

Half-Dose Gadopiclenol versus Standard-Dose Gadobutrol for Contrast-Enhanced 3-T MRI of Meningiomas and Vestibular Schwannomas: Platform- and Protocol-Specific Differences in Routine Clinical Practice

Alexandra Todea

ramona.todea@usz.ch

Department of Neuroradiology, Clinical Neuroscience Center, University Hospital Zurich

Gergely Bertalan

Department of Neuroradiology, Clinical Neuroscience Center, University Hospital Zurich

Joshua Gartlehner

Department of Neuroradiology, Clinical Neuroscience Center, University Hospital Zurich

Zsolt Kulcsar

Department of Neuroradiology, Clinical Neuroscience Center, University Hospital Zurich

Nicolin Hainc

Department of Neuroradiology, Clinical Neuroscience Center, University Hospital Zurich

Research Article

Keywords: Meningioma, Vestibular schwannoma, MRI, high-relaxivity gadolinium contrast agent, gadopiclenol

Posted Date: October 14th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11103708/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Purpose

To compare image quality and quantitative lesion enhancement with half-dose gadopichlenol versus standard-dose gadobutrol in contrast-enhanced 3-T MRI of untreated meningiomas and vestibular schwannomas under routine clinical conditions, with attention to platform-/protocol-specific performance.

Methods

This retrospective, single-center exploratory study included patients undergoing MRI with gadopichlenol (November 2024 to May 2025) or gadobutrol (April 2023 to June 2025). Qualitative image assessment used a 4-point Likert scale. Quantitative metrics included percentage enhancement (E%), lesion-to-background ratio (LBR), and contrast-to-noise ratio (CNR). Because acquisition protocols differed between Siemens and Philips systems, comparisons were stratified by platform/protocol and, exploratorily, by tumor type.

Results

Seventy-six patients with 80 lesions were evaluated (mean ages, 65.8 and 64.2 years, respectively). With the Siemens protocol, E% was higher with gadopichlenol for both readers ($p = 0.01$ and $p = 0.0017$), whereas CNR was higher for Reader 1 only ($p = 0.03$) and LBR did not differ. With the Philips protocol, E%, LBR, and CNR were comparable between agents. Exploratory tumor-specific analyses with the Siemens protocol showed higher E% with gadopichlenol for meningiomas ($p = 0.0001$) and vestibular schwannomas ($p = 0.048$), and higher LBR for meningiomas ($p = 0.03$). Subjective image quality was comparable across settings. Inter-reader agreement was substantial to almost perfect for qualitative assessment (weighted κ , 0.61–0.86) and good for contrast-enhanced quantitative measurements (ICC, 0.78–0.84).

Conclusion

In this retrospective exploratory cohort, half-dose gadopichlenol maintained comparable qualitative image quality to standard-dose gadobutrol, while quantitative enhancement differences varied by acquisition platform/protocol. Higher E% was observed with the Siemens protocol, whereas quantitative metrics were comparable with the Philips protocol.

INTRODUCTION

Meningiomas and vestibular schwannomas are among the most frequently encountered extra-axial brain tumors [1] and are routinely evaluated with MRI after administration of gadolinium-based contrast agents (GBCAs). Given concerns about gadolinium deposition in human tissues following repeated GBCA exposure [2–5], strategies to minimize cumulative gadolinium dose are particularly relevant for patients requiring long-term surveillance. High-relaxivity GBCAs offer the possibility of reducing administered gadolinium dose while preserving diagnostically useful enhancement; however, their performance under heterogeneous routine clinical acquisition conditions remains incompletely characterized.

High-relaxivity GBCAs may provide equivalent or superior diagnostic and enhancement performance at reduced doses [6–9]. Gadopiclenol is a non-ionic macrocyclic GBCA with high kinetic stability which reduces the risk of gadolinium dissociation, addressing safety concerns [10]. It demonstrates approximately two- to threefold higher relaxivity at 1.5–3.0 T compared with previous-generation agents, enabling administration at half the standard gadolinium dose [11, 12]. The randomized double-blind PROMISE [13] and PICTURE [14] trials demonstrated that gadopiclenol at half the conventional gadolinium dose can preserve image quality and diagnostic performance. These controlled trials established reduced-dose efficacy; an important remaining question is how such performance translates to routine neuroradiologic practice across different acquisition platforms and protocols.

Routine clinical MRI is more heterogeneous than controlled trial imaging, with differences in scanner platform, sequence design, acquisition parameters, reconstruction, and post-processing. These factors can alter T1 weighting and measured signal intensity and may therefore influence quantitative comparisons between contrast agents. Evaluating reduced-dose gadopiclenol under such conditions is particularly relevant in meningiomas and vestibular schwannomas, which frequently require serial contrast-enhanced surveillance [15].

Accordingly, the aim of this exploratory study was to compare qualitative image quality and quantitative lesion enhancement with half-dose gadopiclenol and standard-dose gadobutrol in untreated meningiomas and vestibular schwannomas under routine 3-T MRI conditions, with analyses stratified by acquisition platform/protocol.

MATERIAL AND METHODS

Study design and population

This retrospective study was approved by the institutional review board and the ethics committee (BASEC 2025 – 00849), and all patients provided general informed consent.

Consecutive patients with meningiomas or vestibular schwannomas undergoing brain MRI at our institution between November 2024 and May 2025 received gadopiclenol (Elucirem, Guerbet) at 0.05 mmol/kg (0.5 mol solution, 0.1 mL/kg).

The comparator cohort received gadobutrol between April 2023 and June 2025 (Gadovist/Gadavist, Bayer Healthcare) at 0.1 mmol/kg (1.0 mol solution, 0.1 mL/kg). The longer period for gadobutrol cohort reflected eligible comparator examinations.

Eligible participants were adults (≥ 18 years) of either sex, undergoing contrast-enhanced MRI for untreated meningiomas or vestibular schwannomas.

