

# Signal Enhancement of the Dentate Nucleus at Unenhanced MR Imaging after Very High Cumulative Doses of the Macrocyclic Gadolinium-based Contrast Agent Gadobutrol: An Observational Study\*

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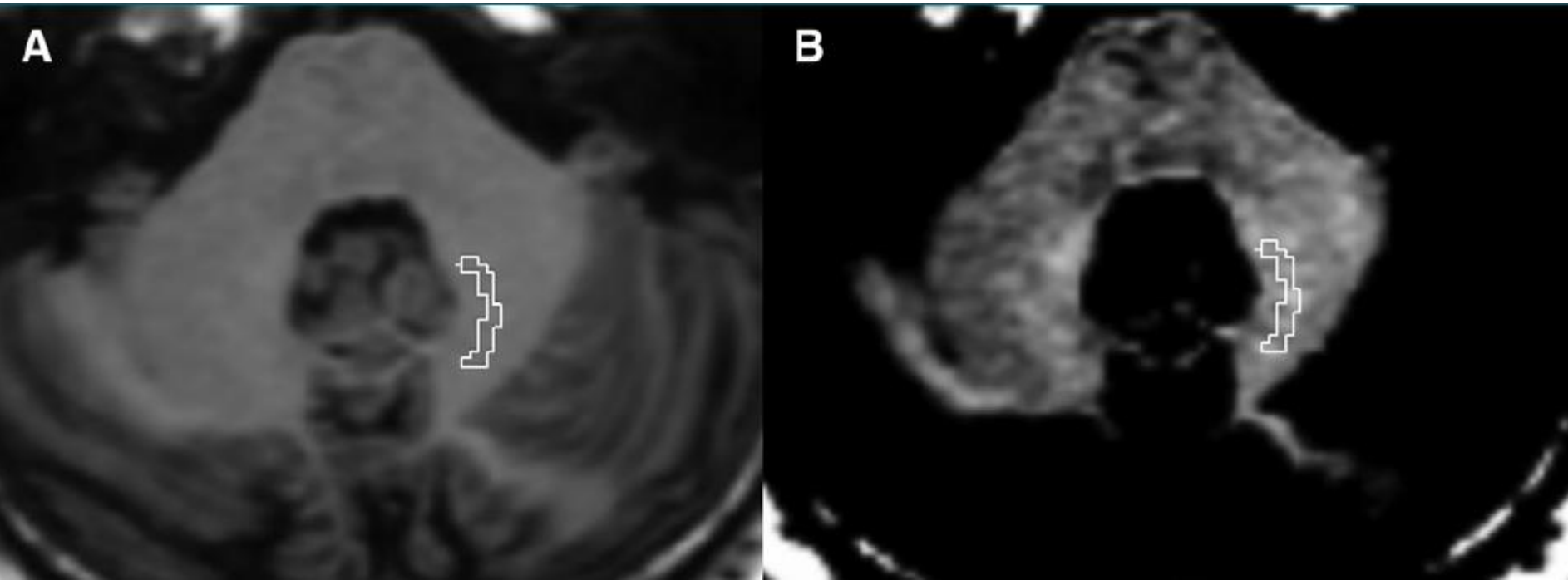
# Conflicts of Interest

I have participated (without honorarium) at a GE Healthcare expert meeting. My department has a research collaboration with GE Healthcare.

