Contrast-Enhanced MRA in Practice: Tips and Caveats

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Introduction

At UCLA, we perform contrast-enhanced MR angiography (CE-MRA) in adults and children* of all ages, covering most vascular territories. In this short article, we will consider thoracic and abdominal applications, although similar principles apply also to carotid and extremity MRA. In some patients, CE-MRA is performed as a stand-alone procedure and in other cases it is combined with cardiac MRI, brain MRI or abdominal MRI. In all cases, some common rules and guidelines apply in the setup and execution of the studies.

Although several non-contrast MRA techniques exist and continue to undergo development, CE-MRA is generally faster, less flow-dependent and more reliable than its non-contrast enhanced counterparts.

First, it is important to realize that CE-MRA is a procedure, not just a pulse sequence, and each step should be planned. A high performance 3D pulse sequence is a prerequisite, but on its own it is insufficient. For first pass imaging, accurate timing of the contrast bolus is crucial and in all cases it is essential to avoid patient motion artifact [1-15]. If we mistime the bolus or the patient moves during the acquisition, the study will be degraded or non-diagnostic, no matter how good the contrast agent or system hardware.

At the time of writing, the U.S. Food and Drug Administration (FDA) has approved the usage of two gadolinium based contrast agents for vascular imaging applications with MR. These are gadofosveset ('Ablavar', Lantheus Medical) and Gd BOPTA ('Multihance', Bracco Diagnostics) [16, 17]. The indication for Ablavar is to evaluate aortoiliac occlusive disease (AIOD) in adults with known or suspected peripheral vascular disease, and Multihance is to evaluate adults with known or suspected renal or aorto-ilio-femoral occlusive vascular disease. All other cardiovascular indications with these agents are off label (performed at the discretion of the physician) and all cardiovascular indications with all other agents are off label.

Although similar physical principles apply when imaging adults and children, there are practicalities of scale and logistics which make it useful to consider them separately.

Prior to scanning, adult patients are deemed suitable if they are alert and co-operative and have no contraindication to gadolinium. Common indications for imaging the thoracic arteries include evaluation of aortic aneurysm, coarctation, dissection, aortic valve disease and vasculitis, as well as assessment for thoracic outlet syndrome. Equipment setup requires ECG leads for monitoring, IV placement for contrast injection, and typically two body array coils.

In our experience, adult patients can typically manage a comfortable breath-hold of around 20 seconds. Some can do more and some less, but we will use this as our typical acquisition period for a high resolution, contrast-enhanced study. Both X-ray CT angiography (CTA) and CE-MRA depend on a timed contrast injection to highlight the enhancing lumen. However, whereas the signal with CTA depends in a fairly straightforward way on how well the vessels are opacified at the instant the slices are being irradiated, CE-MRA uses spatial gradients to encode the signal and in the process it traverses *k*-space. Over the course of the 20 second (or thereabouts) acquisition, *k*-space is traversed at a fairly uniform speed, but in a non-linear way. The center of *k*-space encodes the bulk of the image contrast and should be timed always to occur when the contrast bolus is in the vessels of interest. The time, in seconds from the start of the acquisition to the center of *k*-space can be chosen freely by the user, using the TTC parameter in the exam card. Ideally, all of the *k*-space data (not just the center) will be acquired when the vessels contain the bolus, but if the center is acquired *before* the bolus arrives, only edges or small vessels will be enhanced and the study will be non-diagnostic (see 'point 1' below). If, on the other hand, the center of *k*-space is acquired after the veins enhance, these will appear comparably bright to the arteries. Ideal timing would position the center of *k*-space at the early peak of arterial enhancement, before the veins enhance. It should be noted, however, that in cases of abnormally rapid venous filling, it may not be possible to isolate the arterial phase with a single, long high resolution acquisition, and time resolved techniques may be appropriate for this purpose.

As an aside, time-resolved techniques, such as TWIST, acquire multiple 3D data sets sequentially, but *k*-space is not sampled uniformly. In order to increase the temporal resolution, the central portion (e.g. 10–20%) of *k*-space is acquired more

frequently than the peripheral portion and data from neighboring peripheral *k*-space sets are shared. A detailed consideration of TWIST parameters is beyond the scope of this work, but we will simply state that in all of our CE-MRA studies, we use TWIST with very low dose Gd as a timing run for the high-resolution CE-MRA acquisition and sometimes we acquire an additional breath-held, low dose TWIST between the timing run and the main Gd injection for the high resolution study.

Based on the TWIST timing run, we can read off the time it takes for the test bolus to reach an early peak in the vessel of interest (e.g. aorta). We will then use this time as the starting time for the high-resolution acquisition with infusion of the main contrast bolus. As mentioned above, the center of *k*-space within the high-resolution (20 second) acquisition can be positioned freely by the user, using the TTC parameter in the exam card. Some principles guide our choice of the TTC.

1. The contrast bolus must be in the vessels of interest when we acquire the center of *k*-space. If the center of *k*-space is acquired before the bolus arrives, we will fail to show the major vessels and the study will be non-diagnostic. This is a worst-case scenario and is sometimes referred to as 'high pass filtering' because the low spatial frequencies are compromised and only the high spatial frequencies are 'passed through'. Without low spatial frequency information, the study is useless.
2. The contrast bolus should persist for long enough in the vessels of interest to encompass not just the center of *k*-space, but the periphery also. If the bolus is too short and covers only the center of *k*-space, large vessels may appear bright but the images will be blurred and fine edge detail will be compromised. This is sometimes referred to as 'low pass filtering' because the high spatial frequencies are compromised and only the low spatial frequencies are 'passed through'.
3. We have found that a default TTC of 6 seconds results in reliable CE-MRA in most cases. Six seconds is a typical value for contrast to move from the arterial inflow to the venous outflow of organs such as brain, lungs and kidneys, so the early peak of the arterial signal and the center of *k*-space occur prior to the venous peak. In children or in cases where rapid venous enhancement occurs on the timing run, it may be appropriate to shorten the TTC accordingly.

For many years, we have known that for a 20 second acquisition, a contrast infusion duration of about 15 seconds will provide a wide enough bolus plateau to encompass all of *k*-space adequately. For an adult, this has typically meant that we inject about 30 ml of contrast solution at 2 ml per second, for a 15 second infusion period. We would like the center of *k*-space to occur during the early portion of the plateau and we would like to be acquiring only the peripheral portions of *k*-space by the time the veins fill. This means that we have a high, fairly uniform concentration of contrast in the arteries throughout the acquisition (we 'pass through' both low and high spatial frequencies for the arteries), while we effectively have engineered high spatial frequency filtering of the veins. In this way, the arteries appear bright and well defined while the veins are dark in the center and only their edges are seen. What we have described is an ideal situation, but it can be made to happen pretty routinely with proper timing. If, however, there is substantial contrast in the veins by the time we acquire the center of *k*-space, we will see both arteries and veins with a similar intensity. Depending on the territory and clinical question, this may or may not be a big deal. In any case, if our timing is not ideal, better to err on the side of being a bit late than too early – better to see arteries and veins than neither arteries nor veins!

* MR scanning has not been established as safe for imaging fetuses and infants under two years of age. The responsible physician must evaluate the benefit of the MRI examination in comparison to other imaging procedures.

Contrast agent 'preparation' – we dilute! Why?

In 2007, the association between nephrogenic systemic fibrosis (NSF) and gadolinium administration in patients with renal failure was discovered [18-21]. It became clear that the high doses of Gd used routinely for CE-MRA were particularly problematic, and as a community we implemented immediate and sometimes draconian restrictions and dose reductions in the use of Gd. As a result, NSF has virtually disappeared and no new cases have been confirmed in the past several years.

In the process of evaluating dose reduction regimens for CE-MRA, we were faced with some issues of implementation. The good news is that it has proved feasible to reduce the dose of Gd by a factor of 3-4 at 3T and of 2 at 1.5T, relative to what we used to use in the past. So instead of using double or triple dose (0.2–0.3 mmol/kg) extracellular contrast agents, we can still get very good results with single dose or half-dose (0.05–0.1 mmol/kg) [22]. The challenge is how to administer the lower dose while maintaining the desired time course for the contrast bolus. So, for example, if we used to use 30 ml of undiluted Gd over 15 seconds (injected at 2 ml/s) for an average adult patient at 3T, we might now want to use a quarter of that dose (7.5 ml). If we inject at 2 ml/s, the entire amount is infused in 3.5 seconds and we get a very short peak. This will very likely result in the 'low pass filtering' effect we described above. If we extend the infusion period to our 15 second target by injecting at 0.5 ml/s, timing may become unreliable for first pass imaging because in some patients the small volume of contrast may get held up in the veins of the thoracic inlet. An approach we have found very reliable is to dilute the Gd back up to the original volume (30 ml) and inject the *dilute* solution at the original rate (2 ml/s). The shape of the contrast bolus will be exactly as it was with the full strength Gd, but the peak concentration will be proportionately lower. Experience and theoretical considerations confirm that the reduction in signal-to-noise ratio

(SNR) due to the reduced peak concentration is much less than reduction in contrast dose and the image quality holds up well.

In the examples that follow, we illustrate parameters and contrast dosages and formulations in both adults and children, based on the principles outlined above. More cases, together with movie files and detailed parameters, are available on the UCLA Cardiovascular Imaging Gallery [23].