Exclusion criteria were severe renal insufficiency (estimated glomerular filtration rate [eGFR] < 30 mL/min/1.73 m²; first trimester pregnancy; and previously treated meningiomas or schwannomas.

MRI and image analysis

All patients were scanned on 3 T scanners on Siemens Vida fit 3 T (Siemens Healthineers) and Philips 7700 3 T (Philips Healthcare). For meningiomas, three-dimensional T1-weighted sequences were used. On Siemens, the MPRAGE sequence was used with a repetition time (TR) of 2300 ms, echo time (TE) of 2.98 ms, inversion time (TI) of 900 ms, flip angle (FA) of 9°, field of view (FOV) of 256 × 256 mm², matrix size of 256 × 256, voxel size of 1 × 1 × 1 mm³, slice thickness of 1 mm, and 176 sagittal slices. An equivalent Philips T1-weighted sequence was acquired with the following parameters: AI TFE sequence TR/TE 9.16/4.29 ms, FA 8°, FOV 278 × 280 mm², matrix size of 278 × 280, voxel size of 1 × 1 × 1 mm³, slice thickness of 1 mm, and 188 sagittal slices.

For vestibular schwannomas, two-dimensional axial T1-weighted TSE images were assessed. Siemens: TR/TE 515/12 ms, FA 135°, FOV 403 × 243 mm², matrix 608 × 608, interpolated resolution 0.263 × 0.263, slice thickness 2 mm. Philips: TR/TE 699.1/7.45, FA 80°, FOV 328 × 279, matrix 480 × 480, interpolated resolution 0.375 × 0.375, slice thickness 2 mm.

Post-contrast T1-weighted imaging began approximately 5–6 minutes after contrast administration.

Two board-certified radiologists (AT and NH, both with 13 years of experience) independently evaluated all examinations using Dedalus DeepUnity Diagnost 2.0.2.2 (Dedalus Healthcare GmbH). Both readers were blinded to the contrast agent administered.

Quantitative analyses used region-of-interest (ROI)-based measurements performed on native and contrast-enhanced (CE) T1-weighted images. For each lesion, a circular ROI was placed within the solid enhancing component of the tumor on the post-contrast T1-weighted image, avoiding necrotic, cystic, or hemorrhagic areas. A standardized circular ROI with a mean area of approximately 20 mm² was used, with adjustments made only when required by lesion size or morphology. The ROI was then copied to the corresponding pre-contrast T1-weighted image. A reference ROI was placed in normal-appearing contralateral white matter, while a background noise ROI was positioned in an artifact-free area outside the head to estimate image noise.

For each ROI, mean signal intensity (Avg SI), signal intensity standard deviation (SI SD), and maximum signal intensity (Max SI) were recorded.

Qualitative and Quantitative parameters

Qualitative image assessment used a 4-point Likert scale [13] on native and CE T1-weighted images evaluating: 1) overall image quality, reflecting the general diagnostic acceptability of the images, including contrast, artifacts, and adequacy for tumor evaluation; 2) subjective image noise, referring to the perceived level of background signal variation that could impair visualization of anatomical structures or lesions; 3) border delineation, defined as the clarity of the tumor margins and the ability to distinguish the lesion from adjacent structures; and 4) internal tumor morphology, including the visualization of internal tumor characteristics such as heterogeneity, internal architecture, and structural details. Scores were: 1 = poor non-diagnostic; 2 = mediocre, limited diagnostic value (hard to see details); 3 = good for most diagnoses; 4 = excellent, optimal image quality.

Quantitative analysis included 1) enhancement percentage (E%), 2) lesion-to-background ratio (LBR), and 3) contrast-to-noise ratio (CNR) [14].

The E% represents the increase in the lesion's signal intensity on the contrast-enhanced sequences relative to its baseline (pre-contrast) value. CNR measures the degree to which a lesion can be distinguished from background noise on the image. The LBR quantifies the visibility of a lesion relative to the surrounding normal reference tissue.

Lesion-to-background ratio was calculated as the ratio between the signal intensity of the lesion on CE T1-weighted imaging (SI_{post}) and the signal intensity of the reference tissue (SI_{ref}):

$$LBR = \frac{SI_{post}}{SI_{ref}}$$

Enhancement percentage was calculated from the difference between lesion signal intensity on CE T1-weighted images (SI_{post}) and native T1-weighted images (SI_{pre}), relative to SI_{pre}.

$$E\% = \frac{SI_{post} - SI_{pre}}{SI_{pre}} \times 100$$

CNR was calculated as the difference between lesion signal intensity (SI_{lesion}) and reference-tissue signal intensity (SI_{ref}), divided by the standard deviation of background noise (σ_{noise}):

$$CNR = \frac{SI_{lesion} - SI_{ref}}{\sigma_{noise}}$$

Statistical analysis

Statistical analyses were performed using SPSS Statistics (IBM Corp., Armonk, NY, USA) and Matlab 2022 (The MathWorks, Natick, MA, USA). Both qualitative and quantitative imaging measures were analyzed. Because the Siemens and Philips examinations used different acquisition protocols, comparisons between gadopichlenol and gadobutrol were stratified by acquisition platform/protocol. Tumor-type analyses were considered exploratory subgroup analyses.

For the comparison of enhancement values between contrast agents, lesions were used as the unit of analysis. Two patients contributed two meningioma lesions each. Given this small number of patients with multiple lesions, lesion-level comparisons were performed without additional adjustment for within-patient clustering. Between-group differences were assessed using the Wilcoxon rank-sum test for independent samples. Descriptive statistics are presented as median. Categorical variables were compared using the chi-square test or Fisher's exact test.

In addition, an exploratory reference-centered analysis was performed to quantify gadopichlenol enhancement relative to gadobutrol cohort. For each subgroup, the mean gadobutrol value was used as the empirical reference, and each gadopichlenol measurement was centered by subtracting this reference value. The mean reference-centered difference and corresponding 95% interval were then calculated. These intervals were used for descriptive visualization only and should not be interpreted as conventional confidence intervals for the between-group treatment effect. Statistical inference was based on the Wilcoxon rank-sum tests.

