AJNR

Comparison of bolus and constant infusion methods of gadolinium administration in MR angiography.

G Sze, S N Goldberg and Y Kawamura

AJNR Am J Neuroradiol 1994, 15 (5) 909-912
http://www.ajnr.org/content/15/5/909

Comparison of Bolus and Constant Infusion Methods of Gadolinium Administration in MR Angiography

Gordon Sze, S. Nahum Goldberg, and Yasutaka Kawamura

PURPOSE: To determine whether the method of delivery of gadolinium can alter optimal small-vessel detail in MR angiography. **METHODS:** Six healthy volunteers were studied with MR angiography using both a constant infusion and a bolus method of contrast administration to a total dose of 0.1 mmol/kg. Both three-dimensional time-of-flight and 3-D phase-contrast techniques were used. **RESULTS:** Constant infusion did not prove superior to bolus administration of contrast. With both techniques, gadolinium enhancement uniformly improved visualization of small vessels. Delay from the time of contrast administration to scan acquisition decreased vessel enhancement. **CONCLUSIONS:** Bolus administration of gadolinium is sufficient to improve small vessel visualization with MR angiography. When a series of contrast-enhanced images is to be obtained, MR angiographic sequences should be obtained first.

Index terms: Magnetic resonance angiography (MRA); Contrast media, comparative studies; Contrast media, paramagnetic

AJNR Am J Neuroradiol 15:909–912, May 1994

Increasingly, it seems that contrast enhancement may play a role in specific clinical cases in which magnetic resonance angiography (MRA) is performed. In cases in which fine vascular detail is sought, the administration of gadolinium appears to be of benefit (1–4). The use of contrast in MRA has been noted to improve lumen definition and visualization of small vessels. In specific clinical cases, the diagnosis of occlusive or stenotic disease has been aided and the definition of aneurysms accentuated. Contrast can also be useful to demonstrate the relationship of vascular masses to vessels. In addition, the use of a three-dimensional adaptive-based vessel-tracking algorithm permits differentiation of arteries from enhancing venous structures (3).

Because the mechanism of action of gadolinium in MRA is the shortening of the T1 relaxation time of the blood itself, a method of administration of contrast in which constant infusion is performed has been postulated to be beneficial in maintaining high concentrations of gadolinium throughout the course of the scan and thus maximizing vessel detail. Similar procedures are, of course, routine in computed tomographic scanning. This study was performed to determine whether a constant infusion method of administering gadolinium would be superior to a bolus given just before imaging.

Materials and Methods

Our subjects were six healthy male volunteers, all of whom gave informed consent to undergo a protocol approved by the human investigations committee at our institution. All subjects were studied on 4 separate days. Each patient had a baseline MRA acquisition, after which gadolinium was administered and the MRA was repeated. On 2 of the 4 days, 3-D time-of-flight MRA was performed; on the other days, the 3-D phase-contrast MRA was obtained.

For this study, we used imaging parameters routinely used at our institution for cranial MRA. Previous studies have demonstrated optimal image quality using these settings. In addition, we felt that information from this trial would be most beneficial if the imaging parameters used were identical and thus comparable to routine clinical MRA sequences. For 3-D time-of-flight MRA, the parameters used were 50/6.9/1 (repetition time/echo time/excita-

Received March 26, 1993; accepted pending revision June 18; revision received August 6.

From the Department of Radiology, Yale University School of Medicine, New Haven.

Address reprint requests to Gordon Sze, MD, Yale University School of Medicine, Department of Radiology, 333 Cedar St, New Haven, CT 06510.