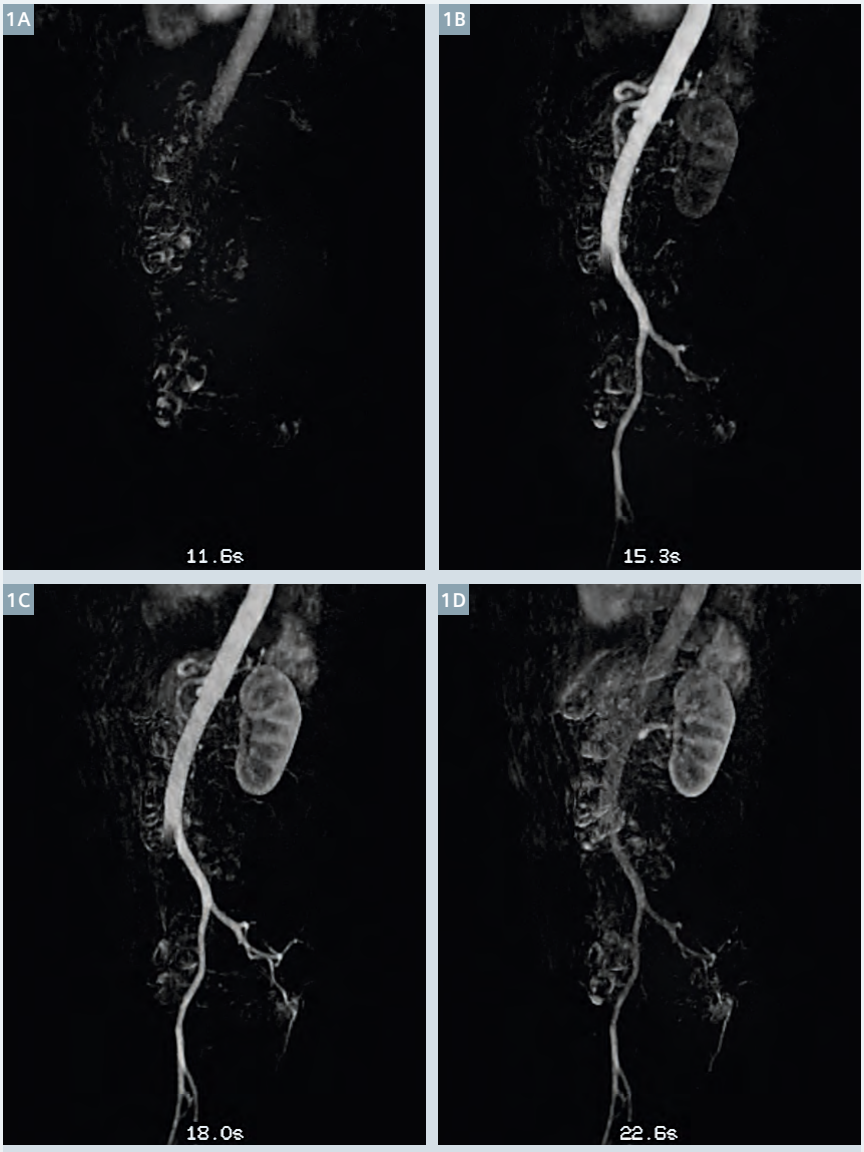
Thoraco-abdominal CE-MRA in adults

With appropriate dilution, the contrast volumes can be made identical at 1.5T and 3T, such that the injection rates and volumes are the same at both field strengths, even though the concentration and dose of Gd is lower at 3T.

With reference to the dilute solution, as a general rule, we perform a sagittal timing TWIST acquisition during free breathing with injection of 3 ml at a rate of 2 ml/s. Then we perform breath-held coronal time TWIST with injection of 7 ml at a rate of 3 ml/s. Finally, we perform coronal high resolution MRA with injection of 30 ml at a rate of 2 ml/s.

The cases below will illustrate these principles. The actual doses and dilution factors may differ slightly from the sample schemes outlined above, but in all cases they will be approximately the same.

Case A: Adult renal arteriovenous fistula



1 Oblique sagittal TWIST timing; full thickness MIP reconstruction.

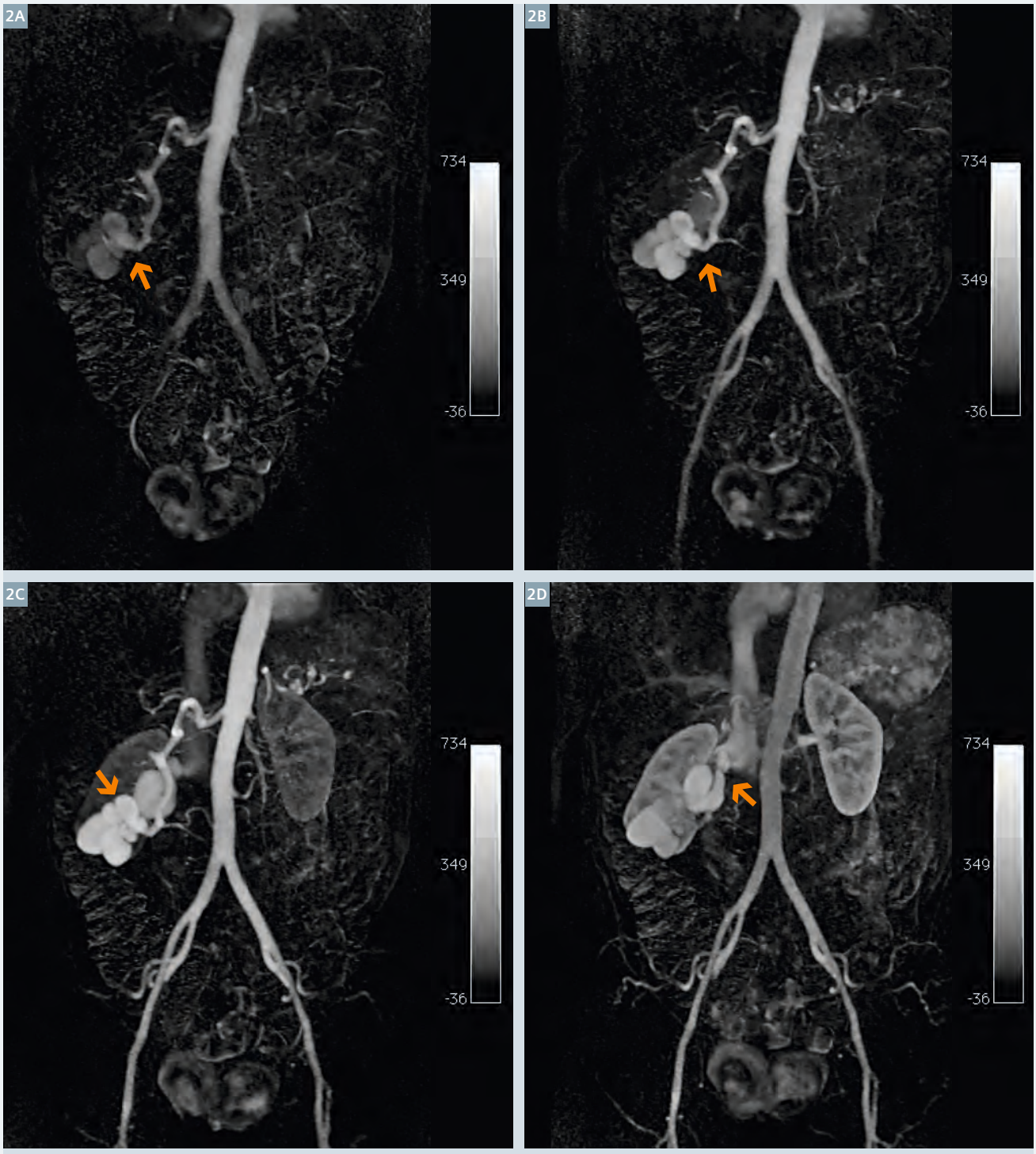
58-year-old female in good general health; incidental finding of renal arteriovenous malformation. She denied symptoms of hematuria, flank pain, dyspnea and did not have any signs of pelvic congestion syndrome. CE-MRA was performed to characterize the vascular malformation prior to possible embolization therapy.

Scanner 3T MAGNETOM Trio, A Tim System

Agent Multihance. 15 ml native formulation of Multihance was diluted to 45 ml with normal saline.

Repetition time (TR)	2.0 ms
Echo time (TE)	0.9 ms
Flip angle	18 degrees
Bandwidth	1015 Hz/pixel
FOV	281 × 500
Matrix	202 × 488
Slice thickness	6 mm
Grappa acceleration factor	2
Temporal resolution	0.9 s
4 ml one third strength Multihance at	2 ml/s

Peak aortic enhancement occurs at 15 seconds and this is the time delay chosen to begin the high-resolution CE-MRA acquisition.