Qualitative scores were analyzed using non-parametric methods. Inter-reader agreement between the two radiologists was assessed using Cohen's weighted kappa coefficient for qualitative parameters and intraclass correlation coefficients (ICC) for quantitative measurements. A two-sided p value < 0.05 was considered statistically significant. Given the exploratory design, modest subgroup sizes, and multiple comparisons, p values were not adjusted for multiplicity and should be interpreted as descriptive evidence rather than confirmatory hypothesis testing. This study was reported according to STROBE.

RESULTS

Study population

The study included 76 patients with 80 lesions: 36 patients received gadopichlenol and 40 gadobutrol. Mean age $\pm$ SD was 65.8 ± 13.4 and 64.2 ± 14.6 years, respectively. The gadopichlenol group comprised 19 patients with meningiomas and 17 with schwannomas; the gadobutrol group comprised 23 and 17, respectively. There were 21 meningiomas and 17 schwannomas in the gadopichlenol group and 25 and 17, respectively, in the gadobutrol group. Two patients in the Philips 7700 subgroup had two meningiomas. All lesions were untreated (Table 1.)

Table 1
Distribution of the patients by tumor type, contrast agent and MRI scanner

Patient and Lesion Distribution in the Gadopiclenol and Gadobutrol Cohorts Across MRI Scanners stratified by tumor type				
Type of tumor	Contrast agent administered	3T MRI scanner	Number of patients	Number of lesions
Meningiomas	Gadopiclenol	Siemens Vida fit	10	10
		Philips 7700	9	11
	Gadobutrol/Controls	Siemens Vida fit	11	12
		Philips 7700	12	13
	Total			42 patients
Schwannomas	Gadopiclenol	Siemens Vida fit	9	9
		Philips 7700	8	8
	Gadobutrol/Controls	Siemens Vida fit	9	9
		Philips 7700	8	8
	Total			34 patients
Total			76 patients	80 lesions

Contrast-enhancement variability by MRI acquisition platform/protocol

Platform-/protocol-stratified results are shown in Table 2. and Figs. 1–2.

With the Siemens Vida Fit protocol, gadopiclenol showed significantly higher E% than gadobutrol for Reader 1 ($p = 0.01$) and Reader 2 ($p = 0.0017$). In the descriptive reference-centered analysis mean differences were 45.75 (95% interval, 20.00–71.50) and 72.20 (28.55–115.86), respectively. Median AvgSI was 209.86 versus 151.24 for Reader 1 and 208.74 versus 140.70 for Reader 2.

CNR was significantly higher with gadopiclenol for Reader 1 ($p = 0.03$; reference-centered difference, 165.13; 95% interval, 13.78–316.49) but not Reader 2. LBR did not differ for either reader (Fig. 1.)

With the Philips 7700 protocol, E% did not differ between agents for Reader 1 ($p = 0.89$; reference-centered difference, – 5.57; 95% interval, – 24.73 to 13.60) or Reader 2 ($p = 0.76$; difference, 3.32; 95% interval, – 17.53 to 24.17). LBR and CNR were also comparable (Fig. 2).

Table 2

Scanner-stratified quantitative enhancement metrics for gadopichlenol and gadobutrol. (AvgSI = average signal intensity; MaxSI = maximum signal intensity; E% = percentage enhancement; LBR = lesion-to-background ratio; CNR = contrast-to-noise ratio.)

MRI platform	Metric	Reader	Gadopichlenol median	Gadobutrol median	Mean reference-centered difference	95% reference-centered interval	p-value
Siemens Vida fit	E%, AvgSI	Reader 1	209.86	151.24	45.75	20.00 to 71.50	0.01
Siemens Vida fit	E%, AvgSI	Reader 2	208.74	140.70	72.20	28.55 to 115.86	0.0017
Siemens Vida fit	E%, MaxSI	Reader 1	227.69	165.23	50.65	21.34 to 79.96	0.02
Siemens Vida fit	E%, MaxSI	Reader 2	248.36	151.69	79.35	39.72 to 118.99	0.0023
Siemens Vida fit	LBR, AvgSI	Reader 1	2.21	2.21	0.35	-0.03 to 0.73	0.17
Siemens Vida fit	LBR, AvgSI	Reader 2	2.27	2.07	0.22	-0.01 to 0.44	0.29
Siemens Vida fit	LBR, MaxSI	Reader 1	2.51	2.49	0.44	-0.22 to 1.09	0.46
Siemens Vida fit	LBR, MaxSI	Reader 2	2.54	2.34	0.11	-0.21 to 0.43	0.56
Siemens Vida fit	CNR, AvgSI	Reader 1	186.42	79.25	165.13	13.78 to 316.49	0.03
Siemens Vida fit	CNR, AvgSI	Reader 2	164.67	150.08	31.94	-23.65 to 87.53	0.31
Siemens Vida fit	CNR, MaxSI	Reader 1	271.43	120.62	211.14	15.84 to 406.45	0.06
Siemens Vida fit	CNR, MaxSI	Reader 2	245.33	227.50	18.36	-41.72 to 78.44	0.64
Philips 7700	E%, AvgSI	Reader 1	62.61	82.15	-5.57	-24.73 to 13.60	0.89
Philips 7700	E%, AvgSI	Reader 2	65.47	64.10	3.32	-17.53 to 24.17	0.77
Philips 7700	E%, MaxSI	Reader 1	59.77	81.75	-4.04	-26.52 to 18.44	0.94
Philips 7700	E%, MaxSI	Reader 2	61.56	81.77	-9.35	-30.81 to 12.11	0.65

