native (noncontrast) three-dimensional (3D) MRA approaches have been employed and correlate well with CTA for aortic annulus sizing [6, 7]. A separate approach that has shown promise for TAVR planning is the use of a non-gadolinium blood pool contrast agent with a long enough intravascular resonance time to allow high-resolution, gated 3D MRA [8]. A unique advantage of this iron-based blood pool contrast agent (ferumoxtyol) is that it is appropriate for patients with renal failure.

The goal of this study was to determine whether there is benefit to using blood pool contrast for high-resolution, gated MRA of the chest. We hypothesized that blood pool contrast would qualitatively and quantitatively improve image quality compared to noncontrast MRA, and that this improved image quality would enable more reproducible measurements of the aortic root.

Materials and methods

We retrospectively collected images from 45 consecutive patients who underwent either gated contrast-enhanced (n = 23) or non-contrast (n = 22) MRA of the chest. Contrast-enhanced MRA with the blood pool agent ferumoxtyol was performed in patients with clinical indications for thoracic imaging and significantly reduced renal function (eGFR < 40 mL/min/1.73 m^2). Institutional review board approval was obtained for all studies. Patient demographical data is shown in Table 1.

MR imaging technique

MRA data were acquired on a whole-body 3T system (Siemens Skyra, Siemens Healthcare, Erlangen, Germany) using an RF-spoiled 3D gradient echo sequence with fat saturation (FLASH). Cardiac gating was performed based on the electrocardiogram (ECG) and respiratory gating with navigators targeting the right hemidiaphragm. Both contrast and noncontrast MRA protocols were designed for diastolic imaging of the thoracic aorta in less than 10 min during free breathing. The field of view was 32 × 32 cm acquired with a matrix size of 256 × 256, producing a true in-plane resolution of 1.25 × 1.25 mm. Data was

acquired in axial or candy cane view covering the aortic root and arch. The numbers of slices were 72 for non-contrast MRA (20% oversampling) and 80 for contrast MRA (10% oversampling). A 7/8 slice partial Fourier, and 50% slice resolution was used, resulting in a through-plane resolution of 2.2 mm. Data was interpolated to a resolution of 0.6 × 0.6 × 1.1 mm^3 voxels by k-space zero filling. GRAPPA was used for parallel acquisition with a reduction factor of 2. Fat suppression was used for both sequences. A standard T2 preparation (40 ms) was used for the non-contrast MRA to improve contrast between the lumen and surrounding tissues [6, 7]. An inversion recovery preparation (200 ms) was used for the contrast-enhanced MRA to enhance the lumen to background contrast, as the contrast media has short T1 values [8]. The non-contrast MRA had a TR/TE of 6.3/3.1 ms, a bandwidth of 399 Hz/pixel, a flip angle of 12°, an echo train length of 45, resulting in a 283 ms acquisition window acquired during diastole. Flow compensation gradients were used in non-contrast MRA to reduce flow-induced artifacts. The contrast MRA had a TR/TE of 2.8/1.2 ms, a bandwidth of 698 Hz/pixel, a flip angle of 20, an echo train length of 45, resulting in a 126 ms acquisition window acquired during diastole. Ferumoxytol was given prior to imaging at a dose of 3 mg/kg administered via slow intravenous infusion in the nursing holding area with continuous monitoring. Patients were scanned 5–10 min after the infusion.

Image analysis

Two experienced chest radiologists who were experienced in cardiovascular imaging independently evaluated the image quality of the major thoracic vessels (aorta, pulmonary arteries and veins, superior and inferior vena cava, aortic valve, and coronary arteries) using a 5-point Likert scale (Fig. 1): (1) Non-diagnostic, (2) Poor quality, (3) Partial visualization of anatomy, (4) Good visualization with mild blurring of borders, (5) Excellent visualization. The reviewers were blinded to the imaging approaches used and patient clinical information.