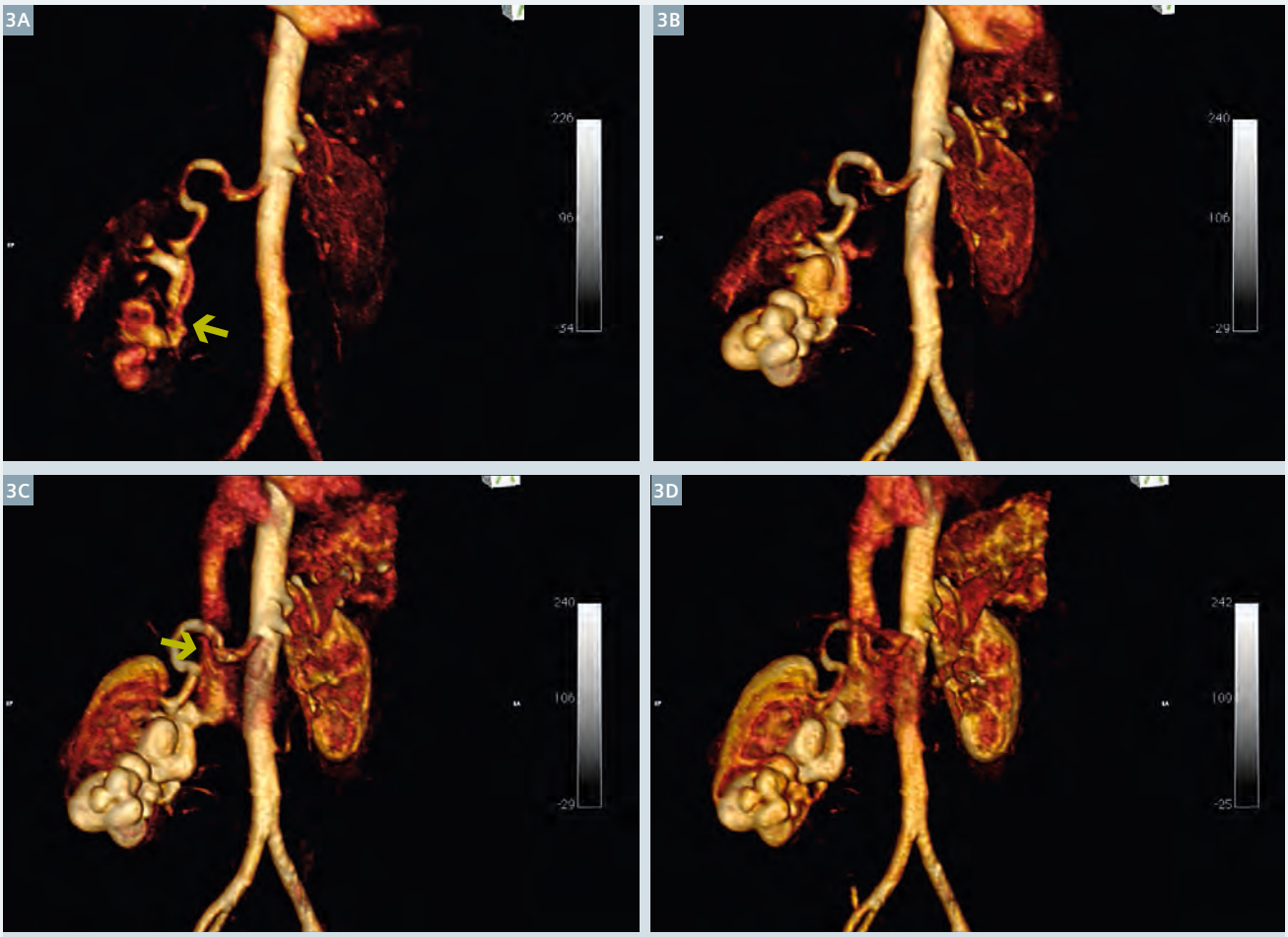


2 Coronal breath-held TWIST; full thickness MIP reconstruction.

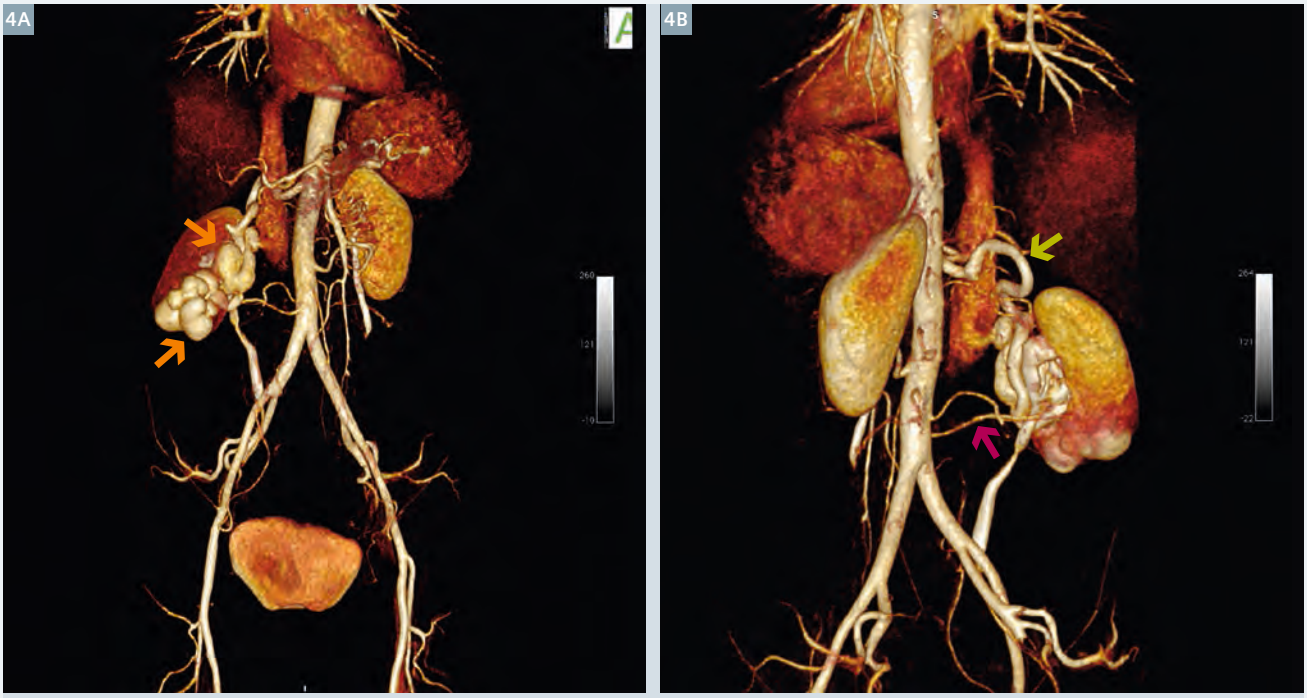
TR	2.0 ms
TE	0.9 ms
Flip angle	16 degrees
Bandwidth	751 Hz/pixel
FOV	312 x 500
Matrix	211 x 512

Slice thickness	4 mm
Grappa acceleration factor	3
Temporal resolution	1.0 s
11 ml one third strength Multihance at	3 ml/s

Note the immediate enhancement of the right renal AVM with direct shunting from the lower pole artery (arrows in figures 2A and 2B) to the grossly enlarged veins (arrows in figures 2C and 2D).



3 Coronal breath-held TWIST; as in figure 2 but with Volume Rendered Reconstruction of the 4D data.



4 High-resolution CE-MRA.

TR	2.64 ms
TE	0.97 ms
Flip angle	18 degrees
Bandwidth	610 Hz/pixel
FOV	375 × 500
Matrix	576 x 389
Slice thickness	1.1
Voxel dimensions =	0.96 × 0.87 × 1.1 mm
Grappa acceleration factor	3

The high-resolution study shows that the malformation (orange arrows) is supplied by an enlarged upper pole renal artery (green arrow). An accessory right lower pole renal artery (red arrow) supplies the uninvolved portion of the kidney. Note that for the high-resolution study, the arterialized veins in the right kidney enhance simultaneously with the arteries, whereas they are separable on the time-resolved TWIST study. In this way, high spatial resolution imaging and high temporal resolution imaging are complementary in highly vascular lesions.

Case B: Coarctation of the aorta

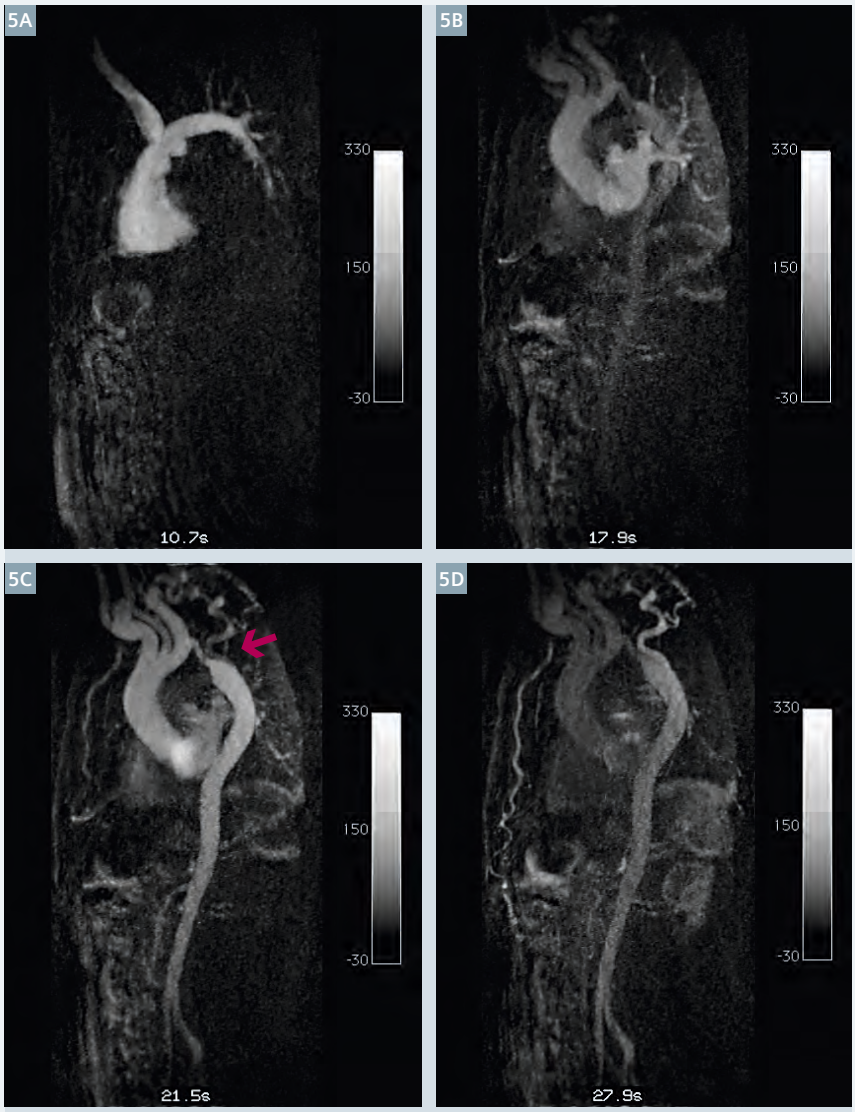
64-year-old male with an 18 month history of walking difficulties, pain and decreased sensation in his lower legs. Past history of hypertension and surgery for coarctation of the aorta at age 18. An MRI /MRA was performed to evaluate cardiac function and vascular anatomy.