MRI platform	Metric	Reader	Gadopichlenol median	Gadobutrol median	Mean reference-centered difference	95% reference-centered interval	p-value
Philips 7700	LBR, AvgSI	Reader 1	2.18	2.02	-0.01	-0.25 to 0.22	0.87
Philips 7700	LBR, AvgSI	Reader 2	2.08	1.81	0.08	-0.09 to 0.24	0.52
Philips 7700	LBR, MaxSI	Reader 1	2.45	2.64	0.02	-0.24 to 0.29	0.79
Philips 7700	LBR, MaxSI	Reader 2	2.18	2.13	-0.03	-0.24 to 0.17	0.98
Philips 7700	CNR, AvgSI	Reader 1	208.00	234.75	33.18	-114.54 to 180.89	0.89
Philips 7700	CNR, AvgSI	Reader 2	520.00	357.00	75.52	-65.40 to 216.44	0.51
Philips 7700	CNR, MaxSI	Reader 1	338.75	232.50	51.86	-124.25 to 227.96	0.79
Philips 7700	CNR, MaxSI	Reader 2	613.00	557.00	-2.89	-159.66 to 153.88	0.91

Exploratory contrast-enhancement analyses by tumor type and MRI acquisition platform/protocol

In exploratory tumor-specific analyses with the Siemens Vida Fit protocol, gadopichlenol showed higher E% than gadobutrol for both tumor types.

For meningiomas, E% was higher with gadopichlenol ($p = 0.0001$; reference-centered difference, 88.04; 95% interval, 47.71–128.37), with median AvgSI values of 239.20 versus 141.50.

For vestibular schwannomas, E% was also higher with gadopichlenol ($p = 0.048$; reference-centered difference, 29.65; 95% interval, 8.65–50.64), with median AvgSI values of 183.50 versus 148.37. Given the exploratory subgroup analysis and multiple comparisons, the borderline p value should be interpreted cautiously.

LBR was higher with gadopichlenol only for meningiomas ($p = 0.03$; medians, 1.98 versus 1.78; 95% reference-centered interval, 0.10–0.81) but did not differ for vestibular schwannomas ($p = 0.64$; 95% interval, -0.2 to 0.3).

CNR did not differ for meningiomas ($p = 0.12$) or vestibular schwannomas ($p = 0.09$); corresponding 95% reference-centered intervals were -2.2 to 278 and 13.1–110, respectively (Fig. 3.)

With the Philips 7700 protocol, E%, LBR, and CNR were comparable between agents for both tumor types (Fig. 4.).

Inter-reader agreement was excellent for native lesion signal intensity (ICC, 0.909–0.944) and good for contrast-enhanced lesion signal intensity (ICC, 0.782–0.839). Agreement was lower for background and non-enhancing white matter measurements. Agreement was higher for contrast-enhanced images, with weighted κ values ranging from 0.79 to 0.86, than for native images, with weighted κ values ranging from 0.61 to 0.78. The highest agreement was observed for overall image quality and subjective noise assessment, whereas border delineation showed comparatively lower agreement. Representative cases are shown in Fig. 5.

DISCUSSION

The principal finding of this retrospective exploratory study is that half-dose gadopichlenol (0.05 mmol/kg) maintained qualitative image quality comparable to standard-dose gadobutrol (0.1 mmol/kg) in untreated meningiomas and vestibular schwannomas under routine clinical conditions, while quantitative enhancement differences varied by acquisition platform/protocol. The most reproducible quantitative difference was higher E% with gadopichlenol using the Siemens Vida Fit protocol; with the Philips 7700 protocol, E%, LBR, and CNR were comparable between agents.

This pattern is important because the study was not designed as a repeat demonstration of reduced dose gadopichlenol efficacy under standardized trial conditions. Rather, it evaluates how the relative quantitative performance of the two agents appears under heterogeneous routine clinical protocols. CNR and LBR findings were less consistent than E%, including reader-specific and tumor-specific differences, emphasizing that isolated nominally significant results should not be interpreted as uniform superiority of one agent across all quantitative measures.

Several studies have assessed gadopichlenol in CNS lesions. Bendzus et al. [16] conducted a double-blind, randomized, controlled cross-over phase IIb study of 240 patients with meningiomas, brain metastases and glial tumors both on 1.5 and 3T scanners. Compared with gadobenate dimeglumine at 0.1 mmol/kg, gadopichlenol at 0.1 mmol/kg achieved significantly higher CNR, LBR and E%, while gadopichlenol at 0.05 mmol/kg demonstrated comparable quantitative performance [16, 17]. The pivotal phase III PICTURE [14] study compared gadopichlenol at 0.05 mmol/kg with gadobutrol at 0.1 mmol/kg. Gadopichlenol demonstrated noninferiority to gadobutrol for all parameters and all readers ($p < 0.0001$). Quantitatively, gadopichlenol showed higher LBR and E% for all readers and higher CNR for two of three readers.

The present study complements these and other controlled data [13, 14, 18, 19] by focusing specifically on meningiomas and vestibular schwannomas imaged in routine practice across two 3-T acquisition settings. The findings were not uniform across platform-/protocol-specific: higher E% with gadopichlenol was reproducible across both readers with the Siemens protocol, whereas quantitative metrics were comparable with the Philips protocol. LBR and CNR differences were less consistent across readers and

tumor subgroups. Taken together, these observations suggest that sequence and protocol characteristics may influence quantitative estimates of relative contrast enhancement and should be considered when translating high-relaxivity contrast-agent data across clinical MRI settings.

A potential explanation for platform-/protocol-dependent differences is variation in MRI sequence design and post-processing. Acquisition parameters such as field strength [20, 21], repetition time, echo time, inversion time, flip angle, and k-space sampling may influence T1-weighting and sensitivity to contrast-agent relaxivity [22, 23]. Vendor-specific reconstruction and post-processing may also modify signal intensity and contrast-to-noise relationships [24]. Importantly, scanner vendor and acquisition protocol were not independently varied in this study. The observed differences therefore cannot be attributed to vendor alone and should be interpreted only as differences between the specific platform/protocol combinations studied. The comparable quantitative performance with the Philips protocol and higher E% with the Siemens protocol nevertheless indicate that half-dose gadopichlenol maintained at least comparable qualitative performance under the routine clinical conditions evaluated.