The myocardial signal intensity was used as a reference for the luminal signal evaluation. The lumen to myocardium contrast ratios were measured in the aorta, pulmonary artery, superior vena cava and left atrium. The method for sharpness quantification was adopted from a previous publication [9] using Micro View software (Parallax Innovations Inc., Ontario, Canada). A straight line was drawn perpendicular to the vessel boundaries and the line intensity profile was generated. Based on the profile, the sharpness was defined as: sharpness = 1/d, where d is the distance between positions of 20 and 80% of the difference of maximum and minimum intensity values (in mm) [9]. The sharpness of the tubular ascending aorta at the level of the pulmonary and of the aortic valve annulus was measured.

Two experienced radiologists independently used standard 3D approaches to measure the diameter of the tubular ascending aorta at the level of the pulmonary artery and the aortic annulus area on both contrast and non-contrast MRAs. The patients who had aortic valve replacement were excluded (n = 5) in the annulus area measurements due to imaging artefacts. The inter-reader reproducibility was evaluated. As a reference for reproducibility, the two radiologists also measured the ascending aorta diameter and aortic annulus area in the last 20 patients studied at our institution with gated CTA for TAVR evaluation.

Statistical analysis

Normality assumptions were formally assessed using the Shapiro–Wilk's test. Distributions were summarized using the median [inter-quartile range (IQR)] or the mean ± standard deviation (SD). Student T-tests or Mann–Whitney tests were used to compare the measurements of two methods. Fisher's exact test was used to compare categorical data. Bland–Altman plots, coefficient of variation (CV) and intraclass correlation coefficient (ICC) was used to evaluate the agreement between two reviewers. CV was defined as the standard deviation of the difference of two measurements over the mean × 100%. A p value of less than 0.05 was considered significant. All p-values were 2-sided. GraphPad prism 5 (GraphPad Software Inc., CA, USA) and R Statistics (version 3.1.3, http://www.r-project.org) was used for data analysis.

Results

Sample images of contrast and non-contrast MRAs are shown in Figs. 1 and 2. There was no significant difference in clinical characteristics between the two groups other than the slightly higher heart rate in the contrast-enhanced MRA group (74.8 ± 11.7 vs. 66.5 ± 11.0, p 0.02). The overall scan time of contrast and non-contrast MRAs was comparable (9:23 ± 4:03 vs. 8:02 ± 3:03, p = 0.20).

The qualitative image quality analysis is shown in Table 2, and the quantitative contrast ratio and sharpness measurements are summarized in Table 3. Contrast MRA had significantly better qualitative image quality on all major thoracic vessels. Quantitative analysis showed contrast MRA had significantly higher contrast ratios (> twofold on average) and somewhat higher sharpness of vessel boundaries. We did not observe obscuration of arterial anatomy by venous signal ("venous contamination") in any cases.

The reproducibility analysis for aorta diameter and annulus area measurements is summarized in Table 4. Contrast and non-contrast MRAs had good reproducibility for aorta diameter measurement, with only slightly lower CVs (2.80 and 3.23%, respectively) compared with the CTA reference (2.46%). Bland–Altman plots showed both MRA techniques had small bias and limit of agreement (Fig. 3). For annulus area quantification, however, the reproducibility was significantly worse for both CTA and MRA (all CVs > 4.5%). Contrast MRA has comparable reproducibility with the CTA reference (CV 4.93 and 4.80%, respectively), but non-contrast MRA was less reproducible (CV 7.32%). Bland–Altman plots showed there was a larger bias and limit of agreement using noncontrast MRA compared with contrast-MRA and the CTA reference (Fig. 4).

Discussion

This study demonstrates that respiratory and cardiac gated magnetic resonance angiography (MRA) is feasible in less than 10 min for ascending aortic evaluation either with or without blood pool contrast at 3T. Qualitative and quantitative measures of vascular image quality are improved with blood pool contrast compared to noncontrast MRA. Noncontrast MRA is appropriate for serial imaging of aortic dilation. Blood pool MRI contrast, however, improves the image quality of all vessels in the chest and enables more reproducible

measurements of the aortic valve annulus area for transcatheter aortic valve replacement (TAVR) planning.