Scanner 1.5T MAGNETOM Avanto

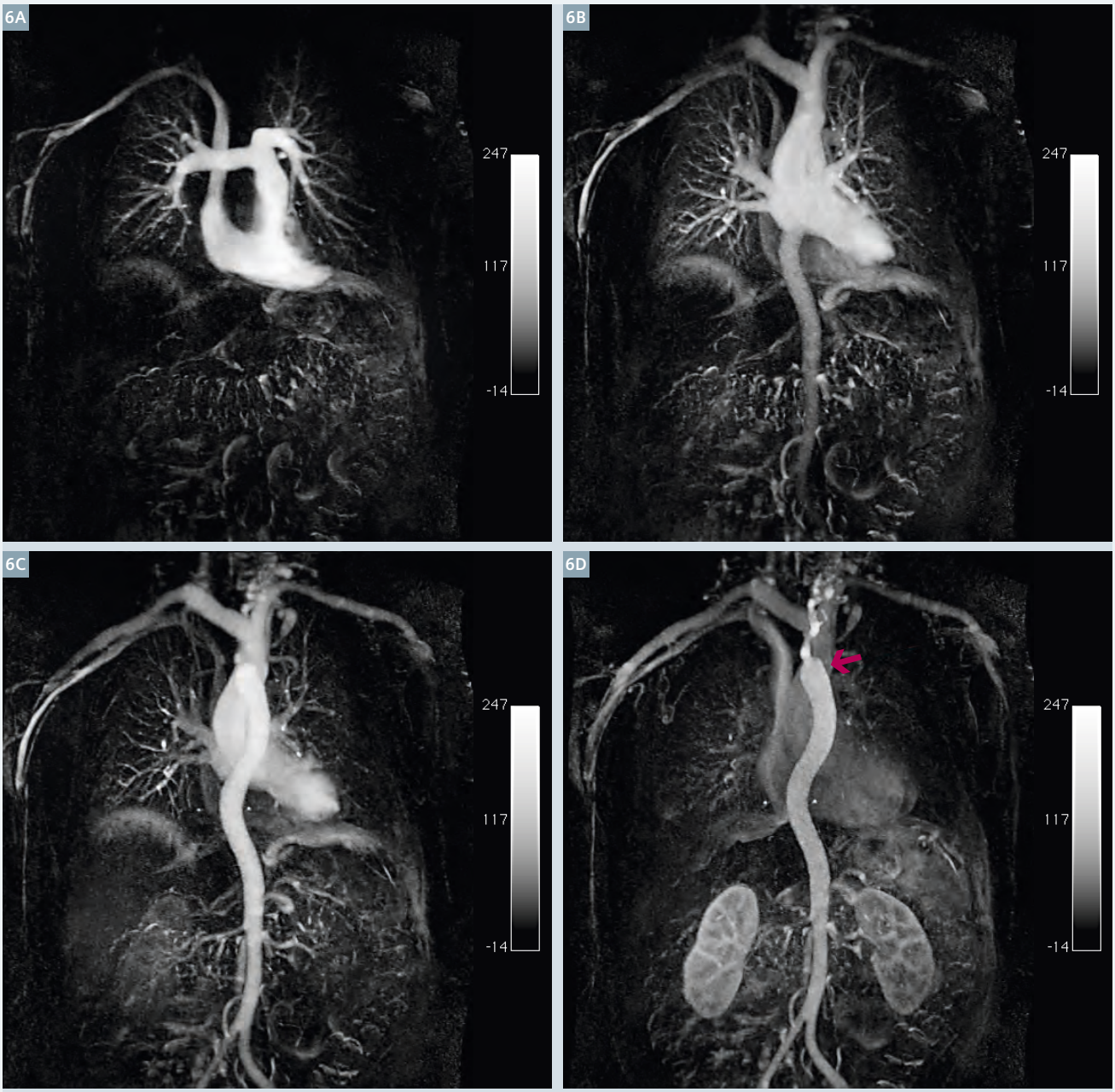
Agent Multihance. 15 ml native formulation diluted to 45 ml with normal saline.

TR	2.0 ms
TE	0.9 ms
Flip angle	18 degrees
Bandwidth	1015 Hz/pixel
FOV	250 × 500
Matrix	180 × 488
Slice thickness	6 mm
Grappa acceleration factor	2
Temporal resolution	0.9 s
4 ml one third strength Multihance at	2 ml/s

Peak aortic enhancement occurs at 22 seconds and this is the time delay chosen to begin the high resolution CE-MRA acquisition.



