Time-Resolved Projection Angiography after Bolus Injection of Contrast Agent

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A method for MR angiography after bolus injection of a normal dose (0.1 mmol/kg) of contrast agent is presented. Projection angiograms are acquired with a non-slice selective Snapshot FLASH sequence with a time resolution of 1 s per image or better. Typically 40 to 60 images are acquired consecutively after bolus injection of a contrast agent. The signal from vessels can be separated from background by postprocessing based on the observed temporal evolution of the signal intensities during bolus passage. The subsecond projection MR-DSA is a reliable and robust technique to produce high resolution anatomical images of the vascular system avoiding the necessity of exact timing of the contrast agent bolus. It also supplies functional information about the hemodynamics in the observed region including perfusion.

Key words: MR angiography; MRA; MR-DSA; pulmonary angiography.

INTRODUCTION

MR angiography (MRA) techniques based on signal intensity changes during the first pass of a contrast agent bolus (1) have become feasible within the last few months due to the development of gradient systems for fast imaging. Three-dimensional acquisition schemes based on gradient echo techniques with short echo times on the order of 2–4 ms and short repetition times of 4–7 ms have been used to acquire three-dimensional datasets *within one* breathhold (1–6). Angiograms of high quality can be reconstructed from these datasets by maximum intensity projection (MIP). The angiographic contrast parameter for these techniques is filling of the vessel as in x-ray angiography rather than vascular flow as in phase contrast-angiography or time-of-flight angiography. A certain problem in three-dimensional data sampling is the fact, that the acquisition time for one dataset is on the order of 20–40 s even on state-of-the-art gradient systems. The γ-shaped intensity curve during bolus passage acts as a filter on the dataset, which leads to some blurring, when the signal maximum coincides with the time of acquiring the data with low phase encoding. If this condition is not met, considerable artifacts can arise (3, 5).

Time-resolved 3D MR angiography (6) alleviates this problem and in addition offers the possibility to observe the dynamics of contrast agent distribution. In connection with a strategy of partial updating of *k*-space, updates can be generated every 2–6 s.

As an alternative approach we have used a projection technique similar to the one published by Wang (7), which creates two-dimensional projection angiograms before, during, and after the bolus passage. This avoids the requirement for exact timing of the bolus administration (5). The subsecond projection MR-DSA also offers the possibility to get functional information about the hemodynamics in the observed region.

MATERIALS AND METHODS

We used a Snapshot-FLASH sequence (8) optimized for projection imaging. Images were either acquired without any slice selection or as projections through thick slabs (60–200 mm thickness). For slice selection Gaussian pulses of duration 200–400 μs were used. Sequences were optimized to a minimum *TE* of 1.4 ms and a *TR* of 3.4 ms by using the standard gradient system of our 1.5 T system (Magnetom Vision. Siemens, Erlangen, Germany) with 25 mT/m maximum amplitude and 0.6 ms rise time. Two hundred fifty-six complex points were acquired for each signal within an acquisition time of 1.28 ms corresponding to an acquisition bandwidth of 200 kHz or 780 Hz/pixel. Asymmetric echo sampling was performed, where the signal maximum occurred after approximately one third of the acquisition time. The flip angle optimally should be around 90° for pulmonary angiograms to maximize signal from vessels versus background. Due to SAR-problems, this was not possible in all patients. Reduction of the flip angle down to 40° did not lead to appreciable deterioration of the quality of the results.

A phased array body coil was used to acquire images of the thorax. RF-spoiling was applied to reduce steady state (SSFP) transverse magnetization. The phase encoding gradient was rewound after signal read out to avoid artifacts from residual SSFP-signals. For our initial experiments a full acquisition matrix of 256 phase encoding steps was used. The experiment was run continuously yielding one image per 950 ms. The additional 80-ms delay over the 256 × 3.4 = 870.4 ms of the imaging cycle itself is caused by additional provisions built into the pulse program, which occur only once per image. This mainly includes a gradient-free time interval before an (optional) ECG-trigger to improve the recognition of the ECG-signal over gradient noise in the ECG-gating unit. For time-sensitive measurements this additional dead time can be significantly reduced, which was, however, not the focus of this study.

