Gadovist® 1.0
Gadobutrol

Valuable Diagnostic Imaging for CNS

Brain Tumor Diagnosis

The Gadovist® effect for imaging of the central nervous system (CNS)

In brain tumor diagnosis, Gadovist® can show comparably higher contrast enhancement than other macrocyclic gadolinium-based contrast agents (GBCAs).[1-3]

In summary, these studies[1-3] show that, in CNS imaging, this:

- enhances lesion detection in brain metastasis
- provides high lesion conspicuity
- enables assessment of malignancy

Why Gadovist® Can Be Preferable to Other GBCAs

Quantitative and qualitative study results show the favorable image quality of Gadovist® for lesion-to-brain contrast compared to competitors and in several MR sequences.[1-3] Readers in these studies favored Gadovist® over ProHance® and Dotarem®.[1-4]

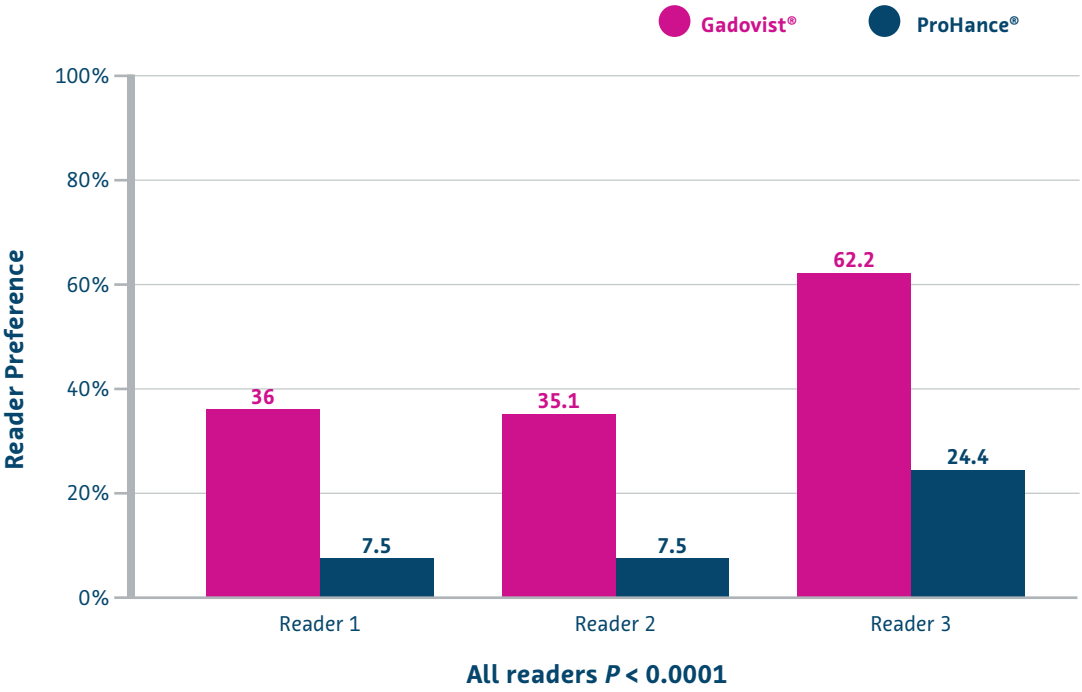
Clear Direction. From Diagnosis to Care.

Clinical Benefits

- **Potential impact on therapeutic decisions**
  Readers' overall preference for Gadovist® in diagnostic image quality indicates a potential impact on therapeutic decisions.[1]
- **Supports early diagnosis and treatment planning in primary and secondary brain tumors**
  High contrast enhancement supports early diagnosis and may have significant relevance for treatment planning in primary and secondary brain tumors.[1-4]
- **Potentially earlier assessment of malignancy with Gadovist®**
  Early diagnosis of poorly enhancing malignant lesions can result in earlier therapeutic intervention.[2]

Image Quality – Reader Preference[2]

Gadovist® vs. ProHance®



Higher preference rate for image quality with Gadovist® compared to ProHance®.[2]

Studies such as these show that Gadovist® can enhance more than just the image. Higher contrast enhancement can lead to faster and more consistent diagnosis, which in turn can mean more effective treatment,[2] helping to improve the patient journey.

MRI Techniques

Getting the Best From Gadovist®

Various MR imaging techniques support different tasks, such as brain tumor diagnosis, treatment response, and multiple sclerosis (MS) monitoring. Each has intrinsically different characteristics and can optimize the enhancement effects of Gadovist®.