5 Oblique sagittal TWIST timing; full thickness MIP reconstruction.

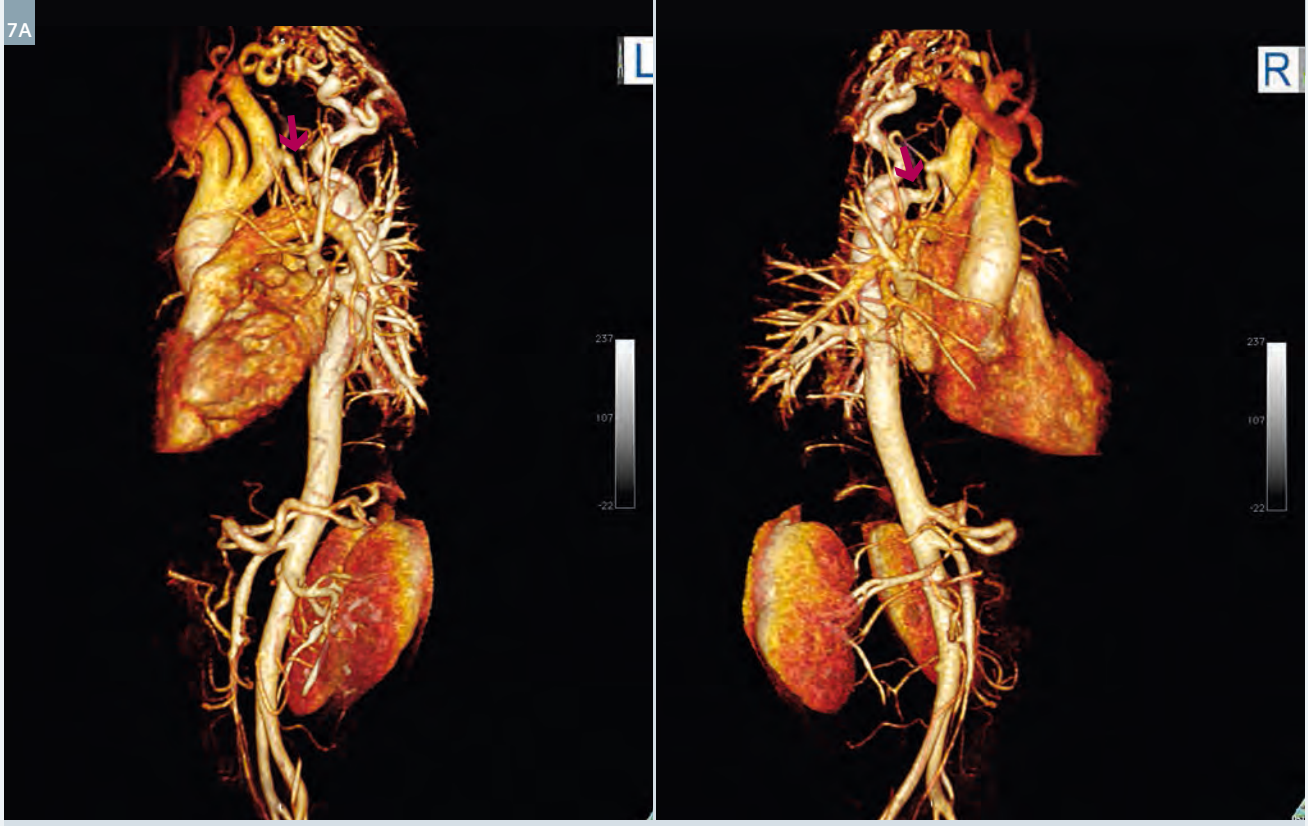


6 Coronal breath-held TWIST; full thickness MIP reconstruction.

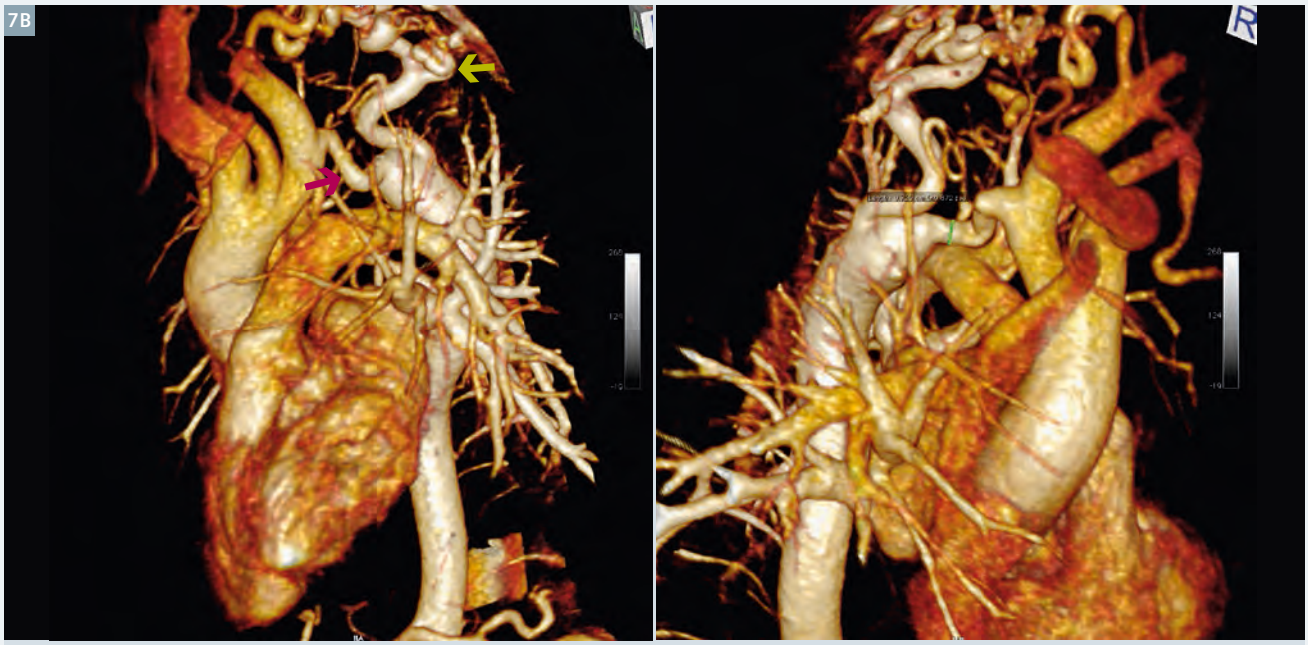
TR	2.0 ms
TE	0.9 ms
Flip angle	16 degrees
Bandwidth	751 Hz/pixel
FOV	406 × 500
Matrix	291 × 512

Slice thickness	5 mm
Grappa acceleration factor	3
Temporal resolution	2.3 s
9 ml one third strength Multihance at	3 ml/s

Note the persistence of signal in the descending aorta (arrow) due to filling via collaterals.



7A High resolution CE-MRA with full FOV Volume Rendered Reconstruction.



7B As in Figure 7A, but zoomed in to focus on the arch hypoplasia and collaterals (arrows). At its narrowest, the arch measures 7.5 mm in diameter.

Parameters for high resolution CE-MRA	
TR	2.28 ms
TE	0.95 ms
Flip angle	29 degrees
Pixel bandwidth	610
FOV	375 × 500
Matrix	288 × 512
Slice thickness	1.3
Grappa acceleration factor	3
34 ml one third strength Multihance at	2 ml/s

Volume rendered full field-of-view (FOV) reconstruction shows persistent hypoplasia of the distal aortic arch (purple arrow) and enlarged intercostal collateral arteries.

Case C: Takayasu's arteritis

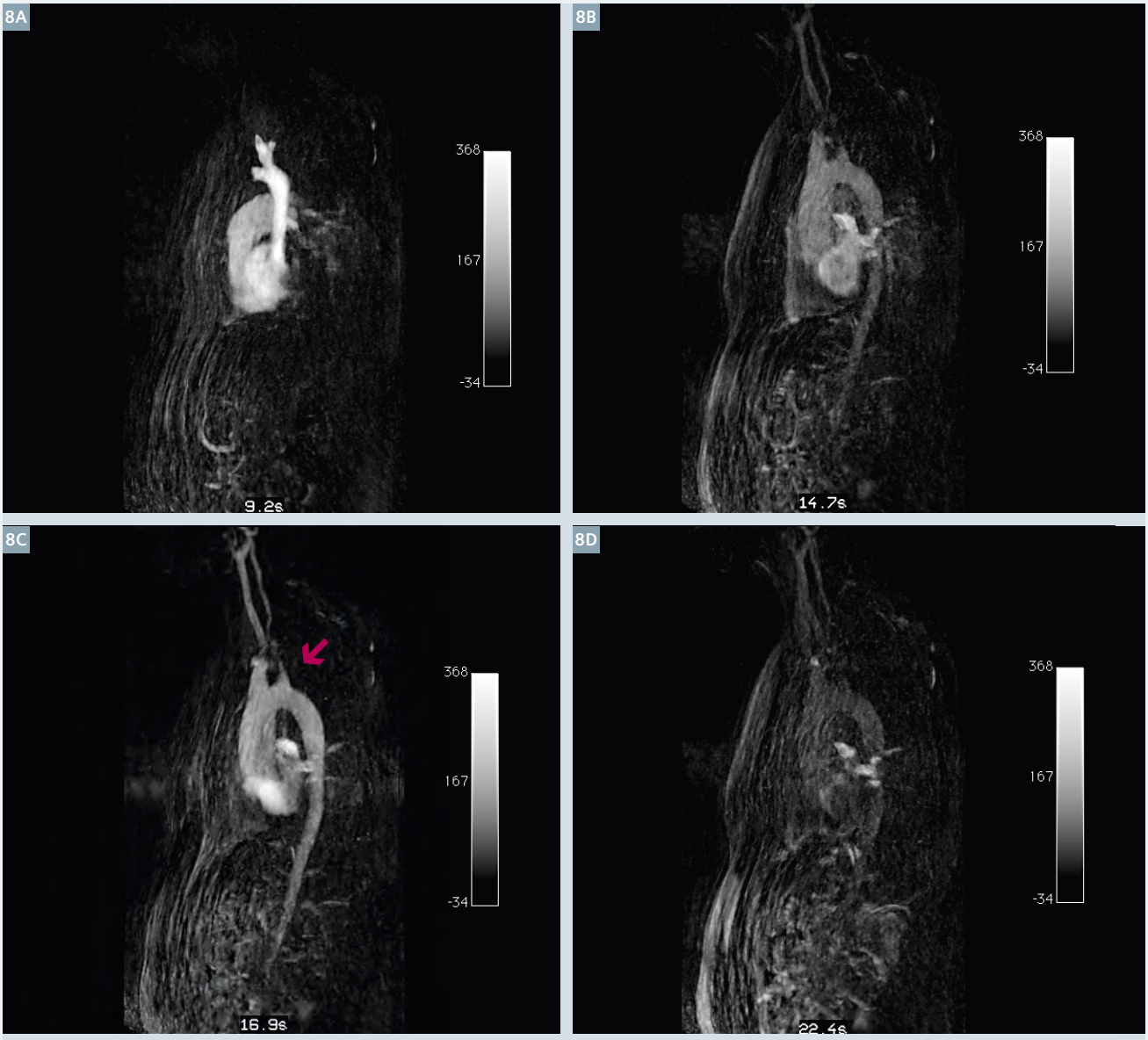
31-year-old female with history of Takayasu's arteritis. Multiple arterial occlusions, including left internal carotid and right subclavian arteries. CE-MRA with 15 cc Multihance. TWIST and 3D high-resolution CE-MRA. Figure 8 shows a volume rendered reconstruction of the heart and great vessels in the anterior (left) and posterior (right) views. Figure 9 shows close up of renal arteries with narrowing.

Scanner 3T MAGNETOM Trio.

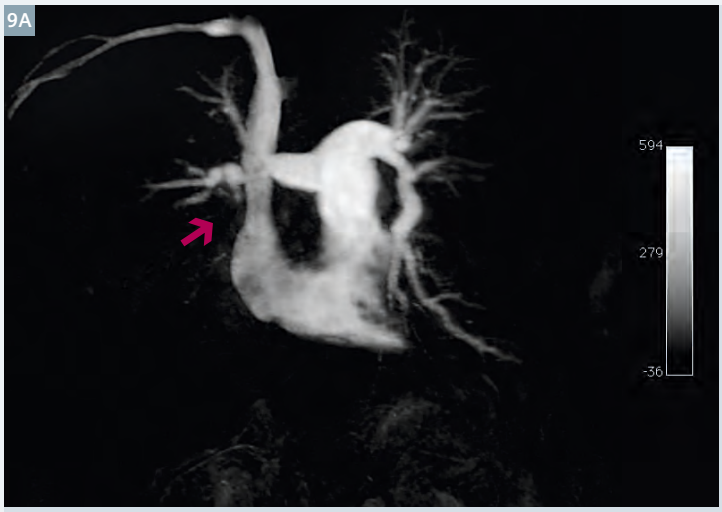
Agent Multihance. 15 ml native formulation of Multihance was diluted to 45 ml with normal saline.