Although real-world clinical data enhance the clinical relevance of the study, several limitations should be acknowledged. The retrospective design and relatively small cohort limit the generalizability of the findings. In addition, the contrast agents were evaluated in different patient cohorts rather than intra-individually, introducing potential inter-individual variability. Furthermore, Siemens and Philips examinations used different acquisition protocols; therefore, the observed differences should be interpreted as platform-/protocol-specific rather than vendor-specific. Finally, because meningiomas and schwannomas typically show conspicuous enhancement, this study focused on image quality and quantitative enhancement rather than lesion detection or diagnostic performance.

In conclusion, half-dose gadopichlenol provided comparable or, for selected quantitative measures, higher lesion enhancement than standard-dose gadobutrol in untreated meningiomas and vestibular schwannomas. The most consistent difference was higher percentage enhancement with the Siemens protocol, whereas quantitative metrics were comparable with the Philips protocol. These findings support the potential use of half-dose gadopichlenol while highlighting the influence of platform- and protocol-specific characteristics on quantitative enhancement measurements.

Abbreviations

GBCAs gadolinium
based contrast agents

T1W

CE T1-weighted contrast enhanced
E% Enhancement percentage

LBR lesion to background ratio

CNR contrast to noise ratio

CNS central nervous system

SD standard deviation

Declarations

Author Contribution

CREDIT Authorship: Conceptualization AT, NH, ZK Methodology AT, NH, GB Software AT, NH, GB Formal analysis AT, NH, GB Investigation AT, NH, GB Resources AT, NH, ZK Data Curation AT, NH, ZK Writing - Original Draft AT, GB Writing - Review & Editing AT, GB, JG, NH, ZK Visualization AT, GB Supervision AT, NH, ZK Project administration AT, NH, ZK

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request, subject to applicable ethical and data protection requirements.

References

1. Price M, Ballard CAP, Benedetti JR, Kruchko C, Barnholtz-Sloan JS, Ostrom QT. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2018–2022. *Neuro-Oncology*. 2025;27(Supplement_4):iv1–iv66. doi: 10.1093/neuonc/noaf194.
2. Kanda T, Ishii K, Kawaguchi H, Kitajima K, Takenaka D. High Signal Intensity in the Dentate Nucleus and Globus Pallidus on Unenhanced T1-weighted MR Images: Relationship with Increasing Cumulative Dose of a Gadolinium-based Contrast Material. *Radiology*. 2013;270(3):834–41. doi: 10.1148/radiol.13131669.
3. Guo BJ, Yang ZL, Zhang LJ. Gadolinium Deposition in Brain: Current Scientific Evidence and Future Perspectives. *Front Mol Neurosci*. 2018;11:335. doi: 10.3389/fnmol.2018.00335.
4. van der Molen AJ, Quattrocchi CC, Mallio CA, Dekkers IA, for the European Society of Magnetic Resonance in Medicine BGREC. Ten years of gadolinium retention and deposition: ESMRMB-GREC looks backward and forward. *European Radiology*. 2024;34(1):600–11. doi: 10.1007/s00330-023-10281-3.
5. Starekova J, Pirasteh A, Reeder SB. Update on Gadolinium-Based Contrast Agent Safety, From the AJR Special Series on Contrast Media. *American Journal of Roentgenology*. 2024;223(3):e2330036. doi: 10.2214/ajr.23.30036.
6. Dapeng Hao MD P, Tao Ai MD, MS, Frank Goerner PhD, Xuemei Hu MD, PhD, Val M. Runge MD, Michael Tweedle PhD. MRI contrast agents: Basic chemistry and safety. *Journal of Magnetic Resonance Imaging*. 2012;Volume 36(Issue 5):pp. 1060–71. doi: <https://doi.org/10.1002/jmri.23725>.

7. Runge VM, Heverhagen JT. Advocating the Development of Next-Generation High-Relaxivity Gadolinium Chelates for Clinical Magnetic Resonance. *Investigative Radiology*. 2018;53(7).
8. Kanal E, Maravilla K, Rowley HA. Gadolinium contrast agents for CNS imaging: current concepts and clinical evidence. *AJNR Am J Neuroradiol*. 2014;35(12):2215–26. doi: 10.3174/ajnr.A3917.
9. Jin T, Ge M, Huang R, Yang Y, Liu T, Zhan Q, et al. Utility of Contrast-Enhanced T2 FLAIR for Imaging Brain Metastases Using a Half-dose High-Relaxivity Contrast Agent. *AJNR Am J Neuroradiol*. 2021;42(3):457–63. doi: 10.3174/ajnr.A6931.
10. Robic C, Port M, Rousseaux O, Louguet S, Fretellier N, Catoen S, et al. Physicochemical and Pharmacokinetic Profiles of Gadopiclenol: A New Macrocyclic Gadolinium Chelate With High T1 Relaxivity. *Investigative Radiology*. 2019;54(8):475–84. doi: 10.1097/rli.0000000000000563.
11. Robert P, Vives V, Grindel AL, Kremer S, Bierry G, Louin G, et al. Contrast-to-Dose Relationship of Gadopiclenol, an MRI Macrocyclic Gadolinium-based Contrast Agent, Compared with Gadoterate, Gadobenate, and Gadobutrol in a Rat Brain Tumor Model. *Radiology*. 2020;294(1):117–26. doi: 10.1148/radiol.2019182953.
12. Napolitano R, Guidolin N, Boccalon M, Fringuello Mingo A, Colombo Serra S, Buonsanti F, et al. Chiral Switch of Gadopiclenol: New Standards in MRI Probes. *Advanced Science*. 2025;12(14):2415321. doi: <https://doi.org/10.1002/adv.202415321>.
13. Kuhl C, Csősz T, Piskorski W, Miszalski T, Lee J-M, Otto PM. Efficacy and Safety of Half-Dose Gadopiclenol versus Full-Dose Gadobutrol for Contrast-enhanced Body MRI. *Radiology*. 2023;308(1):e222612. doi: 10.1148/radiol.222612.
14. Loevner LA, Kolumban B, Hutóczki G, Dziadziuszko K, Bereczki D, Bago A, et al. Efficacy and Safety of Gadopiclenol for Contrast-Enhanced MRI of the Central Nervous System: The PICTURE Randomized Clinical Trial. *Invest Radiol*. 2023;58(5):307–13. doi: 10.1097/rli.0000000000000944.
15. Lancelot E, Raynaud JS, Desché P. Current and Future MR Contrast Agents: Seeking a Better Chemical Stability and Relaxivity for Optimal Safety and Efficacy. *Invest Radiol*. 2020;55(9):578–88. doi: 10.1097/rli.0000000000000684.
16. Bendszus M, Roberts D, Kolumban B, Meza JA, Bereczki D, San-Juan D, et al. Dose Finding Study of Gadopiclenol, a New acrocyclic Contrast Agent, in MRI of Central Nervous System. *Investigative Radiology*. 2020;55(3).
17. Hao J, Pitrou C, Bourrinet P. A Comprehensive Overview of the Efficacy and Safety of Gadopiclenol: A New Contrast Agent for MRI of the CNS and Body. *Invest Radiol*. 2024;59(2):124–30. doi: 10.1097/rli.0000000000001025.
18. Gendron C, Bourrinet P, Dencausse A, Fretellier N. Preclinical Safety Assessment of Gadopiclenol: A High-Relaxivity Macrocyclic Gadolinium-Based MRI Contrast Agent. *Investigative Radiology*. 2024;59(2).
19. Bradu A, Penescu M, Pitrou C, Hao J, Bourrinet P. Pharmacokinetics, Dialysability, and Safety of Gadopiclenol, a New Gadolinium-Based Contrast Agent, in Patients With Impaired Renal Function. *Investigative Radiology*. 2021;56(8).