Typically 40–60 images were acquired consecutively. For angiograms of the lung, ECG gating was optionally used to get images during diastole. The imaging sequence was started immediately after injection of the contrast

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agent with an automatic injector (XD-7000, Fa.Ulrich, Germany). Experiments were performed as an add-on examination on patients, which received a diagnostic contrast agent examination. A clinical dose (0.1 mmol/kg) of Gd-DTPA (Magnevist, Fa.Schering, Berlin) was used.

As yet 24 patients with lung pathologies have been examined. Of these 18 were bronchial carcinoma, 5 had obstructive lung disease, and 1 had a vascular malformation. In addition we acquired exploratory projection angiograms of the lower abdomen and the head.

Cross-correlation images were calculated according to the algorithm proposed for fMRI (9). The time course of the signal in an ROI with 3 × 3 pixel located in the pulmonary trunc was used as a reference signal for the early phase. Alternatively, a signal from the downgoing aorta was used to characterize the late phase. Postprocessing was performed by using our standard fMRI-software (ParaVision, Bruker, Germany) installed on an SGI-workstation.

RESULTS

All 24 patient examinations performed as yet yielded images of consistent high quality, demonstrating the robust performance of the experiment. Segmental and subsegmental arterial branches could be visualized in all experiments. Angiograms of patients who could not hold their breath for more than 5 s due to poor pulmonary conditions (14/24) were of comparable quality to angiograms acquired during breathhold, but precluded more sophisticated cross-correlation analysis. A sensitive clinical workup of this study requires a larger number of patients than this study, which was predominantly undertaken to demonstrate the feasibility of the experimental approach.

Figure 1 shows 4 coronal projection angiograms from a series of 40 images of a patient with lung metastasis. The first 15 images of the series were acquired in breathhold. Figure 2 demonstrates the same images as Fig. 1, but after subtraction of a background image acquired before the arrival of the contrast agent bolus.

In the first image (top left) acquired at td = 6 s after injection, enhancement is seen only in the right ventricle and the pulmonary arteries. The second image (td = 8 s) is acquired at the time of filling of the left ventricle and shows filling of the aorta up to the aortic arch. The third image (td = 11 s) demonstrates the aorta descendens as well as the supra-aortic branches. In the lung predominantly pulmonary veins are shown. The last image (bottom right) was acquired at td = 14 s after bolus injection. The enhancement in the pulmonary vessels has nearly vanished.

