Multiple Sclerosis

Improved Detection of Active Cerebral Lesions With 3-Dimensional T1 Black-Blood Magnetic Resonance Imaging Compared With Conventional 3-Dimensional T1 GRE Imaging

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Objectives: The aim of this study was to assess the diagnostic accuracy of a modified high-resolution whole-brain three-dimensional T1-weighted black-blood sequence (T1-weighted modified volumetric isotropic turbo spin echo acquisition [T1-mVISTA]) in comparison to a standard three-dimensional T1-weighted magnetization-prepared rapid gradient echo (MP-RAGE) sequence for detection of contrast-enhancing cerebral lesions in patients with relapsing-remitting multiple sclerosis (MS).

Materials and Methods: After institutional review board approval and informed consent, 22 patients (8 men; aged 31.0 ± 9.2 years) with relapsing-remitting MS were included in this monocentric prospective cohort study.

Contrast-enhanced T1-mVISTA and MP-RAGE, both with 0.8 mm^3 resolution, were performed in all patients. In a substudy of 12 patients, T1-mVISTA was compared with a T1-mVISTA with 1.0 mm^3 resolution (T1-mVISTA_1.0). Reference lesions were defined by an experienced neuroradiologist using all available sequences and served as the criterion standard. T1-mVISTA, T1-mVISTA_1.0, and MP-RAGE sequences were read in random order 4 weeks apart. Image quality, visual contrast enhancement, contrast-to-noise-ratio (CNR), diagnostic confidence, and lesion size were assessed and compared by Wilcoxon and Mann-Whitney *U* tests.

Results: Eleven of 22 patients displayed contrast-enhancing lesions. Visual contrast enhancement, CNR, and diagnostic confidence of contrast-enhancing MS lesions were significantly increased in T1-mVISTA compared with MP-RAGE ($P < 0.001$). Significantly more contrast-enhancing lesions were detected with T1-mVISTA than with MP-RAGE (71 vs 39, respectively; $P < 0.001$). With MP-RAGE, 25.6% of lesions were missed in the initial reading, whereas only 4.2% of lesions were missed with T1-mVISTA. Increase of the voxel volume from 0.8 mm to 1.0 mm isotropic in T1-mVISTA_1.0 did not affect the detectability of lesions, whereas scan time was decreased from 4:43 to 1:55 minutes.

Conclusions: Three-dimensional T1-mVISTA improves the detection rates of contrast-enhancing cerebral MS lesions compared with conventional 3D MP-RAGE sequences by increasing CNR of lesions and might, therefore, be useful in patient management.

Key Words: 3D black-blood imaging, high resolution, whole brain, T1-mVISTA, MP-RAGE, multiple sclerosis, cerebral lesions, MRI

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Contrast-enhanced magnetic resonance imaging (MRI) is currently the criterion standard for the detection of active lesions in patients with multiple sclerosis (MS) and is necessary for diagnosis according to the revised McDonald and the MAGNIMS consensus guidelines.[1,2] Moreover, contrast-enhanced MRI has been shown to display higher disease activity than suspected by clinical symptoms and is recommended for follow-up and monitoring in clinical studies.[3]

Three-dimensional (3D) T1-weighted (T1w) magnetization-prepared rapid gradient echo sequences (MP-RAGE) are widely used in standard clinical protocols when using contrast-enhanced MRI. However, although precontrast MP-RAGE is widely accepted for anatomical studies and gray and white matter imaging, the choice of the postgadolinium T1w is much more debated: T1w 2-dimensional (2D) spin echo (SE) sequences are recommended for detection of active lesions[3,4] and 3D steady-state spoiled gradient recalled echo sequences (fast angle low shot; FLASH) have been suggested as an option in MS protocols.[4,5]

In general, postcontrast 2D SE sequences are known to provide an increased signal-to-noise ratio compared with 3D GRE sequences such as MP-RAGE or FLASH[6–9] and superior detection rates have been reported on 2D SE compared with 3D GRE.[9,10] On the other hand, other studies reported increased detection rates in 3D GRE sequences as result of a decrease of the partial volume effect due to higher resolution, thinner slices, and the option of multiplanar image reconstruction.[6,11]

Nevertheless, all conventional protocols show only a slight to moderate correlation to clinical manifestations and have limited prognostic value to predict progression of disease.[1,12,13] Indeed, earlier diagnosis, especially in patients with clinically isolated syndrome, can affect therapeutic concepts and might improve long-term outcomes[13,14] because disease activity predicts long-term disability.[14]

Therefore, investigation of new imaging strategies seems to be appropriate.