Gated aortic imaging is needed to minimize the blurring caused by cardiac motion, and allows for precise measurement of the aortic root [10]. Computed tomography angiography (CTA) is frequently used because of its speed and availability, but requires radiation and iodinated contrast. MRA is an alternative approach that has been increasingly used in patients with pre-existing renal failure where iodinated contrast may worsen renal dysfunction. The need for alternative imaging techniques occurs frequently for TAVR patients, in whom pre-existing renal failure is relatively common and periprocedural acute kidney injury is strongly associated with 30-day and 1-year mortality [5]. [11] Steady-state free procession (SSFP) cine MRI has been reported to accurately size the aortic annulus prior to TAVR, but requires a technologist to position the acquisition plane perpendicular to the aortic annulus at the time of imaging [12, 13] More recently, 3D noncontrast MRA has shown promise for gated 3T imaging of the aortic root. Knobelsdorff-Brenkenhoff et al. demonstrated improved image quality and equivalent aortic diameter measurements when comparing native 3D SSFP MRA to first pass contrast-enhanced MRA at 1.5T [6]. SSFP MRA has high SNR and inherent good lumen-to-background contrast, however, off-resonance artifacts at 3T are a limitation for chest MRA. MRA based on the FLASH sequence is a common alternative for chest imaging at 3T. Ruile et al. reported reliable assessment of the aortic annulus with a noncontrast 3D-FLASH MRA, using CTA as the gold standard for comparison [7].

An alternative approach to high resolution, gated MRA in patients with renal failure is the use of iron-based blood pool contrast agents [14]. Ferumoxtyol is one such agent that is approved by the U.S. Food and Drug Administration as an IV treatment for iron-deficiency anemia in patients with chronic kidney disease. With its T1-shortening effect and long intravascular residence time of over 12 h, it is well suited for the steady-state imaging that longer respiratory and cardiac sequences require [15]. In a small cohort of patients, ferumoxtyol-enhanced MRA has shown promise for TAVR planning [8]. An alternative blood pool MRI contrast agent, gadofosveset (Ablavar, Lantheus Medical), was withdrawn from production in 2016. Thus, ferumoxytol is the only available agent for blood pool MR imaging. This fact coupled with recent concerns about deposition of gadolinium in the brain and bone have modified the risk/benefit calculus for ferumoxytol.

We endeavored to determine whether there are advantages to gated MRA with blood pool contrast compared to non-contrast aortic imaging. If the two approaches were comparable, then there would be no compelling reason to use intravenous contrast. Our results show that both noncontrast and blood pool contrast steady-state MRA can be obtained in a clinically acceptable time (less than 10 min) with diagnostic quality images. Blood pool contrast, however, improved both qualitative and quantitative image quality (Table 2). While this better image quality resulted in only marginally improved reproducibility of aortic diameters (CV of 2.80 vs. 3.23%; CTA reference 2.46%), a substantial improvement in the reproducibility of aortic annulus area was demonstrated (CV of 4.93 vs. 7.32%; CTA reference 4.80%). As the accuracy of this measurement is key for procedural success, MRA with blood pool contrast should be considered for TAVR planning.

The improved image quality provided by blood pool contrast has implications beyond that of aortic MRA. Cross-sectional imaging has been increasingly used in the last decade in planning radiofrequency ablation for atrial fibrillation. The clearer depiction of pulmonary venous anatomy afforded by blood pool contrast MRA (Likert 4.58 vs. 2.46, $p < 0.001$) may significantly improve the image guidance for this procedure. Likewise, the improved imaging of the pulmonary arteries (Likert 4.41 vs. 2.88, $p < 0.001$) may aid in the evaluation of pulmonary embolism in patients who are not good CTA candidates, including those with iodinated contrast allergy, renal failure or pregnancy. Additionally, venous imaging, which can be challenging to perform with conventional CT and MRI contrast, is clearly improved with blood pool contrast compared to noncontrast MRA (Likert 4.43 vs. 2.47, $p < 0.001$).