# Methods

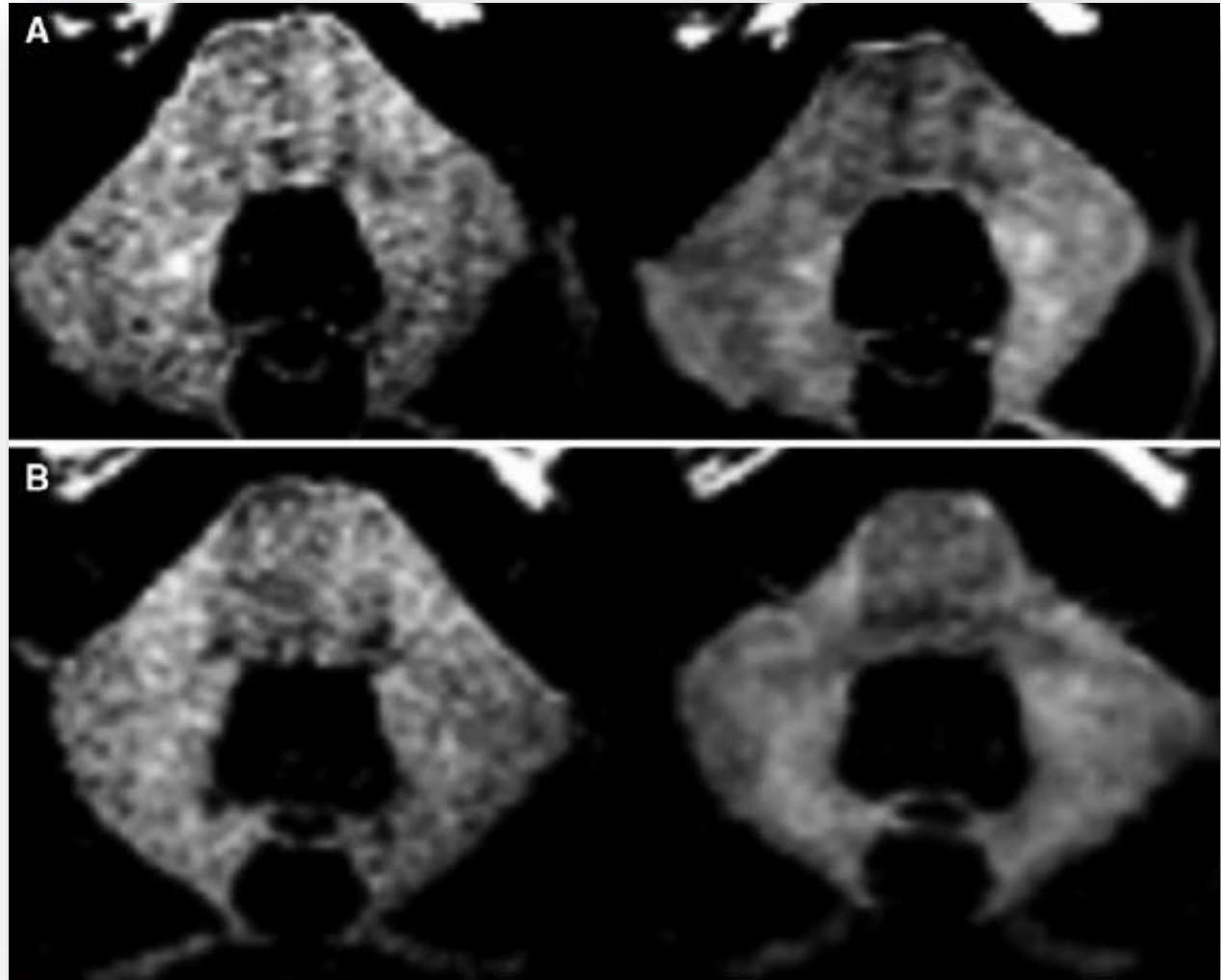
- Retrospective analysis of dentate nucleus (DN) signal enhancement on unenhanced T1-w series in patients with confirmed glioblastoma having received multiple macrocyclic (mc) gadolinium based contrast agent (GBCA) injections
- Exclusion criteria:
  - radiologically confirmed abnormality of the cerebellum and pons at any time
  - any injection of linear GBCA (or unknown GBCA) before entrance or during the glioma treatment monitoring study
  - less than five consecutive, exclusive administrations of 0.2 mmol Gd/ kg b.w of gadobutrol
- Included in analysis: 17 patients having received between 10 and 44 standard doses of the macrocyclic GBCA gadobutrol
- Analysis:
  - relative SI of DN/pons as function of GBCA dose
  - Visual evaluation by 2 neuroradiologists of DN enhancement on window/contrast optimized images (last scan-point vs baseline)

# Results



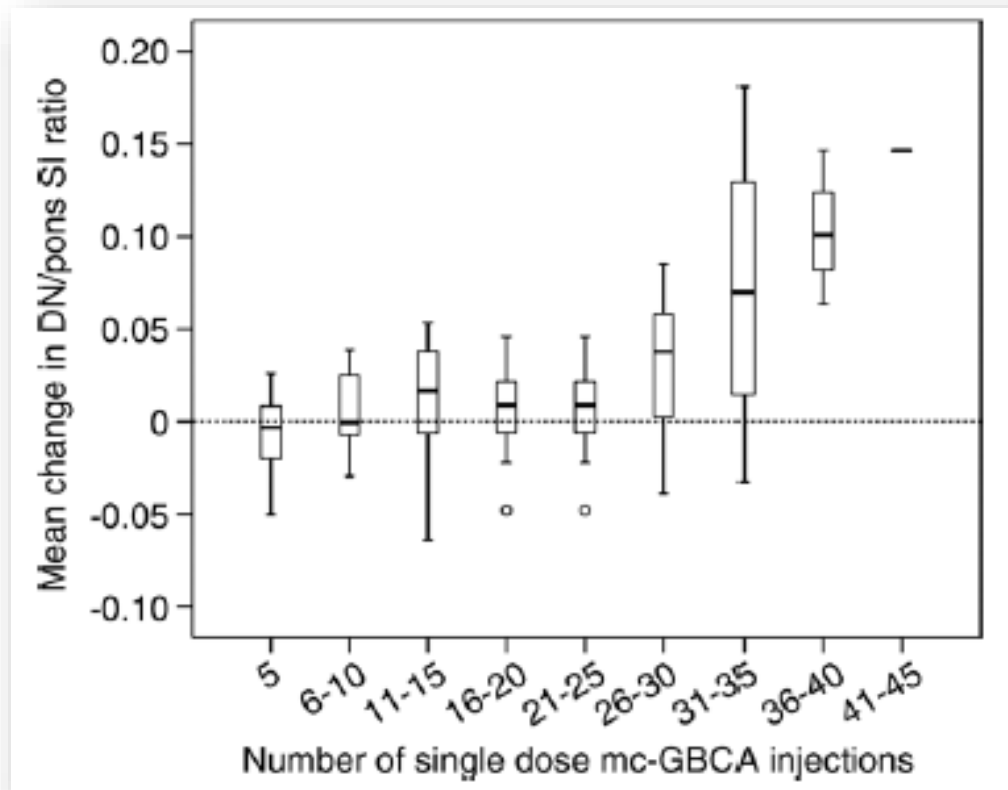
MR images show effect of optimizing image contrast for visualization of subtle intensity differences. A, Standard radiologic image window level and width and, B, optimized level and width. The white outline show the DN region of interest as defined by the radiologist.