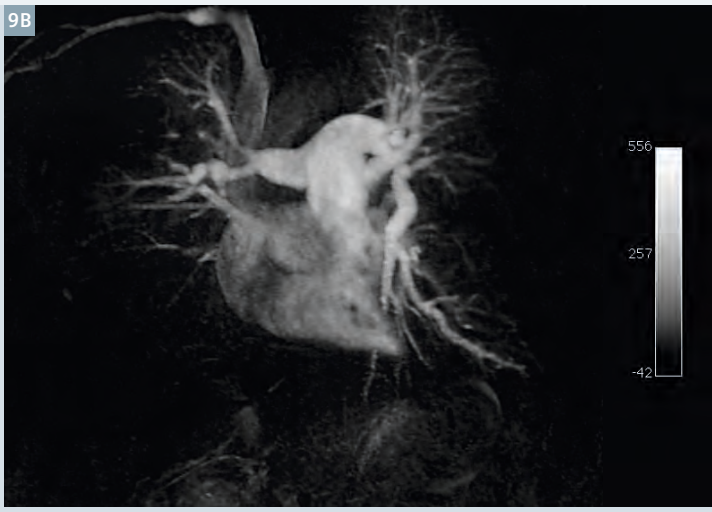
Peak aortic enhancement occurs at 17 seconds and this is the time delay chosen to begin the high resolution CE-MRA acquisition.

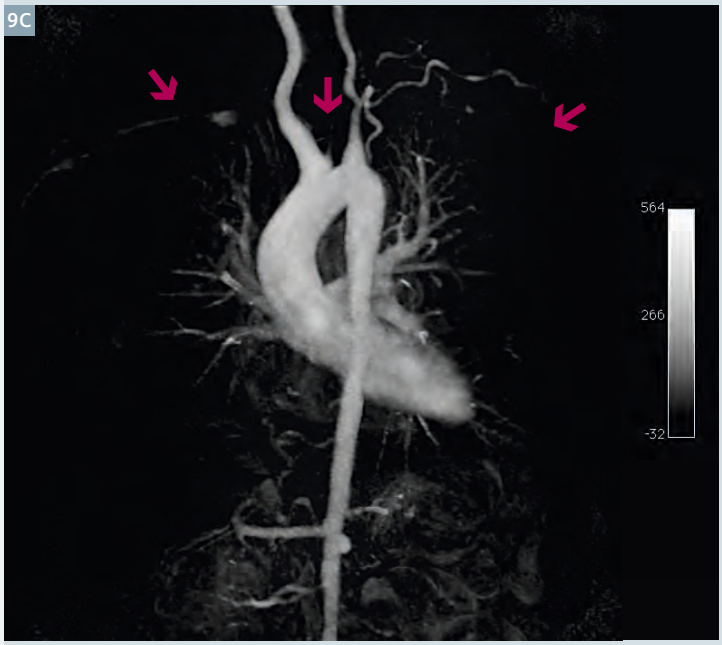
TR	2.0 ms
TE	0.9 ms
Flip angle	18 degrees
Bandwidth	1015 Hz/pixel
FOV	265 × 500
Matrix	190 × 488
Slice thickness	6 mm
Grappa acceleration factor	2
Temporal resolution	1.1 s
3 ml one third strength Multihance at	2 ml/s

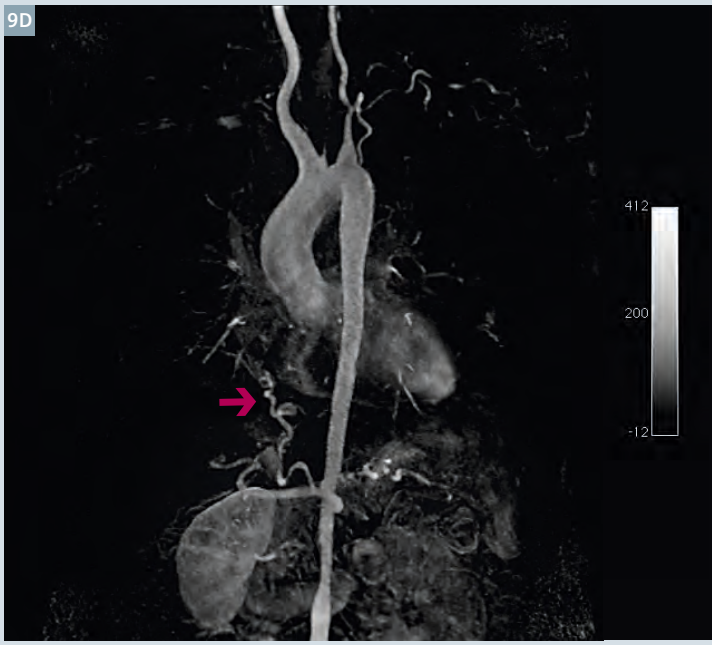


8 Oblique sagittal TWIST timing; full thickness MIP reconstruction.







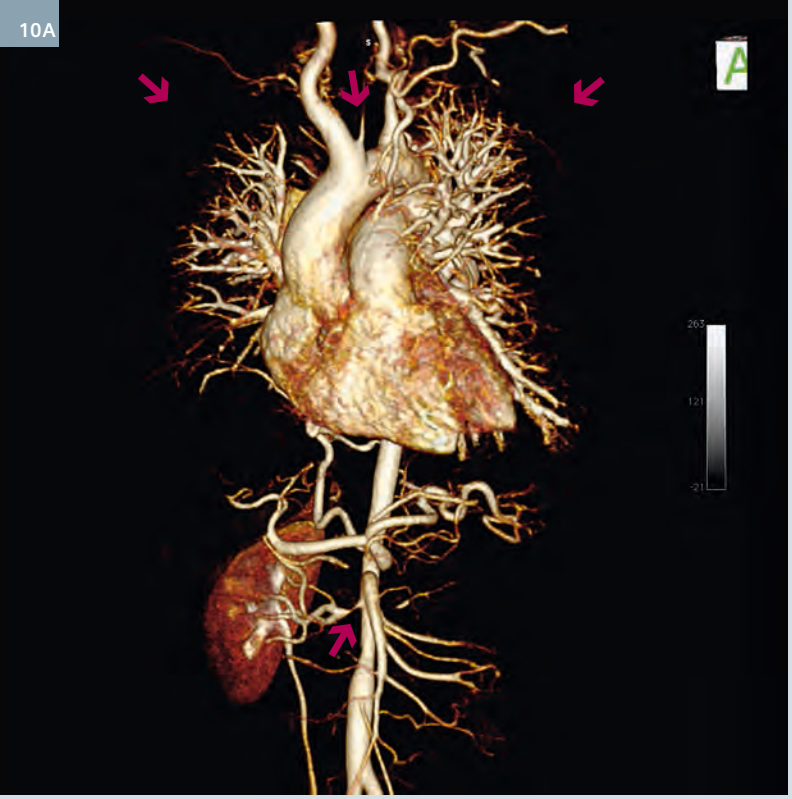


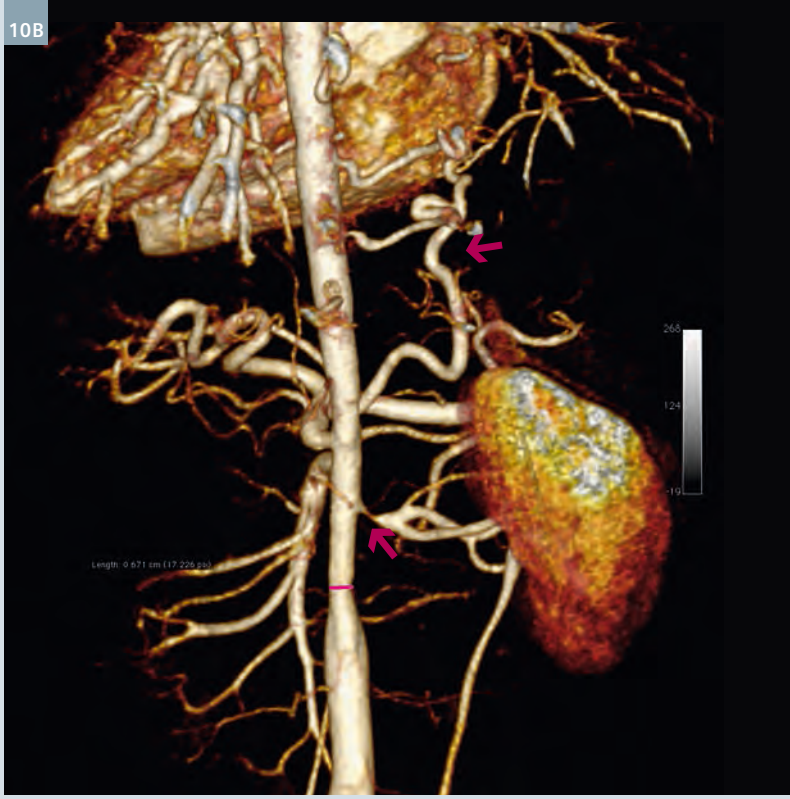
9 Coronal breath-held TWIST; full thickness MIP reconstruction.