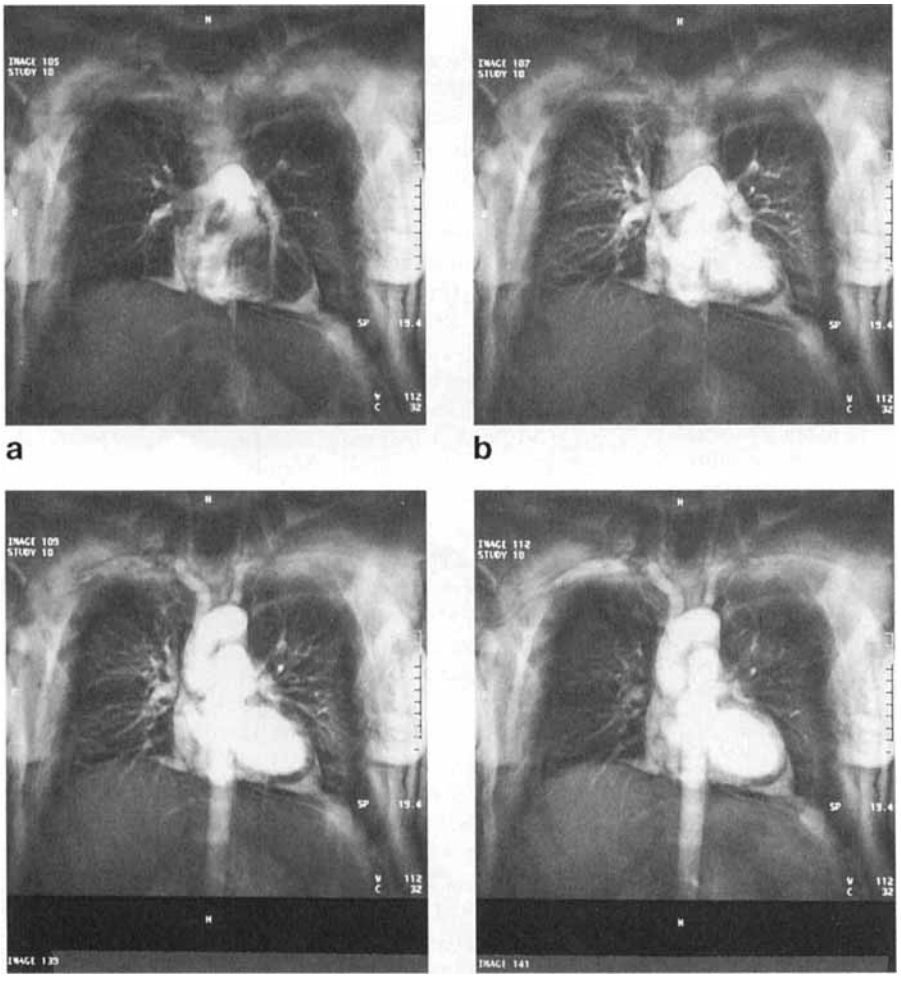

FIG. 1. Four projection angiograms from a sequence of 40 images acquired at 950-ms time intervals after bolus injection of a normal dose of Gd-DTPA. (a) was acquired 6 s after the begin of the injection and shows only enhancement in the right ventricle and the beginning of the pulmonary arteries. At 8 s after injection (b), the enhancement of the pulmonary arteries is fully developed and the left ventricle starts to show up. At 11 s (c), the enhancement has reached the aortic arch and the supra-aortic arteries. 14 s after injection (d), the enhancement in the pulmonary vessels has already strongly decreased and diffuse signals due to organ perfusion show up.

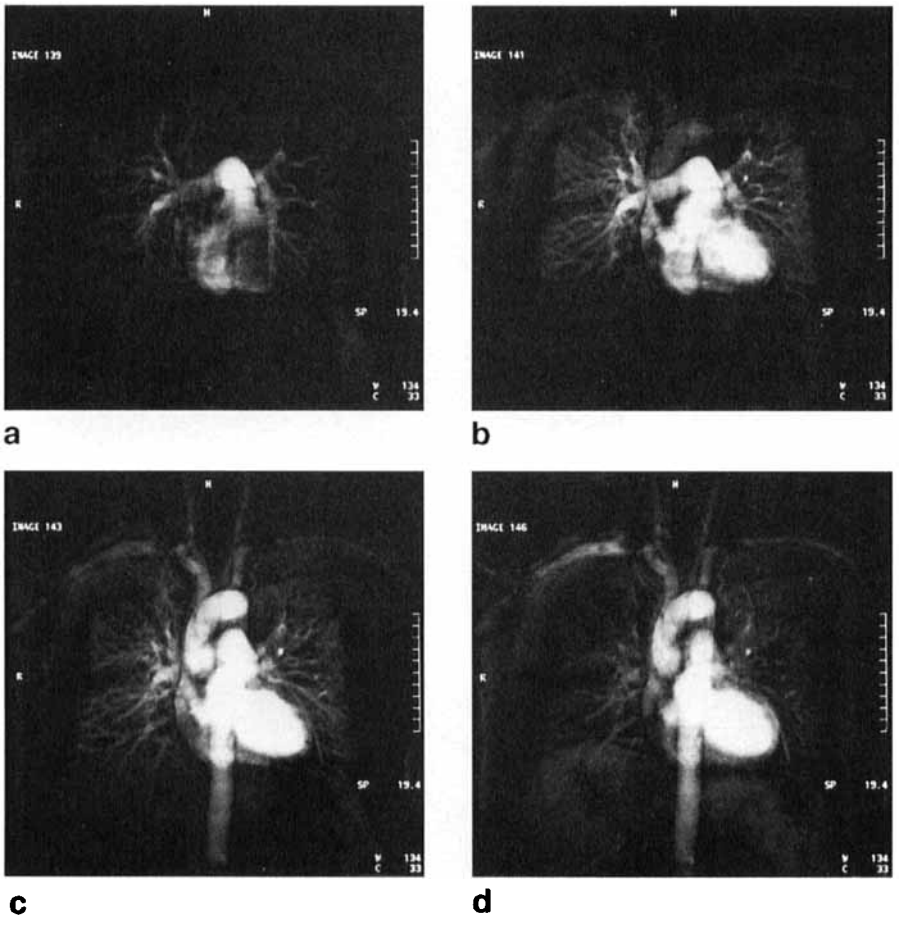

FIG. 2. Same images as Fig. 1, but after subtraction of a reference image acquired immediately before the bolus injection. The very clean background suppression improves the visibility especially of the outer branches of the pulmonary vessels.