AJNR 15:909–912, May 1994 0195-6108/94/1505–0909

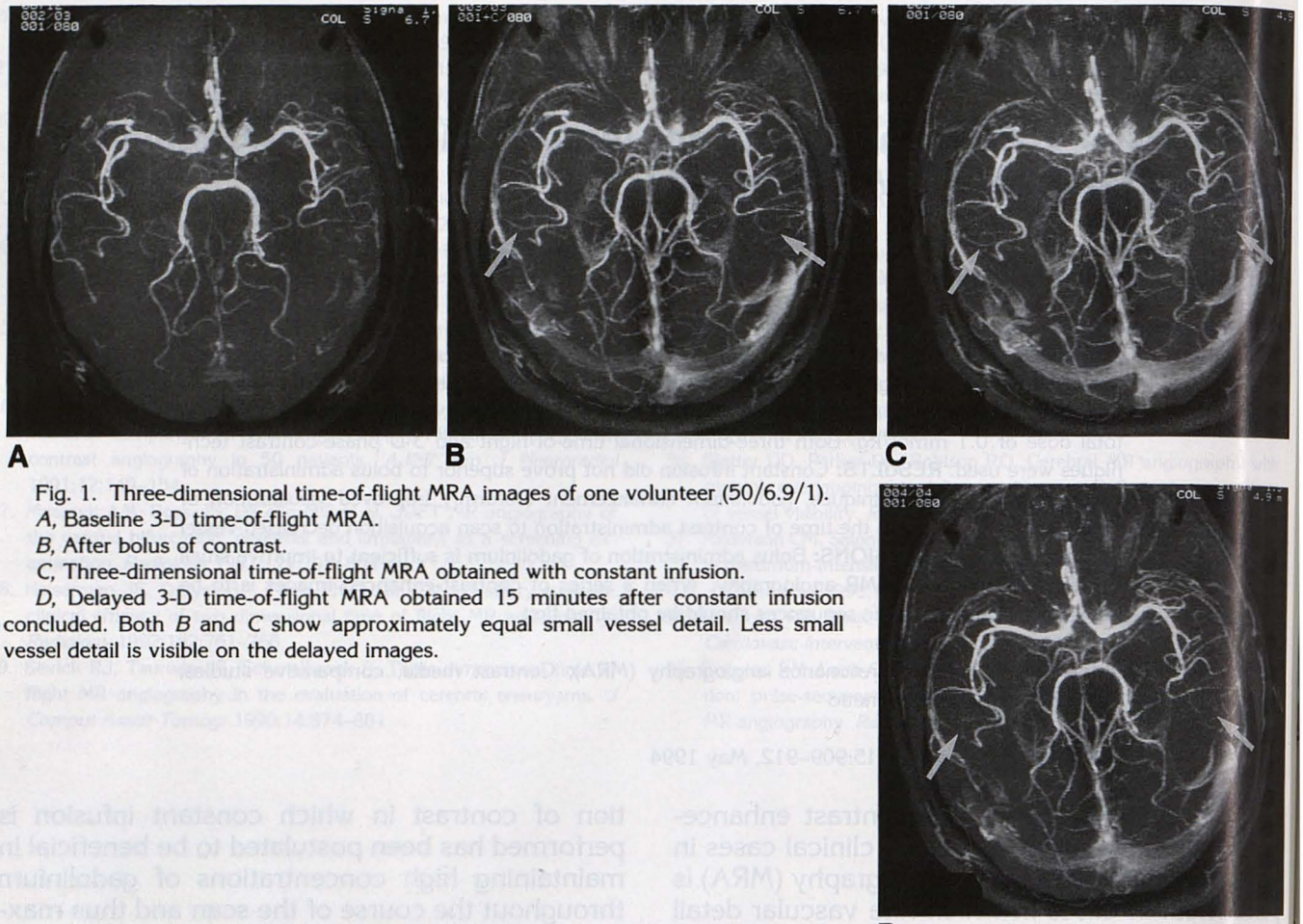

Fig. 1. Three-dimensional time-of-flight MRA images of one volunteer (50/6.9/1).
A, Baseline 3-D time-of-flight MRA.
B, After bolus of contrast.
C, Three-dimensional time-of-flight MRA obtained with constant infusion.
D, Delayed 3-D time-of-flight MRA obtained 15 minutes after constant infusion concluded. Both *B* and *C* show approximately equal small vessel detail. Less small vessel detail is visible on the delayed images.

tions), 20° flip angle. Sixty images of 0.9 mm were used in the 3-D reconstruction for a total slab thickness of 54 mm. The matrix was 256 × 192. Imaging time was 10 minutes 16 seconds. For 3-D phase-contrast MRA, the parameters used were 30/7.2/1, 20° flip angle. The velocity encoding was 50 cm/sec. Slab thickness was 25.2 mm, as 28 sections of 0.9 mm were used. The matrix was 256 × 192. Imaging time was 12 minutes 20 seconds.