Optimizing the Contrast Rate

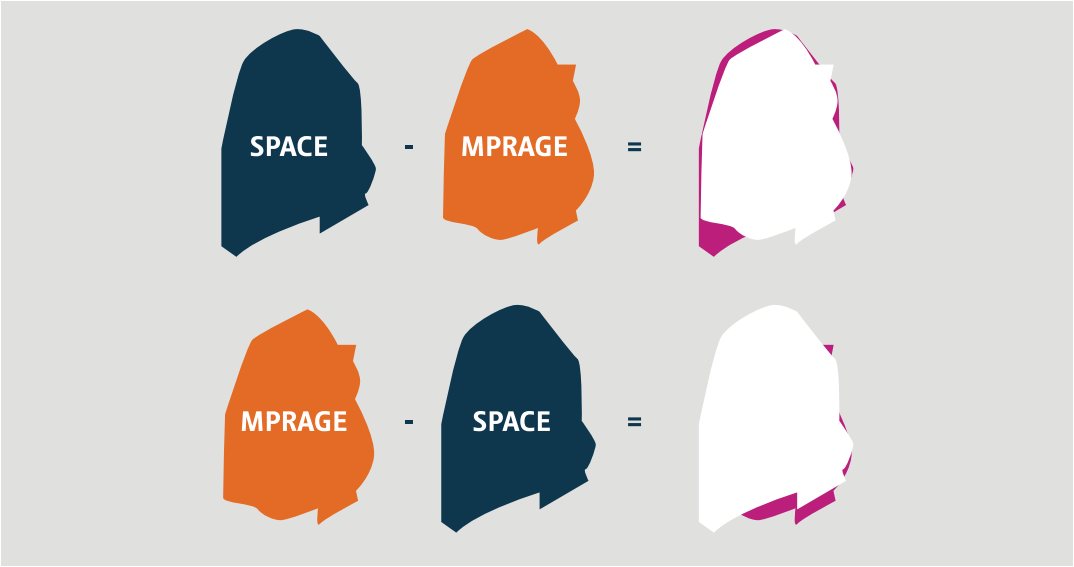
Sequence such as MPRAGE images exhibit suboptimal post-gadolinium enhancement. When using Gadovist®, both SPACE and VIBE obtain higher contrast rate, contrast-to-noise ratios, and visual conspicuity ratings in both gliomas and metastases.

Brain Tumors: See More Using Gadovist® with SPACE* and VIBE**

A recent study suggests that selecting special sequences such as SPACE and VIBE (compared with MRPAGE) enables additional information from a Gadovist®-enhanced brain tumor MRI.[5]

Clinical Benefits

- More accurate guiding of biopsy sampling and consequent correct histologic grading
- Optimized treatment decision-making
- More favorable patient outcomes due to achieving maximal tumor resection



Contrast-enhancing lesion margin extent discrepancy between SPACE and MPRAGE. Segmentations obtained with MPRAGE or with SPACE are reciprocally subtracted, revealing the spatial mismatch of the tumor border segmentation obtained with MPRAGE (red margins).

* Sampling perfection with application optimized contrasts using different flip angle evolution (the abbreviation was invented by Siemens Healthineers)

** Volumetric interpolated brain examination

In both gliomas and metastases, Gadovist®-enhanced SPACE and VIBE techniques provide:

- higher contrast-to-noise ratios
- higher visual conspicuity ratings

This results in potentially more accurate enhancement of lesion boundary delineation.

Brain Tumors: Visualizing Tumor Aggressiveness with Gadovist®

In patients with glioblastomas, diffuse cerebral infiltration of gliomas may be missed on a conventional MRI. In one study, quantitative T1-difference maps obtained using Gadovist® could deliver additional clinical benefit.[6]

These maps may indicate tumor cell infiltration, not only in the glioblastoma itself, but also in the edema region and beyond.

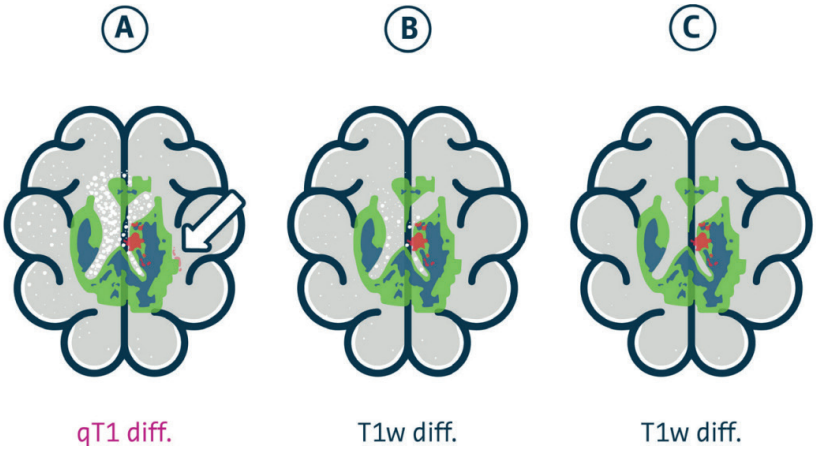
- In patients with untreated glioblastomas, quantitative T1-difference maps may clearly delineate Gadovist® leakage beyond the enhancing tumor areas.
- Gadovist® enhancement in the edema region and even beyond indicates a deficient blood brain barrier (BBB), and therefore most likely infiltration with tumor cells.

Clinical Benefits

Quantitative T1-difference mapping may be a useful tool for initial tumor characterization and for monitoring treatment effects.