Until recently, the use of 3D T1w turbo spin echo (TSE) sequences was restricted by reaching the limits of the specific absorption rate due to long echo trains combined with short repetition times and associated high levels of radio frequency energy applied. New MRI techniques, such as parallel imaging techniques, allow significant reduction of acquisition times.[15,16] In addition, the use of variable refocusing angles allows a further decrease of acquisition time and specific absorption rate, whereas image resolution can be increased.[17,18]

Initial studies in patients with intracranial metastases have shown that the use of 3D T1w TSE sequences with variable refocusing angles lead to a significant increase in signal intensity of lesions through a significant increase of the contrast-to-noise ratio (CNR), thus, leading to a superior detectability of lesions.[19,20] Moreover, black-blood (BB) contrast was reported to be supportive for detection of contrast-enhancing brain metastasis, as distracting signal from blood vessels is suppressed.[21,22] However, up to now, BB suppression was only achievable by using double inversion recovery resulting in small 2D stacks of a few centimeter[23] or in 3D sequences by using a motion-sensitized driven equilibrium prepulse, which suffers from decreased T1 contrast, as it

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is based on a T2-prep pulse.[24] We recently developed a novel 3D T1w TSE BB sequence with variable refocusing flip angles sweeps (T1-weighted modified volumetric isotropic TSE acquisition [T1-mVISTA]).[25] This sequence provides a submillimeter isotropic resolution, coverage of the whole brain, reconstruction in all planes, and scan times under 5 minutes. In an initial study in patients with cerebral metastases, detection rates with T1-mVISTA were nearly doubled, especially in small lesions under 5 mm.[25]

The aim of this study, therefore, was to evaluate the accuracy of a contrast-enhanced 3D T1-mVISTA in comparison to the standard contrast-enhanced 3D MP-RAGE sequence for the detection of active cerebral lesions in patients with relapsing-remitting MS (RRMS).

MATERIALS AND METHODS

Study Design and Study Population

The study was designed as a prospective monocentric cohort study and followed the principles of the Declaration of Helsinki. Approval by the institutional review board was given, and written informed consent was obtained from all patients. Patients were recruited between October 2013 and January 2016.

Inclusion Criteria

Patients with RRMS diagnosed by an experienced neurologist according to the McDonald criteria were included.

Exclusion Criteria

Patients with (*a*) vasculitis, (*b*) a tumor, (*c*) stroke, and (*d*) typical MR contraindications as well as (*e*) RRMS patients with corticosteroid therapy within the last 4 weeks were excluded.

MRI Protocol

Scans were performed on a 3 T scanner (Ingenia; Philips Healthcare, Best, the Netherlands) using a commercial 8-channel head coil. All patients underwent MRI for clinical reasons.

All patients received a standard brain-protocol including 3D T2w fluid attenuation inversion recovery (FLAIR; repetition time [TR], 4800; echo time [TE], 335; TI, 1650; matrix, 224 × 224), axial T2w TSE (TR, 3965; TE, 80; matrix, 420 × 270), diffusion-weighted imaging (TR, 3690; TE, 63; matrix, 152 × 129), and nonenhanced and contrast-enhanced T1-mVISTA and MP-RAGE sequences, both with 0.8 mm^3 resolution. We additionally performed a contrast-enhanced T1-mVISTA with 1.0 mm^3 resolution (T1-mVISTA_1.0) in a subgroup of the cohort for analysis of the acquisition time and image quality of T1-mVISTA_1.0 as a proof of concept. Detailed scan parameters for T1-mVISTA and MP-RAGE are listed in Table 1. To increase the signal-to-noise ratio, all images were reconstructed with a slice thickness of 1.5 mm.