Our study has several limitations. While our cohort is relatively small ($n = 45$), we feel that our results clearly demonstrate the improved image quality of blood pool MRA. The same patients were not studied with the two MRA approaches. In practice, it was challenging to run both approaches in the same patients because that would require two separate imaging sessions. Guidelines for Ferumoxytol administration at our institution require that the USPIO contrast should be slowly infused in the nursing station under close monitoring [16]. However, the two groups studied were roughly equal in size, age, and indication for imaging (mainly aortic valve replacement and aortic dilation). We do not have a gold standard for our measurements. Our aim, however, was not accuracy of measurement, but rather reproducibility related to differences in image quality. Furthermore, we included a CTA reference for reproducibility of measurements to provide context for our data. In a previous publication, we found USPIO MRA had comparable measurement of aortic annulus area with trans-esophageal echocardiography (TEE) as the gold standard using a similar 3D MRA protocol [8]. The blood pool contrast agent used (ferumoxtyol) has a higher reported incidence of anaphylaxis than gadolinium (1:10,000) [16]. We followed the recommended safety precautions to minimize the risk of allergic reaction, including the slow infusion of contrast in the nursing holding area with continuous monitoring before the MRI, and also obtained consent prior to contrast administration [16].

In conclusion, both gated noncontrast and blood pool contrast MRA can provide diagnostic imaging of the thoracic aorta in a clinically acceptable time frame. Qualitative and quantitative assessment of image quality is improved with blood pool contrast. While this only marginally improves the reproducibility of aortic diameter measurements, it results in substantially improved reproducibility of aortic annulus area, which is key for TAVR planning.

Acknowledgments

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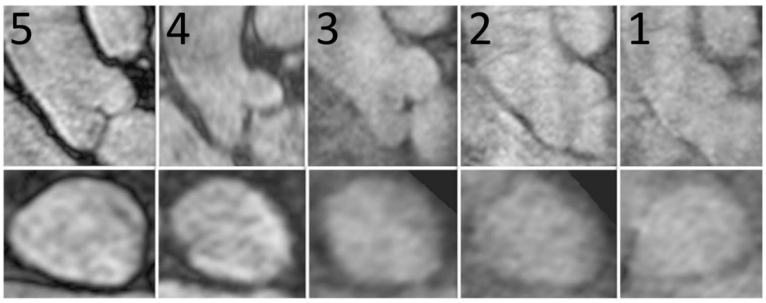

Fig. 1.

5-point Likert scale with representative images for the aortic root and annulus. 1—non-diagnostic, 2—poor quality, 3—partial visualization of anatomy, 4—good visualization with mild blurring of borders, 5—excellent visualization. Note that the images for 4- and 5— were obtained using blood pool contrast

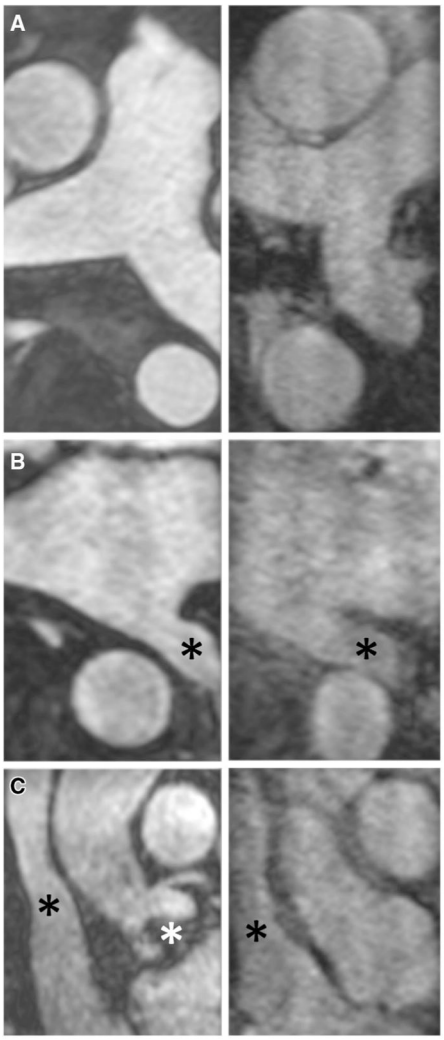

Fig. 2.