20. Rinck PA, Muller RN. Field strength and dose dependence of contrast enhancement by gadolinium-based MR contrast agents. *European Radiology*. 1999;9(5):998–1004. doi: 10.1007/s003300050781.
21. Rohrer M, Bauer H, Mintorovitch J, Requardt M, Weinmann H-J. Comparison of Magnetic Properties of MRI Contrast Media Solutions at Different Magnetic Field Strengths. *Investigative Radiology*. 2005;40(11).
22. Marth T, Froehlich JM, Nanz D, Sutter R. Gadolinium concentration dependent signal enhancement profiles using routine clinical sequences with gadopichlenol, gadoterate, gadobutrol, and gadoxetate at 1.5, 3 and 7 Tesla. *European Journal of Radiology*. 2025;191:112322. doi: <https://doi.org/10.1016/j.ejrad.2025.112322>.
23. van der Velden BHM, van Rijssel MJ, Lena B, Philippens MEP, Loo CE, Ragusi MAA, et al. Harmonization of Quantitative Parenchymal Enhancement in T1-Weighted Breast MRI. *Journal of Magnetic Resonance Imaging*. 2020;52(5):1374–82. doi: <https://doi.org/10.1002/jmri.27244>.
24. Keenan KE, Gimbutas Z, Dienstfrey A, Stupic KF, Boss MA, Russek SE, et al. Multi-site, multi-platform comparison of MRI T1 measurement using the system phantom. *PLOS ONE*. 2021;16(6):e0252966. doi: 10.1371/journal.pone.0252966.

Figures

Comparison of quantitative enhancement metrics between gadopixelenol (0.05 mmol/kg) and gadobutrol (0.1 mmol/kg) on 3T Siemens Vida fit

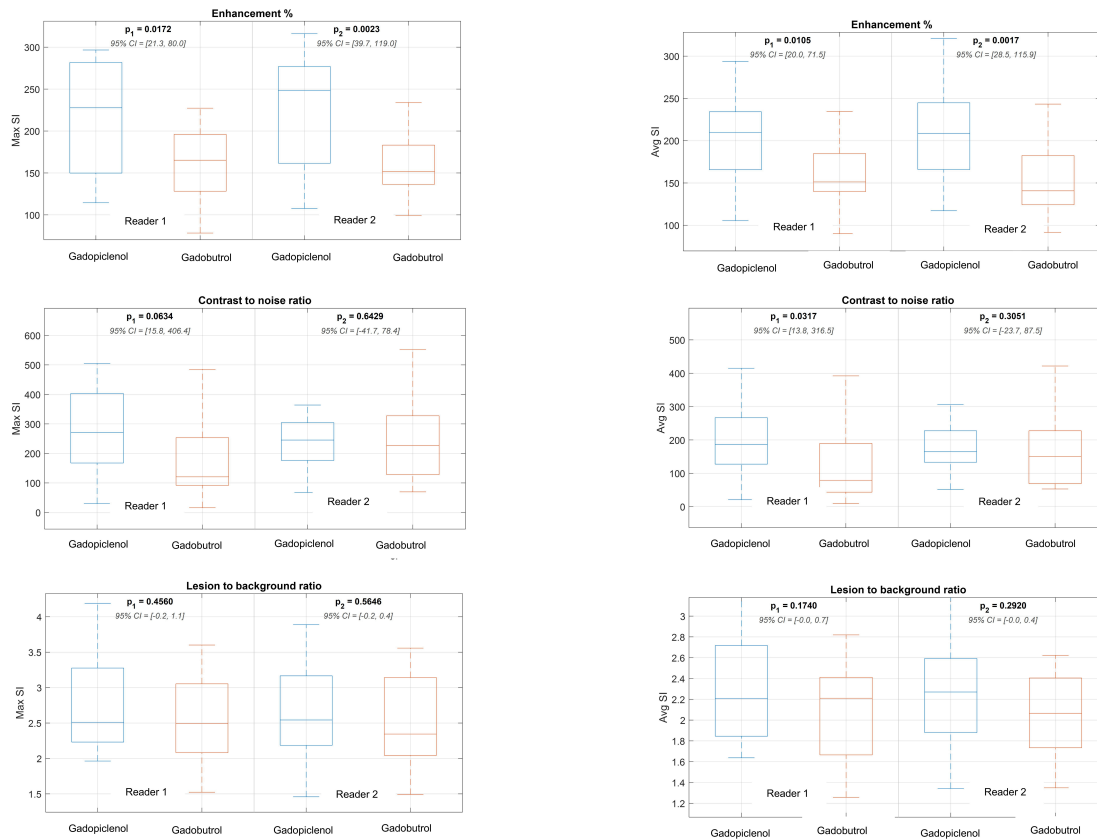


Figure 1

Comparison of quantitative enhancement metrics between gadopixelenol (0.05 mmol/kg) and gadobutrol (0.1 mmol/kg) on a 3T Siemens Vida fit scanner for brain meningiomas and schwannomas analyzed together (Avg SI – average signal intensity; Max SI – maximal signal intensity).