It is interesting to note, that the inflow of the bolus to the right ventricle can not be seen even with the normal dose of Gd-DTPA used throughout our experiments. This indicates, that the T_2* shortening wipes out the signal even at echo times as low as 1.4 ms. Bright signal appears only after mixing of the bolus with blood in the right heart chamber.

A correlation image based on the pixel time course of the signal located in the pulmonary artery is demonstrated in Fig. 3. The early phase (positive correlation coefficient) is clearly distinguished from the later stages (negative correlation coefficient). Background signal is efficiently suppressed. Note the clear delineation of the myocardium due to (late) perfusion.

Figure 4 demonstrates the possibility to acquire biplanar angiograms in a patient who was unable to hold his breath for more than 5 s due to total obstruction of the vessels of the left lung by a bronchial carcinoma. Image acquisition was alternated every 890 ms between sagittal (Fig. 4a) and coronal (Fig. 4b) projections.

DISCUSSION

Subsecond projection MR-DSA has demonstrated to be a very reliable and robust technique to acquire projection angiograms of the lung. Even for patients who can not hold their breath due to their clinical condition, angiographic images of diagnostic quality can be acquired. Background noise can be easily eliminated by difference formation to a reference images. Further postprocessing using more sophisticated algorithms developed for functional imaging can be used to further distinguish vessels from background. Cross-correlation on a signal defined by the time course in a region of interest placed into a pulmonary vessel does not reduce background noise very efficiently. The correlation coefficients also offer a means to derive functional information.

After leaving the left ventricle, the bolus has already been diluted considerably. In our first experiments using subsecond projection MR-DSA on the femoral arteries, we had thus to reduce the flip angle to 30° to avoid saturation of the blood signal. Nevertheless good angiograms could be produced after background subtraction or cross-correlation.

Similar considerations apply to the application of subsecond projection MR-DSA for angiography of the head and neck, where the possibility to distinguish arterial from venous phase with very high temporal and spatial resolution appears to be especially attractive. Due to the strong overlay of multiple vessels when projection images are acquired through the entire head, it is advisable to restrict the projection volume to the volume of interest. For further information about the in depths position of vessels, we have used a time series of images acquired

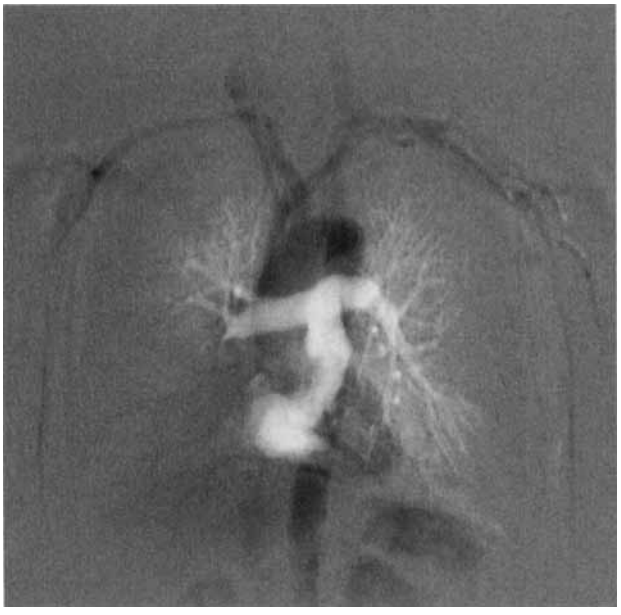

FIG. 3. Cross-correlation image from the experiment shown in Figs. 1 and 2. The pixel time courses were correlated to the signal in the pulmonary trunc. Positive correlation (bright) corresponds to the early phase. Later enhancement leads to negative correlation shown in black. Note the diffuse late enhancement in organ tissues including the myocardium.

under different projection angles. Alternating data acquisition between two different projection angles already yields information about the vessel position in space, which is sufficient for most purposes. The reduced temporal resolution of the sequential acquisition to about 2 s per updated view is still highly sufficient to observe the bolus passage.