- The extent of resection of the enhancing part of a glioblastoma correlates with the survival time of the patients.
- Visualizing the infiltration areas would allow their inclusion in therapy.

Visual Assessment of Contrast Agent Leakage Beyond the Edema Region



Enhancing tumor (red), edema (blue), and 5 mm zone (green). The qT1-difference map (A) shows enhancement (white arrow) beyond the left-side edema region and 5 mm zone, which is not visible in the T1w difference images (B,C).[6]

Adapted from Nöth et al. 2020.

Study details

- Gadovist® leakage in at least a part of the edema region in 32/33 patients (24 clear, 8 weak)
- Gadovist® leakage in areas beyond the pathology in 21/33 patients (10 clear, 11 weak)

GADOVIST® 1.0 mmol/mL solution for injection. **Composition:** GADOVIST 1.0 is a clear, sterile, aqueous solution. Each mL of GADOVIST 1.0 contains 604.72 mg (1.0 mmol) of gadobutrol, 1.211 mg trometamol, 0.013 mg sodium (0.00056 mmol), and 0.513 mg calcium sodium butrol in water for injection. The pH of GADOVIST 1.0 is adjusted to between 6.6 and 8.0 with hydrochloric acid. **Indications:** GADOVIST 1.0 (gadobutrol) is a medicinal product for diagnostic use only. GADOVIST 1.0 (gadobutrol) is indicated in adults and children of all ages including term newborns for: contrast enhancement during cranial and spinal MRI investigations and for contrast-enhanced magnetic resonance angiography (CE-MRA); contrast enhanced MRI of the breast to assess the presence and extent of malignant breast disease, and MRI of the kidney. GADOVIST 1.0 is particularly suited for cases where the exclusion or demonstration of additional pathology may influence the choice of therapy or patient management, for detection of very small lesions and for visualization of tumours that do not readily take up contrast media. GADOVIST 1.0 is also suited for perfusion studies for the diagnosis of stroke, detection of focal cerebral ischemia and tumour perfusion. **Contraindications:** GADOVIST 1.0 should not be administered to patients who have experienced a life-threatening reaction to GADOVIST 1.0 previously. **Serious warnings and precautions for use:** Gadolinium-based contrast agents (GBCAs) increase the risk for Nephrogenic Systemic Fibrosis (NSF) in patients with: chronic severe renal insufficiency (glomerular filtration rate <30 mL/min/1.73m^2), or acute renal failure / acute kidney injury. In these patients, avoid use of GBCAs unless the diagnostic information is essential and not available with noncontrast-enhanced magnetic resonance imaging (MRI). NSF may result in fatal or debilitating systemic fibrosis affecting the skin, muscle, and internal organs. Screen all patients for renal dysfunction by obtaining a history and/or laboratory tests. When administering a GBCA, do not exceed the recommended dose and allow a sufficient period of time for elimination of the agent from the body prior to any readministration. **Adverse reactions:** Patients with a history of previous reaction to contrast media, allergic disorders or bronchial asthma suffer more frequently from hypersensitivity reactions than others. As with other contrast media, delayed allergoid reactions occurring hours or days after administration have been observed, though rarely. Anaphylactoid reactions may occur. Transient sensations of taste or smell perversion may occur during or immediately after injection of GADOVIST 1.0.

Literature:

1. M. Koenig et al., “Intra-individual, randomised comparison of the MRI contrast agents gadobutrol versus gadoteridol in patients with primary and secondary brain tumours, evaluated in a blinded read,” Eur Radiol 23, no. 12 (Dec 2013): 3287-95.
2. Juan E Gutierrez et al., “Safety and Efficacy of Gadobutrol for Contrast-enhanced Magnetic Resonance Imaging of the Central Nervous System: Results from a Multicenter, Double-blind, Randomized, Comparator Study,” Magn Reson Insights (Apr 2015): 1-10.
3. M Anzalone et al., “Cerebral neoplastic enhancing lesions: multicenter, randomized, crossover intraindividual comparison between gadobutrol (1.0M) and gadoterate meglumine (0.5M) at 0.1 mmol Gd/kg body weight in a clinical setting,” Eur J Radiol 82, no. 1 (Jan 2013): 139-45.
4. Ulrike I Attenberger et al., “Evaluation of gadobutrol, a macrocyclic, nonionic gadolinium chelate in a brain glioma model: comparison with gadoterate meglumine and gadopentetate dimeglumine at 1.5 T, combined with an assessment of field strength dependence, specifically 1.5 versus 3 T,” J Magn Reson Imaging 31, no. 3 (Mar 2010): 549-55.
5. L Danieli et al., “Brain Tumor-Enhancement Visualization and Morphometric Assessment: A Comparison of MPRAGE, SPACE, and VIBE MRI Techniques,” AJNR Am J Neuroradiol 40, no. 7 (Jul 2019): 1140-1148.
6. Ulrike Nöth et al., “Quantitative T1 mapping indicates tumor infiltration beyond the enhancing part of glioblastomas,” NMR Biomed 33, no. 3 (Mar 2020): e4242.

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