Contrast-Enhanced MRA in the NSF Era: Potential for Contrast Dose Reduction

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Purpose: Higher doses of gadolinium-based contrast agents (GBCA) are often used for contrast-enhanced MRA (CE-MRA). Patients with moderate-to-severe (stages 3-5) chronic kidney disease undergoing contrast-enhanced MR imaging are known to be at increased risk for developing nephrogenic systemic fibrosis, particularly with higher doses or repeated exposure to GBCA (1-2). Herein we review information on the application of lower doses of the higher-relaxivity gadobenate dimeglumine (MultiHance; Gd-BOPTA) for CE-MRA.

Materials and Methods: A total of 183 subjects were studied in 7 intraindividual crossover studies comparing gadobenate dimeglumine (Gd-BOPTA) to conventional contrast agents for CE-MRA (3-9). In 5 studies, equal 0.1 mmol/kg doses of Gd-BOPTA and gadopentetate dimeglumine (Gd-DTPA) were compared for MRA of the abdominal and renal arteries (N=10), peripheral vessels (N=110), pelvic vessels (N=5), and supra-aortic vessels (N=12). In 2 studies, 0.1 mmol/kg Gd-BOPTA was compared to 0.2 mmol/kg Gd-DTPA for MRA of the carotid arteries (N=12) or renal arteries (N=34). Contrast enhancement was evaluated in a blinded manner using both qualitative and quantitative metrics.

Results: In all territories investigated, the high relaxivity agent performed better than the non-protein binding comparator (Table 1). In the two studies in which a single dose of Gd-BOPTA was compared with a double dose of another gadolinium agent, Gd-BOPTA resulted in significantly greater increases in SI and SNR than the comparator despite the lower administered dose (Table 2).

Table 1: Studies Comparing Gd-BOPTA with comparator Gd agents at a Dose of 0.1 mmol/kg

Territory	N	Main Findings
Abdominal/ renal vessels (3)	10*	• Significant ($p<0.05$) ↑in signal peak duration, max SI, and AUC with Gd-BOPTA vs Gd-DTPA
Run-off vessels (4)	14*	• Significant ↑ in SI with Gd-BOPTA vs Gd-DTPA at all levels • No qualitative difference in abdominal vessels; preference for Gd-BOPTA in pelvic vessels; markedly better performance for Gd-BOPTA in femoral/tibial vessels
Run-off vessels (5)	96†	• Global diagnostic preference of readers 1, 2, and 3 for Gd-BOPTA in 75 (82%), 75 (82%), and 70 (76%) patients, vs 4 (4%), 7 (8%), and 8 (9%) patients for Gd-DTPA ($p\leq0.0001$; all readers) • Significant ($p\leq0.0001$) preference for Gd-BOPTA for qualitative endpoints in each vascular territory • Significant ($p\leq0.0001$) ↑ in CNR with Gd-BOPTA for each vascular territory
Pelvic vessels (6)	5*	• SNR and CNR with Gd-BOPTA (81.2 and 68.9) as well as standard (84.3 and 71.6) diluted (79.2 and 66.3) 1M gadobutrol significantly ($p<0.02$) higher vs Gd-DTPA (50.0 and 38.2) • Difference between either form of gadobutrol and Gd-BOPTA not statistically significant ($p>0.3$) • Small vessels delineated better both with gadobutrol and Gd-BOPTA vs Gd-DTPA
Supraaortic vessels (7)	12*	• Significant ↑ in median vessel delineation score with Gd-BOPTA vs Gd-DTPA (4.3 vs. 3.7; $p=0.005$) • Significant ($p\leq0.026$) preference for Gd-BOPTA globally and for assessments of extracranial arteries, Circle of Willis, and vessels distal to Circle of Willis • Significant ($p\leq0.021$) ↑ in CNR with Gd-BOPTA: overall increases of 23.3%, 26.7%, and 28.5% noted for internal carotid, middle cerebral, and basilar arteries, respectively

*Healthy volunteers

†Patients with known or suspected stenoocclusive disease of the vessels of interest

Table 2: Studies Comparing 0.1 mmol/kg Gd-BOPTA with Gd-DTPA at a Double Dose (0.2 mmol/kg)

Territory	N	Main Findings
Carotids (8)	12†	• ↑ in SI and CNR (latter statistically so [$p=0.002$]) with Gd-BOPTA over Gd-DTPA, despite lower dose
Renal vessels (9)	34†	• Mean SNR and CNR values for Gd-BOPTA and Gd-DTPA nearly identical in suprarenal aorta but, with Gd-BOPTA, greater ↑ at progressively lower levels: at infrarenal aorta, mean SNR 48.3 vs 40.6 and mean CNR 44.2 vs 36.4 with Gd-BOPTA vs Gd-DTPA, respectively ($p=0.05$ for both), despite lower dose

†Patients with known or suspected stenoocclusive disease of the vessels of interest

Conclusions: Intraindividual CE-MRA studies in various vascular territories demonstrate that the higher-relaxivity Gd-BOPTA may be used at lower dose without compromise of diagnostic efficacy, potentially limiting patient exposure to GBCA.

References

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