Enhancing lesions of the brain: intra-individual quantitative and qualitative comparison of contrast enhancement after gadobenate dimeglumine (Gd-BOPTA) versus established gadolinium comparators

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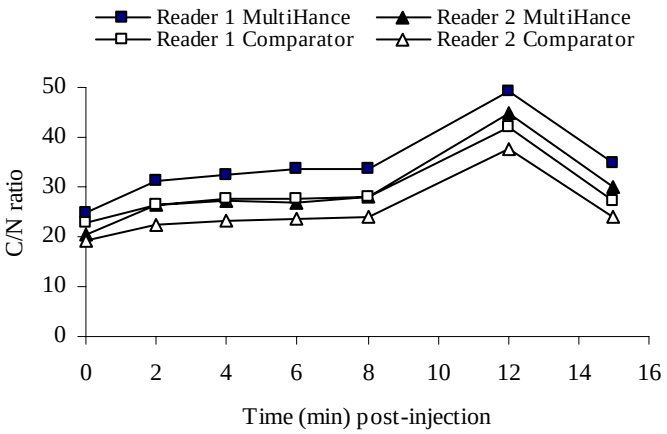
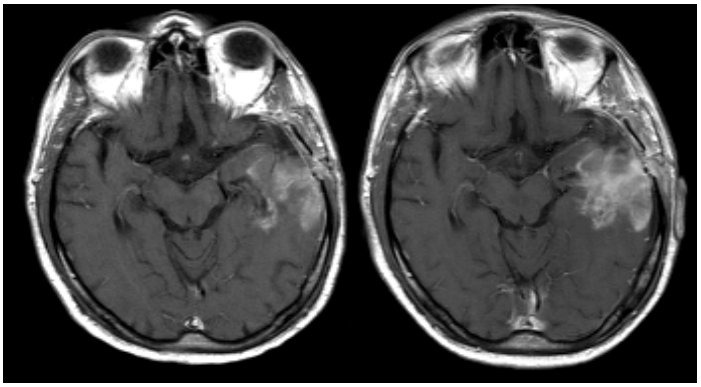
Synopsis: Gd-BOPTA at 0.1 mmol/kg bodyweight was compared intra-individually with equivalent doses of either Gd-DTPA (n=23) or Gd-DOTA (n=22) for contrast enhancement of enhancing intracranial brain tumors. T1w spin echo (T1wSE) images were acquired at 2,4,6,8,10, and 15 min post-contrast with a T1wSE-MT sequence at 12 min. Quantitative comparison by two independent blinded off-site readers revealed significantly greater % signal enhancement (%En; $p<0.0001$), lesion-to-brain ratio (L/B; $p<0.003$) and contrast-to-noise ratio (C/N; $p<0.03$) for Gd-BOPTA-enhanced images at all time-points from 2 min post-contrast. Qualitative assessment revealed significant preference for Gd-BOPTA over combined comparator for lesion border delineation ($p<0.004$, both readers), lesion internal morphology ($p<0.008$, both readers), global contrast enhancement ($p<0.0001$, both readers) and global diagnostic preference ($p<0.0005$, both readers).

Purpose: Gadobenate dimeglumine (Gd-BOPTA, MultiHance®, Bracco Imaging SpA, Milan, Italy) is a paramagnetic contrast agent whose T1 relaxivity *in vivo* ($r1=9.7\ mmol \bullet L^{-1}s^{-1}$) is approximately twice that of Gd-DTPA, Gd-DOTA and other available gadolinium agents due to a unique capacity for weak and transient interaction with serum albumin (1,2). This feature may contribute to the improved detection, delineation and conspicuity of enhancing intracranial lesions for which blood-brain barrier breakdown results in elevated levels of serum proteins (3). Presented are the results of a fully blinded, independent off-site evaluation of the quantitative and qualitative enhancement obtained after a dose of 0.1 mmol/kg Gd-BOPTA, compared with that obtained after an equivalent dose of either Gd-DTPA or Gd-DOTA.

Methods and Materials: 45 patients (31M/14F) with suspected glioma or cerebral metastasis underwent two successive randomized, double-blinded MR exams with Gd-BOPTA and either Gd-DTPA (n=23) or Gd-DOTA (n=22) at equal dose (0.1 mmol/kg). The imaging parameters and equipment were identical for the two examinations for each patient. The contrast agents were administered by power injector at 2 ml/s with the second agent administered between 24 hours and 14 days after the first agent. Images were acquired pre-dose (T1wSE, T2wFSE sequences) and post-dose (sequential T1wSE sequences at 2,4,6,8,10,15 min with a T1wSE-MT sequence at 12 min) at either 1T (Philips; 16 patients) or 1.5T (Siemens; 29 patients) using a head coil. Quantitative (lesion-to-brain ratio (L/B), contrast-to-noise ratio (C/N) and % lesion enhancement (%En)) and qualitative assessment of lesion enhancement was performed by two independent fully-blinded off-site readers. Statistical significance for quantitative evaluations was determined using paired t-tests while significance for qualitative evaluations was determined using the Wilcoxon signed rank test.

Results: Images from 43/45 patients were available for quantitative assessment. After correction for pre-contrast values, significantly greater L/B ($p<0.003$), C/N ($p<0.03$) (Fig. 1) and %En ($p<0.0001$) was noted by both readers for Gd-BOPTA-enhanced images at all time-points from 2 min post-contrast. Qualitative matched-pairs assessment of all 45 patients revealed significant preference for Gd-BOPTA over combined comparator for lesion border delineation ($p<0.004$, both readers), lesion internal morphology ($p<0.008$, both readers), global contrast enhancement ($p<0.0001$, both readers) and global diagnostic preference ($p<0.0005$, both readers). Although not designed to evaluate lesion detection, more lesions were detected on post-dose images after Gd-BOPTA than after comparator agent (reader 1: 75 vs. 72; reader 2: 77 vs. 72). Similarly, inter-reader agreement was significantly greater after Gd-BOPTA (weighted kappa for contrast enhancement = 0.244; 95% C.I. 0.065, 0.422 after Gd-BOPTA vs. 0.094, 95% C.I. –0.078, 0.267 after comparator).





Gd-DTPA **Gd-BOPTA**

Conclusion: This extensive, fully blinded intra-individual comparison confirms that Gd-BOPTA has preferential contrast enhancing characteristics compared to conventional gadolinium agents. The superior contrast enhancement achieved with Gd-BOPTA may impact positively on overall patient management as well as pre-surgical planning and post-surgical follow-up. Moreover, the significantly greater enhancement at early post-contrast time-points may be clinically highly advantageous in permitting a greater daily throughput of patients.

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