Comparison of quantitative enhancement metrics between gadopixelenol (0.05 mmol/kg) and gadobutrol (0.1 mmol/kg) on a 3T Philips 7700 scanner

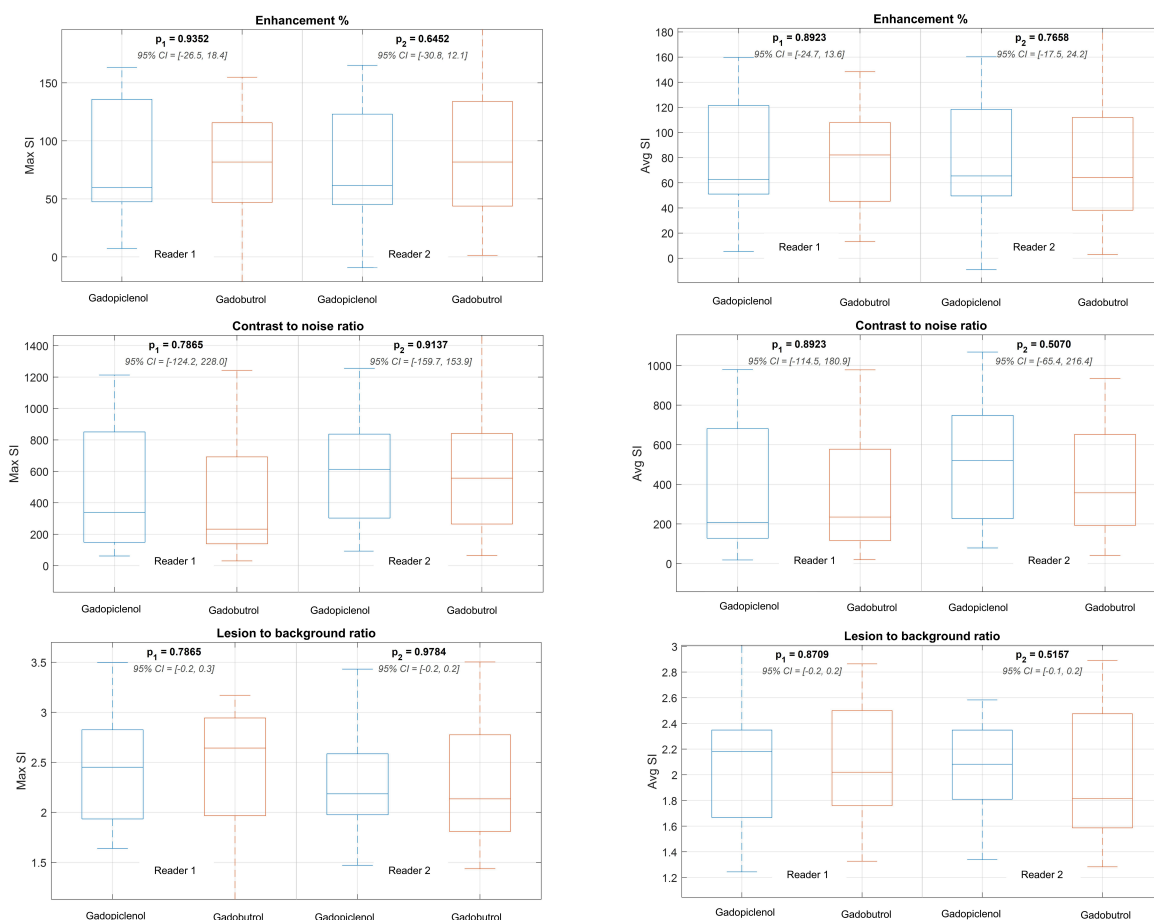


Figure 2

Comparison of quantitative enhancement metrics between gadopixelenol (0.05 mmol/kg) and gadobutrol (0.1 mmol/kg) on a 3T Philips 7700 scanner for brain meningiomas and schwannomas analyzed together (Avg SI – average signal intensity; Max SI – maximal signal intensity).

Comparison of quantitative enhancement metrics between gadopixelenol (0.05 mmol/kg) and gadobutrol (0.1 mmol/kg) on Philips 7700 scanner stratified by tumor type