Representative images of non-aortic anatomy with contrast (left) and noncontrast (right) MRA: bifurcation of the pulmonary artery (**a** Likert 4.5 vs. 3), left lower lobe pulmonary vein (**b** with asterisk, Likert 5 vs. 2.5), and superior vena cava (**c** with asterisk, Likert 4 vs. 2.5). Note that the contrast MRA for the superior vena cava demonstration has an aortic valve replacement (white asterisk)

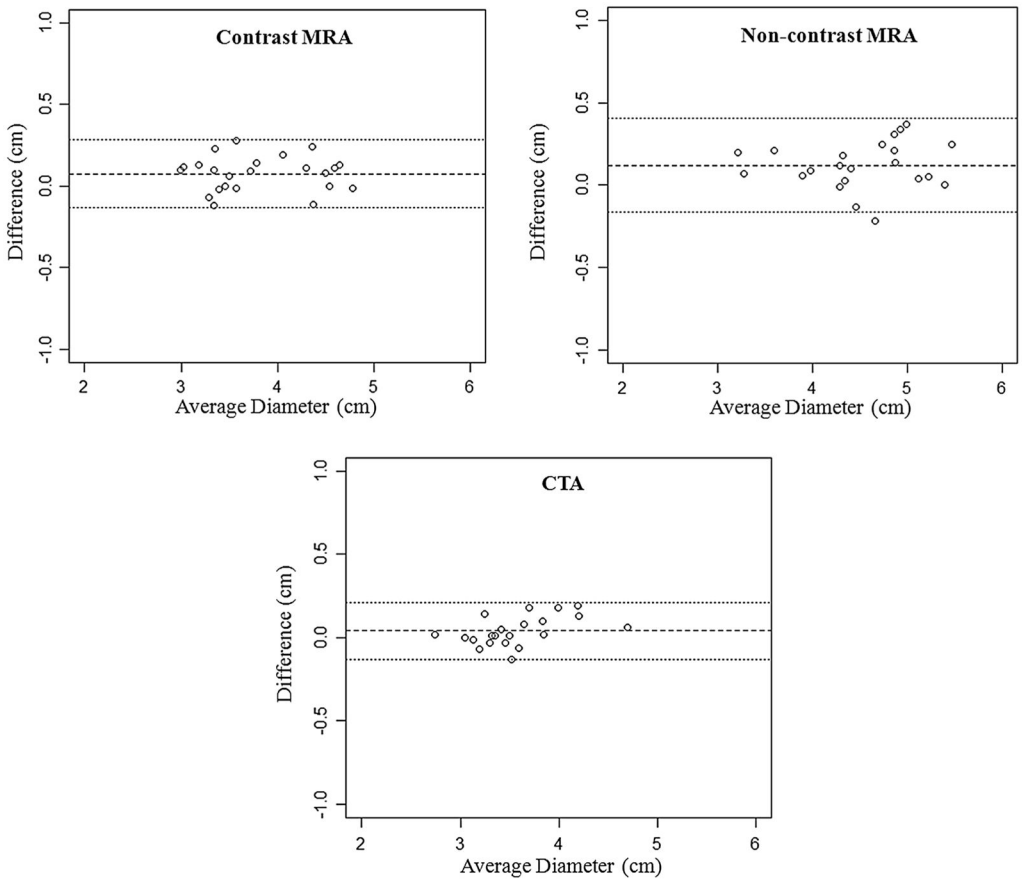

Fig. 3.
Bland–Altman plots of ascending aortic diameter measurements

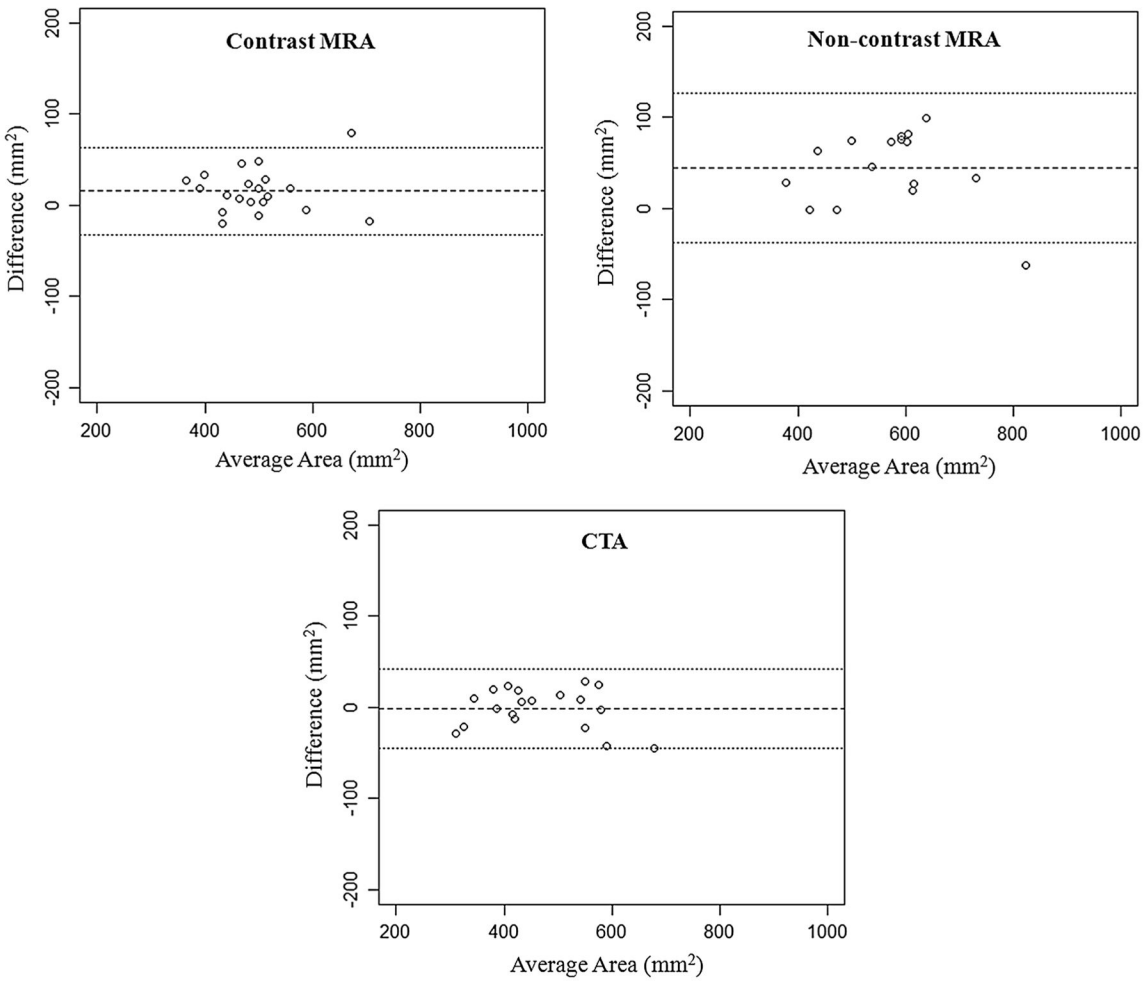

Fig. 4.
Bland–Altman plots of aortic valve annulus area measurements

Table 1

Patient demographics

	Contrast-MRA (n = 23)	Non-contrast MRA (n = 22)	P values
Age (years)	73.0 ± 8.6	69.0 ± 12.9	0.22
Sex (male)	22	22	1.00
Indications			
Aortic dilation	11	13	0.55
Aortic valve replacement	8	9	0.76
Others[a]	4	0	0.11
Height (cm)	175.1 ± 6.2	177.1 ± 7.9	0.38
Weight (kg)	92.7 ± 20.6	93.1 ± 19.0	0.94
Body Mass Index (kg/m^2)	30.5 ± 6.8	28.6 ± 5.5	0.34
Heart rate	74.8 ± 11.7	66.5 ± 11.0	0.02
Respiratory gating efficiency (%)	35.0 ± 8.2	33.1 ± 7.9	0.49