In the current implementation using the full acquisition data matrix of 256 phase encodes subsecond projection, MR-DSA already gives sufficient time resolution to observe the passage of the contrast agent in various steps over the time of bolus passage.

The temporal resolution of the updates can be easily further improved by using fewer phase encoding steps per image. With 192 phase encoding steps, a time resolution of about 700 ms can be reached without significant reduction of the image quality. This already allows crude quantification of flow by observing the frame-to-frame progression of the bolus maximum. By using keyhole techniques with down to 32 phase encoding steps per frame, a temporal resolution of about 110 ms can be achieved, which already allows quite reliable quantification of vascular flow.

Further studies are required to evaluate whether this intrinsic gain in time resolution by roughly one order of magnitude compared with dynamic 3D angiography (6) is of clinical relevance. Advantages of the 2D technique is certainly the higher temporal resolution, which is crucial for non-breathhold imaging and for applications to vessels near the heart, which show strong ECG-related motion. 3D acquisitions have a higher SNR than 2D scans by a factor of $\sqrt{n}$, where n is the number of 3D partitions. After averaging, the signal-to-noise per unit time should

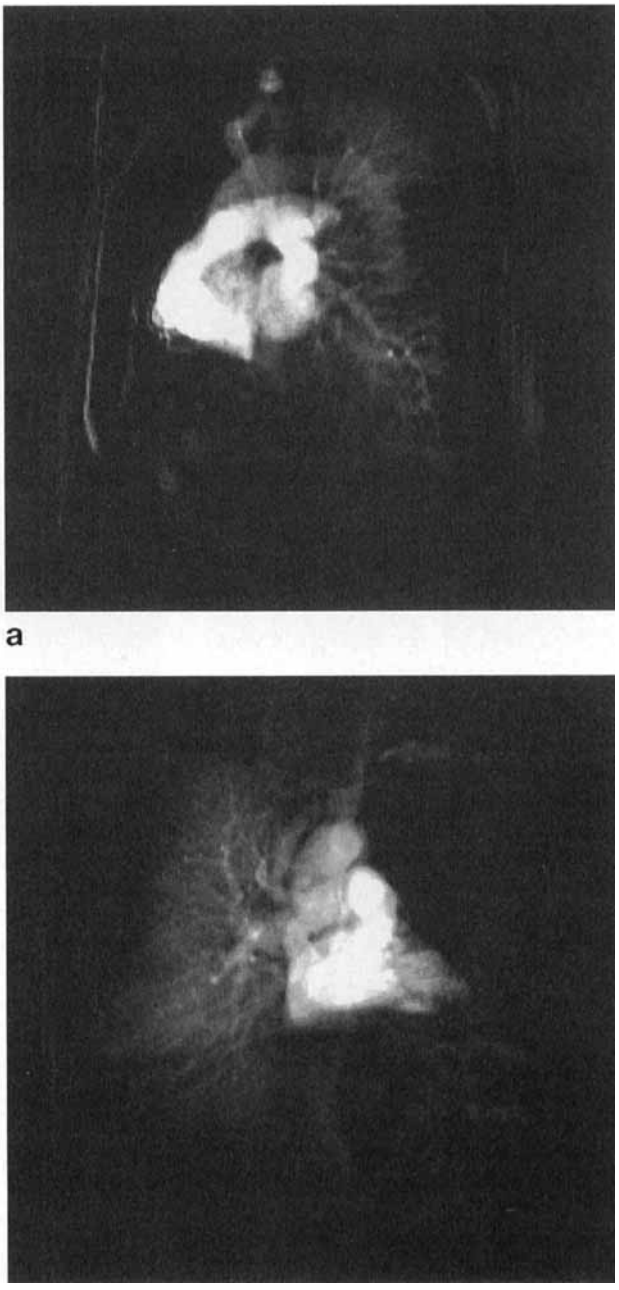

FIG. 4. Sagittal (a) and coronal (b) subsecond projection MR-DSA of a patient with a bronchial tumor obstructing the left lung. Images were acquired in alternate fashion with TE = 1.4 ms, TR = 3.4 ms. The acquisition of the sagittal image (a) preceded the coronal image (b) by 890 ms. The sagittal image (a) shows the heart and the pulmonary trunc as well as segmental and subsegmental pulmonary arteries in the right lung. Some slight enhancement can be seen in the aortic arch. In (b), the diffuse "flush" of the capillaries in the right lung is clearly visible. Signal from the left lung is totally missing demonstrating total occlusion of the left pulmonary artery. Images are subtraction images from a reference image acquired immediately preceding the bolus application of contrast agent. Background subtraction works quite satisfactorily, although the patient was unable to hold his breath for more than 5 s. The bright vertical line to the left of the heart in (a) is a residual artifact due to misalignment between the two images used for subtraction.

be identical for 2D and 3D acquisitions, if the same pulse sequence and the same parameters are used.