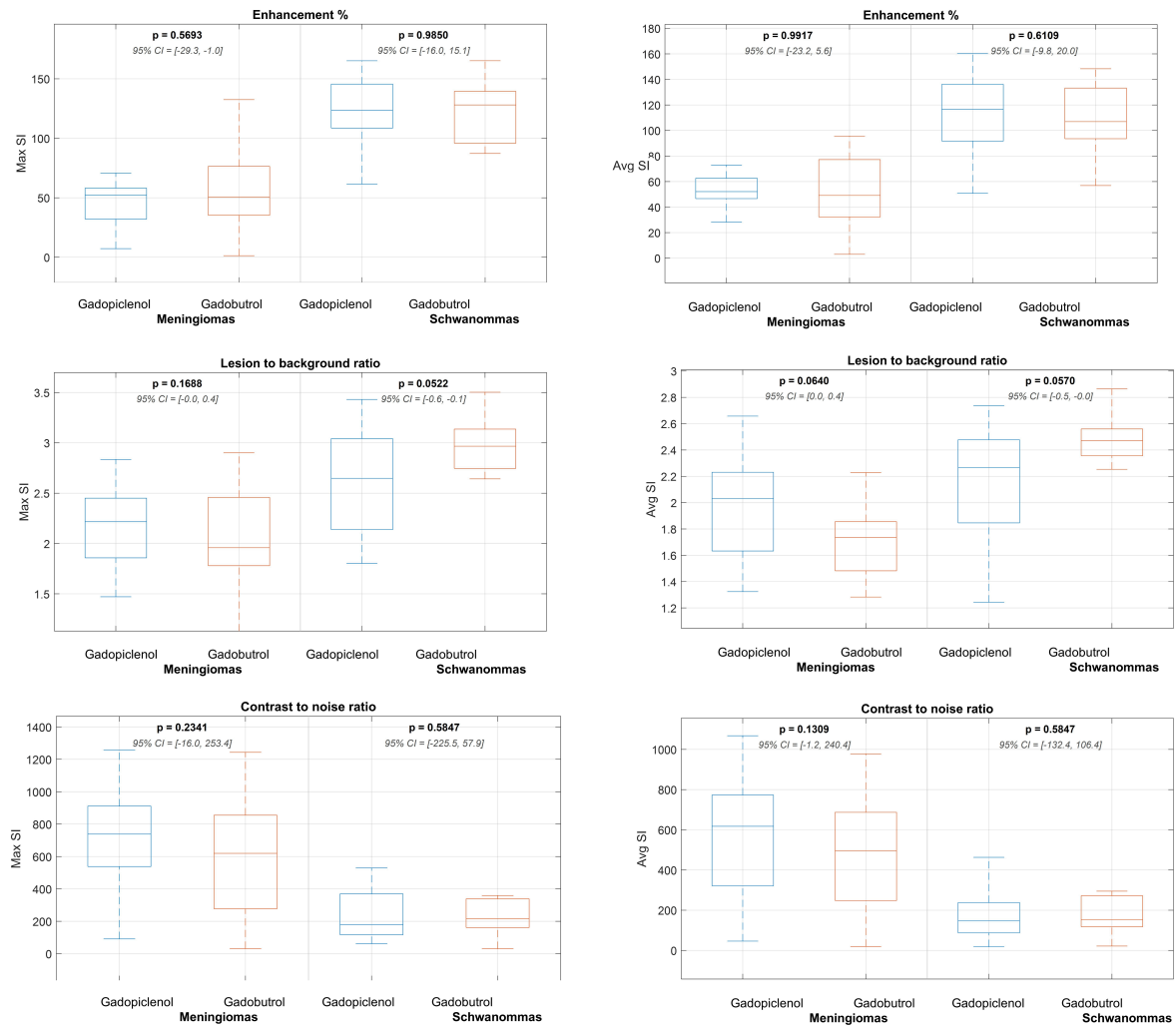


Figure 4

Comparison of quantitative enhancement metrics between gadopixelenol (0.05 mmol/kg) and gadobutrol (0.1 mmol/kg) on a Philips 7700 scanner for two readers, stratified by tumor type, in brain meningiomas and vestibular schwannomas (Avg SI = average signal intensity; Max SI = maximum signal intensity).

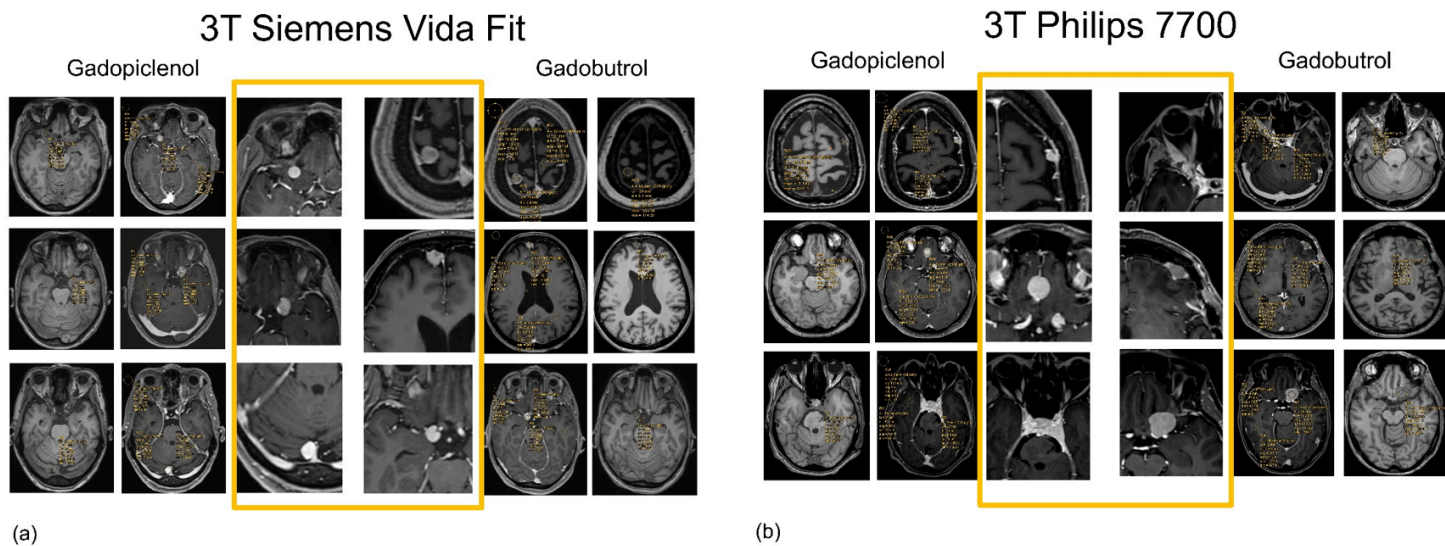


Figure 5

Example of enhancement of meningiomas on (a) Siemens Vida fit and (b) Philips 7700