[a]Other indications include aortic dissection, aortic screening and left atrial mapping

Table 2

Qualitative image scores of thoracic vessels for contrast and non-contrast MRA

	AO	PAs	PVs	AoV	SVC/IVC	Coronary	Average
Reader 1							
Contrast MRA	4.4 ± 0.5	4.8 ± 0.4	4.7 ± 0.6	4.5 ± 0.6	4.3 ± 0.9	3.7 ± 1.0	4.4 ± 0.8
Non-contrast MRA	2.9 ± 0.9	2.9 ± 0.8	2.5 ± 0.6	2.2 ± 0.7	2.3 ± 0.8	2.5 ± 0.8	2.6 ± 0.7
P values	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Reader 2							
Contrast MRA	4.0 ± 0.7	4.1 ± 0.6	4.5 ± 0.5	4.3 ± 0.6	3.8 ± 0.9	3.4 ± 0.8	4.0 ± 0.8
Non-contrast MRA	2.9 ± 0.8	2.8 ± 0.8	2.4 ± 0.9	2.7 ± 1.0	2.6 ± 0.9	2.4 ± 1.0	2.6 ± 0.8
P values	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

AO aorta, *PAs* pulmonary arteries, *PVs* pulmonary veins, *AoV* aortic valve, *SVC/IVC* superior vena cava/inferior vena cava

Table 3

Quantitative image quality measurements

Lumen to myocardium contrast ratio					
	AO	**PA**	**SVC**	**LA**	**Average**
Contrast MRA	4.71 ± 2.84	5.66 ± 3.33	4.86 ± 3.03	5.79 ± 3.88	5.26 ± 3.27
Non-contrast MRA	2.03 ± 0.49	2.07 ± 0.51	1.45 ± 0.44	2.03 ± 0.43	1.90 ± 0.53
P values	<0.001	<0.001	<0.001	<0.001	<0.001

Sharpness of vessel boundaries			
	Ascending Aorta	**Annulus**	**Average**
Contrast MRA (mm^{-1})	0.87 ± 0.16	0.70 ± 0.16	0.79 ± 0.18
Non-contrast MRA (mm^{-1})	0.62 ± 0.16	0.56 ± 0.14	0.59 ± 0.15
P values	<0.001	0.008	<0.001

AO aorta, *PA* pulmonary artery, *SVC* superior vena cava, *LA* left atrium

Table 4

Measurement reproducibility

Aorta-diameter					
	Reader 1 versus 2 (cm)	**Bias ± 95% LOA (cm)**	**P value**	**CV (100%)**	**ICC**
Contrast MRA	3.85 ± 0.58 versus 3.77 ± 0.58	0.08 ± 0.21	0.002	2.80	0.975
Non-contrast MRA	4.57 ± 0.64 versus 4.44 ± 0.63	0.11 ± 0.28	<0.001	3.23	0.957
CTA	3.59 ± 0.47 versus 3.55 ± 0.43	0.04 ± 0.17	0.05	2.46	0.978

Annulus area					
	Reader 1 versus 2 (mm^2)	**Bias ± 95% LOA (mm^2)**	**P value**	**CV (100%)**	**ICC**
Contrast MRA	503.7 ± 87.3 versus 488.0 ± 88.9	15.8 ± 47.9	0.01	4.93	0.916
Non-contrast MRA	593.1 ± 111.7 versus 548.7 ± 87.3	44.4 ± 81.9	<0.001	7.32	0.870
CTA	466.0 ± 101.3 versus 467.2 ± 105.4	−1.3 ± 43.9	0.81	4.80	0.978

LOA limit of agreement, *CV* coefficient of variance, *ICC* intraclass correlation coefficient