Evaluation of Gadolinium Concentration in Morphologic Assessment of Brain Tumors: Results of a Multicenter Intraindividual Crossover Comparison of Gadobutrol Versus Gadobenate Dimeglumine (the MERIT Study)

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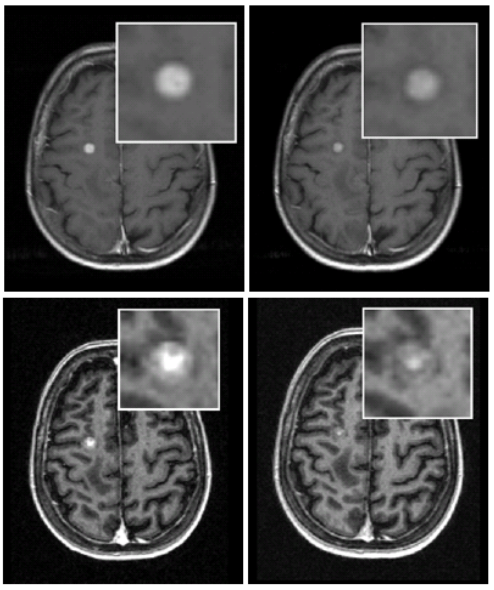
Purpose: To intraindividually compare 0.1 mmol/kg doses of standard concentration gadobenate dimeglumine (0.5M) with double concentration gadobutrol (1.0M) for the evaluation of brain tumors on magnetic resonance (MR) images at 1.5T.



58 year old woman with metastases from melanoma. Greater enhancement and conspicuity achieved on T1SE (A,B) and T1GRE images (C,D) with gadobenate dimeglumine (A,C) than with gadobutrol (B,D)

Materials and Methods: 122 patients (67m/55f, mean age 56.1±12.6y) with known or suspected brain tumors were enrolled at 12 study centers and underwent two MR imaging examinations 3 to 14 days apart. Patients were randomized to Group A (n=59) which received gadobenate dimeglumine for the first examination and gadobutrol for the second, or Group B (n=63) in which patients received gadobutrol first. Contrast agents were administered at 0.1 mmol/kg, corresponding to 0.2 mL/kg for gadobenate dimeglumine and 0.1 mL/kg for gadobutrol. Injection durations were comparable for the two agents. T1W spin-echo (T1SE) and T2W fast spin-echo (T2FSE) sequences were performed pre-contrast injection and T1SE and 3D T1W gradient-echo (T1GRE) sequences post-contrast injection. All images were evaluated by 3 expert radiologists blinded to agent or clinical information. Qualitative (lesion border delineation, disease extent, lesion morphology, lesion contrast enhancement, and overall diagnostic preference), quantitative (contrast-to-noise ratio [CNR] and lesion-to-background ratio [LBR]), and safety assessments were performed.

Results: 114 patients were evaluable for efficacy. Diagnoses included mostly primary glial tumors or metastases. Readers expressed global preference for gadobenate dimeglumine compared with gadobutrol (P<0.0001 for all readers; Table 1). A corresponding significant preference for gadobenate dimeglumine was noted for each individual qualitative diagnostic information endpoint (P<0.0001 for all readers for all endpoints). Reader agreement was consistently good (κ=0.414-0.629). Gadobenate dimeglumine demonstrated significantly greater mean percent enhancement than gadobutrol on post-dose T1SE images for all readers (reader 1: 119.9±68.7 vs 97.3±58.2; reader 2: 121.6 ±65.9 vs 99.8±56.9; reader 3: 111.9±62.3 vs 89.7±55.9; P<0.0001 for all readers). Quantitatively, significant increases in CNR and LBR were noted for gadobenate dimeglumine compared with gadobutrol on T1SE images (CNR: P=0.0186, P<0.0001, P=0.0007 for readers 1, 2, and 3, respectively; LBR: P<0.0001 for all readers), and on T1GRE images (P<0.0001, all readers for both endpoints). The incidence of adverse events (AE) was similar: 6.8% after gadobenate dimeglumine and 5.9% after gadobutrol. AE were mild except one moderate case of injection site inflammation after gadobutrol.

Conclusions: Despite the differences in concentration, significantly greater qualitative and quantitative brain tumor enhancement is achieved with the use of gadobenate dimeglumine compared with gadobutrol.

Table 1. Qualitative Assessments of Three Independent Blinded Readers

Qualitative Endpoint	Gadobenate Dimeglumine Preferred (range for 3 readers) n (%)	Gadobutrol Preferred (range for 3 readers) n (%)	P-Value
Global diagnostic preference	46 (40.7) - 54 (47.4)	6 (5.3) – 7 (6.1)	<0.0001
Lesion border delineation	37 (34.0) - 43 (38.1)	3 (2.6) – 5 (4.4)	<0.0001
Definition of disease extent	18 (15.9) - 21 (18.4)	1 (0.9) – 3 (2.6)	<0.0001
Visualization of lesion internal morphology	35 (30.7) - 39 (34.5)	1 (0.9) - 5 (4.4)	<0.0001
Lesion contrast enhancement	50 (43.9) - 62 (54.4)	7 (6.1) - 10 (8.8)	<0.0001

N=113 for Reader 1 and N=114 for Readers 2 and 3.