TR	2.5 ms
TE	0.9 ms
Flip angle	20 degrees
Bandwidth	751 Hz/pixel
FOV	375 × 500
Matrix	288 × 512

Slice thickness	4 mm
Grappa acceleration factor	3
Temporal resolution	1.0 s
6 ml one third strength Multihance at	3 ml/s

Note the immediate occlusion of the right lower lobe pulmonary artery (arrow in 9A) and of both subclavian arteries and stenosis of the left common carotid artery (arrows in 9C). The later enhancement of the right inferior phrenic artery (arrow in 9D) highlights its role as a collateral (see figure 10).





10 High resolution CE-MRA with full FOV **(10A)** and zoomed **(10B)** Volume Rendered Reconstruction.

Again shown in greater detail is occlusion of both subclavian arteries and stenosis of the left common carotid artery (arrows in 10A). Note the enlarged right inferior phrenic artery (upper arrow in 10B) and the critically stenosed right renal artery (arrows 10A, B). The left renal artery is occluded.

Parameters for high resolution CE-MRA	
Field strength	3T
TR	2.8 ms
TE	1.06 ms
Flip angle	18 degrees
Pixel bandwidth	620 Hz/pixel
FOV	375 × 500 mm
Matrix	389 × 576 mm
Slice thickness	1.1 mm
Grappa acceleration factor	4
36 ml one third strength Multihance at	2 ml/s

Thoraco-Abdominal CE-MRA in Children

Here, we will consider only very young children* who differ significantly from adults both in physical scale and their inability to cooperate with the study. Where detailed evaluation of thoracic and/or abdominal vascular anatomy is required, it is necessary to avoid motion artifact and to acquire images with sufficient spatial resolution. We use the head coil or extremity coil for neonates or very small infants. For larger children, coil options include small or large flex coils and the body array coil, depending on patient size.

We routinely request that small children are anesthetized and intubated. In this way, the airway is protected and the anesthesiologist or neonatal intensivist can prevent respiratory motion artifact by controlled ventilation. A stable IV line is mandatory and children must be monitored closely throughout the procedure with pulse oximetry, non-invasive blood pressure measurement, ECG and end-expiratory CO2 monitoring.

Whereas the size of the target vessels in small children is less than in adults, the time required to image them is not. In fact, the resolution requirements are more stringent so we need to do what we can to maximize signal-to-noise ratio (SNR). SNR can be increased in a variety of ways, for example by using small multi-element coil arrays, using high relaxivity contrast agents and imaging at 3T (see case D). In children with complex congenital heart disease, the cardiac index may be very high (relative to normal adults) so we routinely aim to deliver 'double dose' contrast.

In general, for high resolution imaging in children, we aim for similar acquisition times as in adults i.e. about 20 seconds. Breathing can be safely suspended for 20 seconds or more in the majority of ventilated children, especially if higher inspired oxygen concentration and mild hyperventilation are used in the run up to the apneic period. The same principles apply to the timing of the image acquisition relative to the contrast injection as in adults. So, we want to infuse the timed contrast bolus over about 15 seconds to

encompass most of the acquisition period. Because the requisite dose of contrast agent may be contained in less than one milliliter of the native formulation, infusing this over 15 seconds requires that we dilute the contrast substantially. In children weighing 3 kg or less, we infuse at 0.3 ml/s. At this rate, in 15 seconds we will infuse 4.5 ml, so 4.5 ml must contain our required dose of (whatever) contrast agent. For example, if we aim to use 0.2 mmol/kg Multihance in a 2.5 kg patient, we want to deliver 1 ml of native contrast in 15 seconds, so our dilution is 1 part contrast and 3.5 parts saline. Practically, we might draw up 10 ml of Multihance into the syringe, draw up 35 ml saline into the same syringe and agitate the mixture. We now have a 1 in 4.5 strength solution of Multihance. Because the total volume we will inject is less than the dead space in the injector tubing, we prime the dead space with dilute contrast and we do *not* use a saline flush. For Ablavar (or other agents) the principles are the same, but the appropriate dilution factor will vary, depending on the total dose ('double dose' Ablavar is 0.06 mmol/kg) and the concentration of the native agent (Gadavist is formulated as a more concentrated solution at 1 mmol/ml).

*MR scanning has not been established as safe for imaging fetuses and infants under two years of age. The responsible physician must evaluate the benefit of the MRI examination in comparison to other imaging procedures

Case D: Shone's Complex

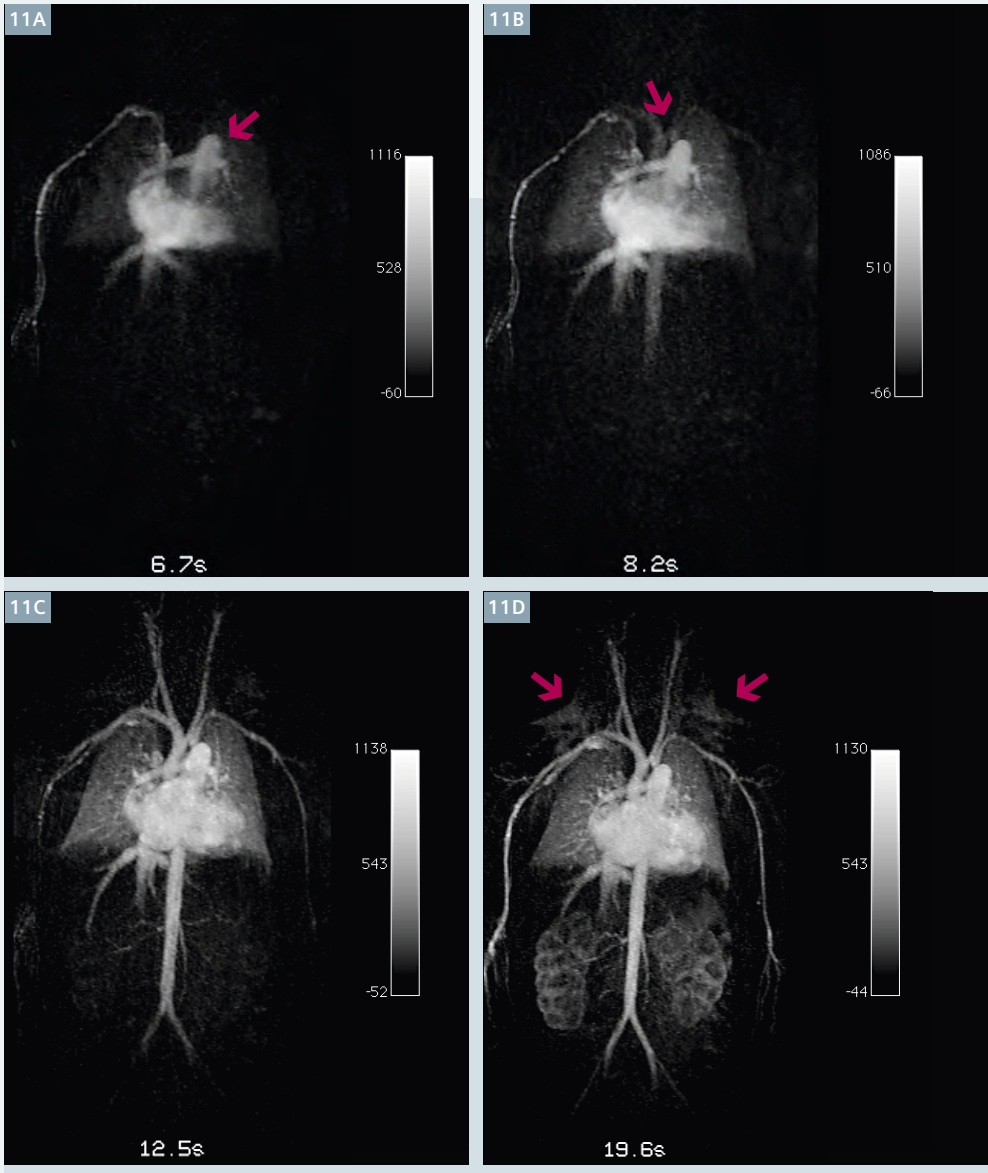
3-day-old female neonate with complex congenital heart disease (Shone's complex) and multiple corrective surgeries after birth. MRI / MRA ordered to evaluate anatomy prior to further planned corrective surgery.

Scanner Images have been acquired on a 3T MAGNETOM Trio, A Tim System, using the 15-channel knee coil

Agent Ablavar. Native formulation diluted by a factor of 8 with normal saline.