Gadopentetate dimeglumine (0.1 mmol/kg) was administered either as a bolus, immediately before scanning, or as a minibolus, followed by constant infusion. This dosage of gadolinium was chosen because it is the standard regimen used for most conventional imaging sequences. For MRA scans acquired with the bolus method, the total dose of gadolinium was administered intravenously in less than 15 seconds, followed by immediate scan acquisition. The constant infusion was performed by giving a bolus of the first 5 mL of gadolinium, followed by constant intravenous administration of the remainder of the gadolinium, diluted in normal saline to a volume of approximately 150 mL, at a rate of approximately 15 mL/min. In all patients, the gadolinium dilution entered the patient during the 10- to 12-minute interval required for each acquisition. MRA scanning was begun immediately after the drip infusion was begun. In addition, in all six phase-contrast and five of the time-of-flight cases in which the constant infusion method was used, an additional postcontrast MRA sequence was obtained immediately after the infusion was completed. Approximately 15 minutes elapsed between contrast administration and the completion of this delayed scan. The purpose of this sequence was to permit direct comparison of the infusion method with a semibolus method while the patient was in the exact same position in the scanner and also to evaluate the effect of a brief delay on image quality.

The images were photographed in a manner that omitted any information regarding method of administration of gadolinium. For each MRA technique, time-of-flight or phase-contrast, and for each patient, four sets of images were displayed on an alternator in a random fashion. These four sets were the baseline MRA, the MRA obtained with constant infusion, the MRA obtained immediately after bolus, and the MRA obtained after constant infusion was concluded. These images were ranked by three neuroradiologists in the order in which fine vascular detail was seen. Attention was particularly given to branches of the anterior and middle cerebral arteries. The series of images with overall clearer definition of small vessels was defined as the better scan. In cases where no difference between

two scans could be ascertained, an equal rank was given to both.

To ensure accuracy and reproducibility in interpretation of the readings, images were reviewed twice by each radiologist on different days separated by 2 months. Inter- and intraobserver reliability were compared and analyzed with κ statistics.

From these raw data, a nonblinded radiologist compared the unenhanced images with those with contrast enhancement, the images enhanced with the bolus method with those with constant infusion, and the constant infusion images with images acquired at a delay from gadolinium injection. Statistical analysis of these comparisons was then performed using Friedman's rank test (F), with these results analyzed to calculate the number of standard deviations F falls from the expected mean of a normal Gaussian distribution.

Results

In all comparisons (n = 138), the administration of gadolinium permitted much greater delineation of fine vascular structures ($F = 1083$; $P \ll .001$). More venous structures were appreciated on the time-of-flight scans of two of the volunteers studied. However, the constant infusion method of administration did not provide better vascular detail when compared with the bolus method. In the phase-contrast studies, the constant infusion method was determined to be superior for 10 comparisons, the bolus method was better in 19, and no significant difference was ascertained in 7 readings. Thus, Friedman's test yielded a result of 2.25, corresponding to a P value greater than .15, with a moment of .88 SD from the expected mean. For time-of-flight studies, results were even more similar with the bolus method determined to be superior in 14 readings, the constant infusion method in 13, and no significant difference noted in 9, corresponding to F of 0.03, $P > .9$. When analyzed, this represents a result approaching the mean of the Gaussian distribution (0.0 moments).

Comparing the constant infusion images with the delayed images, the constant infusion method appeared superior. In the phase-contrast studies, the constant infusion images were determined to be superior for 20 comparisons, the delayed images were better in 7, and no significant difference was ascertained in 9 readings. Thus, Friedman's test yielded a result of 4.70, corresponding to a P value less than 0.04, with a moment of 2.6 SD from the expected mean. For time-of-flight studies, results were even more significant with the constant infusion determined to be superior in 25 readings, and no significant difference noted in 5. This corresponds to an F of 20.83, and a $P < .005$. When analyzed, this represents a result 14 moments from the mean of the Gaussian distribution.