# Results



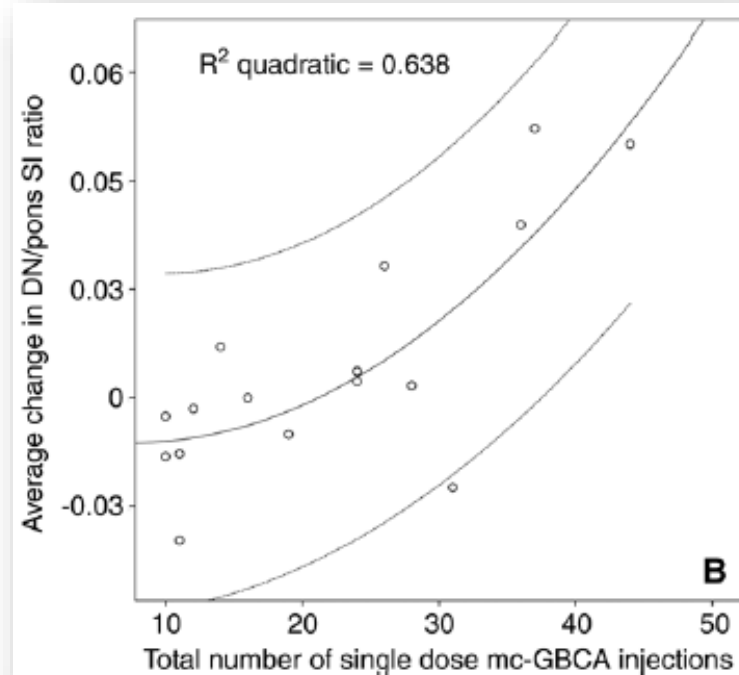
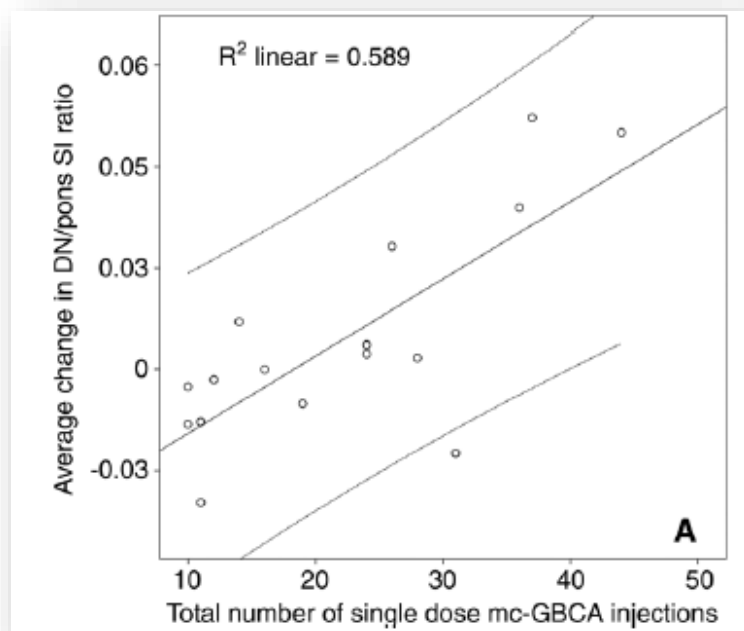
Unenhanced T1-weighted images from the two patients who were radiologically scored to have visible or strong DN enhancement at last time point (right column) and no DN enhancement at baseline examinations (left column).

# Results



Boxplot of mean change in DN-to-pons unenhanced T1-weighted SI ratio from baseline MR imaging examination as function of number of macrocyclic (*mc*) GBCA injections.

# Results



Scatterplots show change in DN-to-pons unenhanced T1-weighted SI ratio from baseline MR imaging examination to mean intensity ratio throughout all postbaseline examinations as function of number of single-dose macrocyclic (*mc*) GBCA injections. The corresponding, *A*, linear and, *B*, quadratic regression lines (center lines) and 95% confidence intervals (outer lines) are shown. Best fit was obtained with quadratic function.

# Conclusions

- We measured a small but statistically significant dose-dependent T1-weighted nSI enhancement in the DN after multiple administrations of the macrocyclic GBCA gadobutrol.
- The effect could only be radiologically visualized in two patients who received a very high cumulative dose of gadobutrol.
- Our results must be confirmed in larger and better controlled prospective studies, but they suggest that both linear and macrocyclic GBCAs can cause gadolinium retention, albeit at very different levels of total gadolinium exposure.