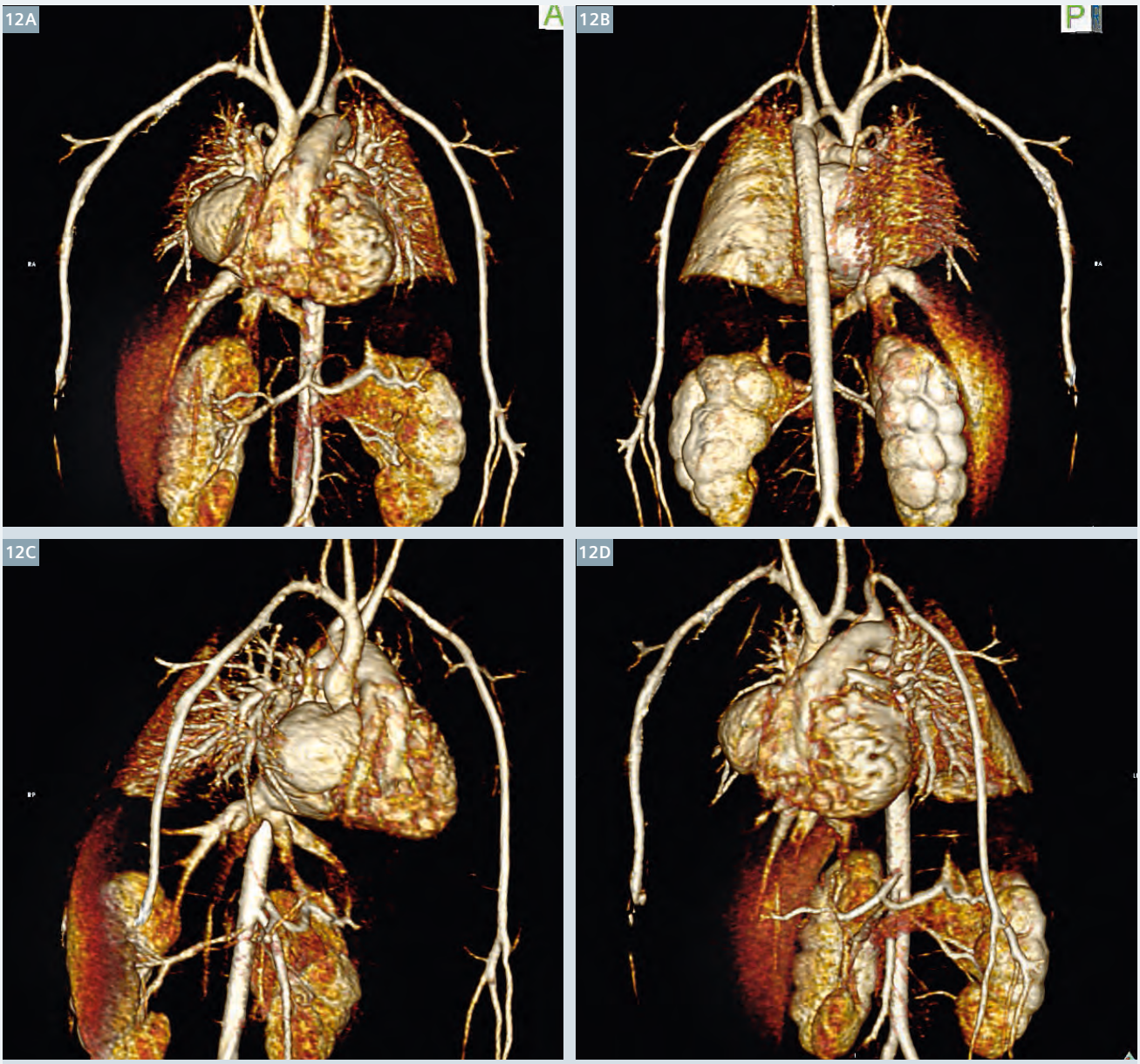
TR	2.8 ms
TE	1.08 ms
Flip angle	13 degrees
Bandwidth	698 Hz/pixel
FOV	131 × 300 mm
Matrix	157 × 488 mm
Slice thickness	3 mm
Grappa acceleration factor	3
Temporal resolution	1.43 s
1 ml one eighth strength Ablavar at	0.3 ml/s

Note the enlarged ductus arteriosus (arrow in 11A) and early shunting to the aortic arch (arrow in 11B). Incidentally noted is enhancement of brown fat in the shoulder regions bilaterally (arrows in 11D). The coronal TWIST acquisition in this case was used to optimize the timing for the high resolution study below.



11 Coronal breath-held TWIST; full thickness MIP reconstruction.

High resolution cardiac gated CE-MRA with full FOV Volume Rendered Reconstruction.

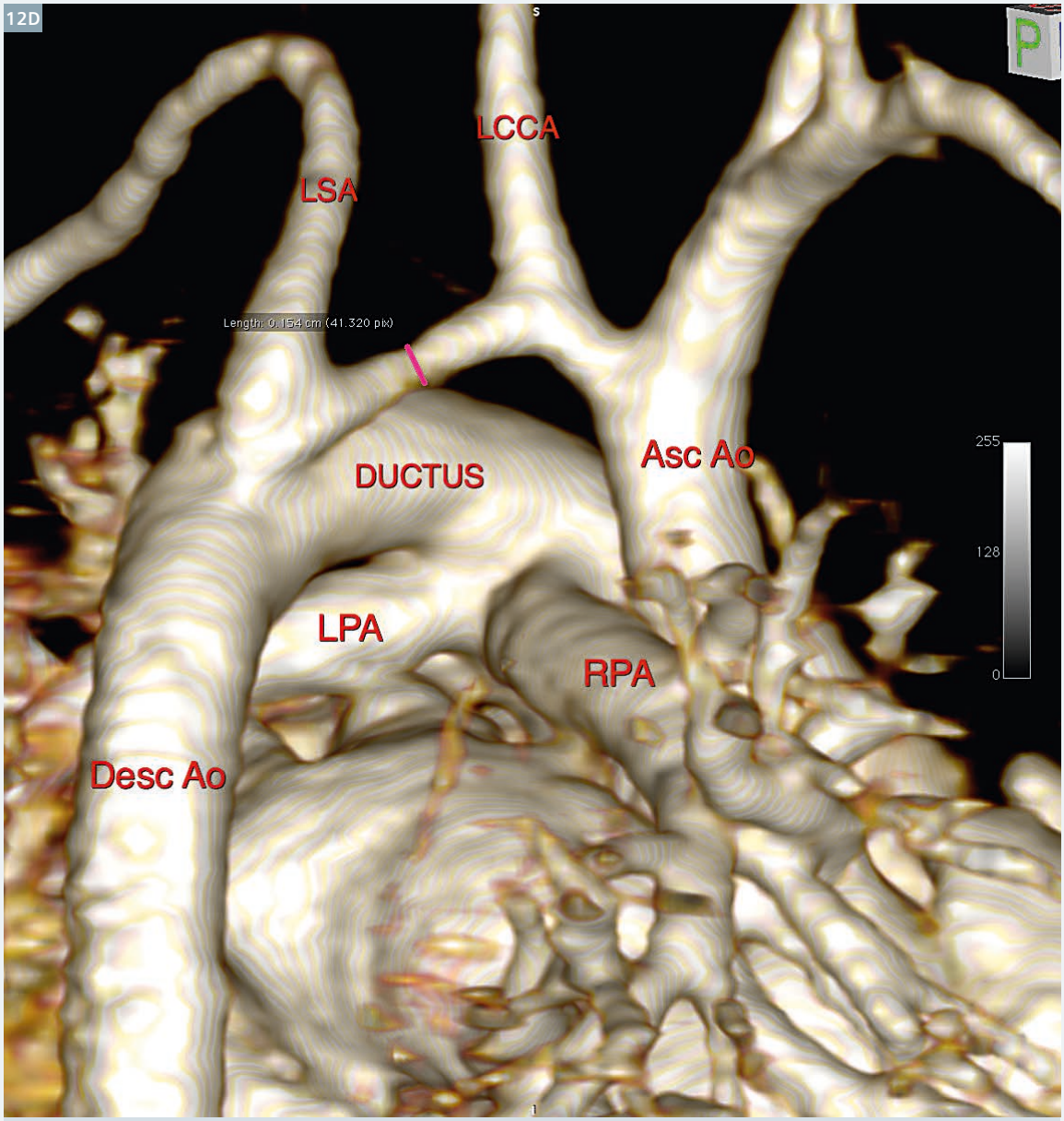


12 High resolution cardiac gated CE-MRA with full FOV Volume Rendered Reconstruction.

Four representative views of the full FOV, cardiac gated acquisition show clear definition of cardiac chamber anatomy and renal fetal lobation. More detailed vascular anatomy is depicted in the zoomed images in figure 12D.

Parameters for high resolution CE-MRA	
Field strength	3T
TR	3.09 ms
TE	1.15 ms
Flip angle	14 degree
Pixel bandwidth	610 Hz/pixel
FOV	131 × 300 mm

Matrix	161 × 512 mm
Slice thickness	0.80
Voxel dimensions	0.8 × 0.6 × 0.8 mm^3
iPAT	3
Effective TTC	11 s
Acquisition time	23 s
5 ml one eighth strength Ablavar at	0.3 ml/s



12D High resolution cardiac gated CE-MRA with zoomed Volume Rendered Reconstruction.
From the same dataset as figure 12A–C, the zoomed images maintain detail because of the high resolution, cardiac gated acquisition. Annotated are the right and left pulmonary arteries (LPA and RPA), taking origin abnormally from the large ductus arteriosus (DUCTUS). The aortic arch is markedly hypoplastic, measuring 1.5 mm in diameter. This patient went on to have surgical correction on the basis of the MRI findings.

Further Information

More cases, together with movie files and detailed parameters, are available on the UCLA Cardiovascular Imaging Gallery

http://www.radnet.ucla.edu/safaridemos/showcase/gallery

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