Intraobserver comparisons yielded an overall observed percent agreement of 85.8% with a κ test result of .83 indicating significant agreement between individual readings of each reader. The correlation of interobserver review was likewise excellent with an observed percent agreement of 84.8% and a κ of .81, indicating significant agreement among readers.

Discussion

Both this study and one by Bradley et al (Comparison of Routine and Gadodiamide Enhanced 3-D Time of Flight MR Angiography in the Brain (abstr), presented at the 78th Annual Meeting of the Radiological Society of North America, Chicago, 1992) demonstrate increased conspicuity of fine vascular detail using gadolinium contrast during MRA scanning. In addition, Chung et al (Contrast Material Enhanced MR Angiography for Intracranial Aneurysms with 3-D Time of Flight and 3-D Phase Contrast Techniques (abstr), presented at the 78th Annual Meeting of the Radiological Society of North America, Chicago, 1992) noted improved intracranial aneurysm detection when gadolinium enhancement was used. The use of gadolinium, however, also increased the visualization of venous structures which obscured arterial anatomy in several patients in Chung's study. Therefore, gadolinium may potentially help to improve diagnosis in appropriately selected cases, but may also obscure findings.

Although the use of contrast can improve image quality in cases in which MRA is performed to visualize small vascular structures, neither constant infusion nor bolus of gadolinium provide clinically or statistically better results for image enhancement. The bolus method is probably easier to administer. In both cases, MRA should be obtained as the first postcontrast sequence to maximize small vessel visualization. This advice corroborates the recommendations of Lin et al that scan acquisitions should be obtained within 15 minutes of gadolinium administration to maximize blood vessel enhancement (3).

Previous work has suggested that the use of routine doses of gadolinium reduces the T1 relaxation time of blood by a factor of 2 immediately after injection (Lin W et al, High Resolution MRA

with Gadopentetate Dimeglumine: Preliminary Results in the Intracranial Circulation, presented at the Annual Meeting of the Society of Magnetic Resonance Imaging (abstr), New York, 1992). The relaxation time returns to three fourths of its normal value after 30 minutes. Giving the gadolinium, preparing for the scan, and the actual imaging take at least 15 minutes; thus, if a delay occurs, a substantial decrease in intravascular concentration of contrast will occur.

In this study, 3-D techniques were used rather than 2-D techniques. First, 3-D techniques are more prone to saturation of spins, particularly in slow flow, because of the thickness of the slab. Spin saturation depends not only on blood flow velocity but also on slab thickness. Contrast may be particularly helpful in 3-D acquisitions. Two-dimensional techniques are less sensitive to saturation; however, the voxel size is larger and image resolution is lower. Therefore, in cases in which visualization of small structures is necessary, a 2-D approach would probably not be as useful.

An optimal contrast agent for MRA would remain in the intravascular compartment during the imaging time. Experimental compounds such as gadolinium-DTPA polylysine and gadolinium-DTPA albumin have been studied (4). Until then, contrast-enhanced MRA will rely on gadolinium compounds that rapidly pass out of the intravascular compartment.

References

1. Creasy JL, Price RR, Presbey T, et al. Gadolinium enhanced MR angiography. *Radiology* 1990;175:280–283
2. Marchal G, Michiels J, Bosmans H, et al. Contrast enhanced MRA of the brain. *J Comput Assist Tomogr* 1992;16:25–29
3. Lin W, Haacke EM, Smith AS, Clampitt ME. Gadolinium-enhanced high-resolution MR angiography with adaptive vessel tracking: preliminary results in the intracranial circulation. *J Magn Reson Imaging* 1992;2:277–284
4. Marchal G, Bosmans H, Van Hecke P, et al. Experimental Gd-DTPA polylysine enhanced MR angiography: sequence optimization. *J Comput Assist Tomogr* 1991;15:711–715