A problem of projection imaging is dephasing of spins across the projection direction. Depending on the overall field inhomogeneity and on local susceptibility effects, the signal from within the vessels is not necessarily in phase signal from the background. For generating subtraction angiograms, this problem can be alleviated using complex subtraction as long as vessels do not overlap (7). For projections through complex vascular structures like pulmonary vessels, however, it is essential to minimize the echo time of the sequence to avoid loss of image quality due to signal cancellation. Our experience on MR-DSA of pulmonary vessels show, that TE = 1.4–1.9 ms leads to very satisfactory results at least for our applications, whereas initial experiments with longer TE (3.0–4.5 ms) led to images with severely deteriorated quality. For TE = 1.4 ms two signals will be out-of-phase, if their frequency difference is roughly 360 Hz or 5.5 ppm at 1.5 T. Local susceptibility effects can be easily 3 ppm or more, which illustrates, that minimizing TE to even below 1 ms is a desirable goal for MR-DSA.

A different acquisition strategy has to be applied, for flow-related phase changes, which will also lead to signal cancellation in overlapping vessels. Flow compensation will invariably lead to an increase in te and thus to increased sensitivity to susceptibility effects. Further studies are required to optimize the acquisition strategy for a given application. In general, flow-compensation seems to be indicated for observing vessels with fast flow in tissues with low susceptibility effects. Minimizing TE is advisable for observing medium to slow flow vessels in areas of high local susceptibility.

As yet, we have not undertaken a systematic study for finding the optimal dose and concentration of the contrast agent. For angiography of the pulmonary vessels, the normal dose has proven to be sufficient. Higher dose will lead to a longer bolus passage. This could be used for contrast-to-noise improvements by averaging over several time frames. The reduced sharpness of the bolus would, however, be disadvantageous for the assessment of the hemodynamics of the observed vascular system.

For subsecond projection MR-DSA angiography downstream from the aorta, a higher dose promises to improve the results significantly. As an alternative, catheter angiography can be used to achieve a high local bolus intensity. Due to the considerably increased invasiveness of such a procedure, it should be restricted, to patients that already have a catheter in position. Possible clinical applications are cases in which a selective catheter placement is not possible and conventional x-ray angiography consequently produces unsatisfactory results.

CONCLUSIONS

The subsecond projection MR-DSA technique offers an approach for fast and reliable technique for projection angiography. The continuous acquisition during the bolus passage avoids the necessity of exact timing of the bolus to the data acquisition. Only minimal postprocessing is required to get diagnostic angiograms including information about the hemodynamics in the observed region. Applications of subsecond projection MR-DSA as a method for coronary angiography appear feasible and are under way in our department.

It should be noted that the basic image information afforded by subsecond projection MR-DSA is identical to that offered by digital subtraction angiography (DSA) (10). Diagnostic protocols, which have been developed for the clinical application of DSA over the years for various diagnostic applications, can thus be translated after appropriate modification into a MR protocol. A potentially important difference of the MR technique is the strong nonlinear signal behavior with only slight variations of the signal intensity with the concentration of the contrast agent at the high concentrations occurring during bolus passage. This nonlinearity reduces the signal attenuation on dilution of the contrast agent, but, as demonstrated above, also leads to signal loss close to the point of c.a. injection.

Further studies are required to establish the pitfalls and advantages resulting from this different contrast behavior of the MR technique. Other differences include a reduced and much more homogeneous background signal in MR, which yields acceptable angiograms even without subtraction (Fig. 1), but also at least the currently higher spatial resolution of DSA. A thorough discussion, which is beyond the scope of this paper, needs to take all these factors into account to reveal applications for which MR offers a significant diagnostic advantage above the general benefit of the lack of ionizing radiation.

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