The field of view covered the whole brain, reaching from the vertex to the medulla oblongata. An amount of 0.2 mL/kg body weight of gadoteric acid (DOTAREM 0.5 mmol/mL; Guerbet, Roissy, France) was administered. The first postcontrast scan was started 4 minutes after injection.[26] Contrast-enhanced MP-RAGE and T1-mVISTA were acquired in alternating random order to prevent bias due to the potential increase of contrast agent uptake by increased time after injection.[27]

Definition of Criterion Standard

Our criterion standard was based on predefined reference lesions, which were assessed by reading all available sequences by an experienced neuroradiologist, who did not act as a reader. A contrast-enhancing MS lesion was defined as a focal enhancement on the postcontrast image corresponding to a T2 FLAIR hyperintensity. Images were provided in axial, sagittal, and coronar reformation.

Image Analysis

The first reader, with more than 15 years of experience, analyzed contrast-enhanced T1-mVISTA, T1-mVISTA_1.0, and MP-RAGE sequences in a random order 4 weeks apart. Sequences were provided in axial, sagittal, and coronal planes with a reconstructed slice thickness of 1.5 mm. Three-dimensional T2w FLAIR images and the corresponding

TABLE 1. MR Parameters

	T1-mVISTA	T1-mVISTA_1.0	MP-RAGE
Sequence	3D T1w TSE	3D T1w TSE	3D T1w GE
TR, ms	700	700	12
TE, ms	28	23	6.7
Fat suppression	SPIR	SPIR	No
SENSE factor (A/P, R/L)	1.7/2.5	2.0/2.5	1.8/2
TFE factor	NA	NA	119
Echo spacing/ETL	4.0/243	3.3/232	NA
Flip angle, degrees	Variable	Variable	8
NSA	2	2	1
Scan FOV, mm^3	200 × 251 × 160	200 × 251 × 160	240 × 250 × 190
Recon matrix	267 × 335	200 × 251	300 × 312
No. slices	427	320	476
Voxel size, mm^3	0.75 × 0.75 × 0.75	1.0 × 1.0 × 1.0	0.8 × 0.8 × 0.8
Recon voxel size, mm^3	0.39 × 0.39 × 0.35	0.49 × 0.49 × 0.50	0.58 × 0.58 × 0.4
Scan time, min	4:43	1:55	4:46
Flow compensation	No	No	Yes
Slice orientation	Sagittal	Sagittal	Sagittal

A/P indicates anterior posterior; ETL, echo train length; FOV, field of view; GE, gradient echo; MP-RAGE, magnetization-prepared rapid gradient echo; NA, not applicable; NSA, number of signal averages; R/L, right left; SPIR, spectral presaturation with inversion recovery; SENSE, sensitivity encoding; TE, echo time; TFE, turbo field echo; TR, repetition time; TSE, turbo spin echo; T1w, T1-weighted; T1-mVISTA, T1-weighted modified volumetric isotropic TSE acquisition; T1-mVISTA_1.0, T1-weighted modified volumetric isotropic TSE acquisition with 1.0 mm^3 resolution; 3D, 3-dimensional.

non–contrast-enhanced T1-mVISTA or MP-RAGE, respectively, were provided for decision making of an enhancing lesion. The reader was blinded regarding the clinical outcome, advised to mark every contrast-enhancing MS suspect lesion and to assess the visual contrast enhancement (VCE; 0 = no; 1 = slight; 2 = moderate; 3 = strong contrast enhancement) and the diagnostic confidence (DC; probability of contrast-enhancing MS lesion is: 1 = unlikely; 2 = vague; 3 = likely; 4 = high; 5 = very high). Furthermore, the reader had to assess the image quality of T1-mVISTA and MP-RAGE sequences as follows: 1 = poor, diagnosis strongly impaired; 2 = adequate, major artifacts; 3 = good, only minor artifacts; and 4 = excellent, no artifacts.

A second reader, who was aware of the reference lesions, rereviewed the marked lesions from the first reader and transferred the results to an Excel sheet. Subsequently, the second reader performed a side-to-side comparison for determination of the CNR and for size measurements of the lesions. For CNR measurements, regions of interest (ROIs) were placed in the center of the maximum signal intensity (SI) of each lesion and the adjacent brain parenchyma in a side-to-side comparison with the same area of ROI in each sequence.

Contrast-to-noise-ratio was estimated using the following formula:

$$CNR = \left(\mu_{lesion} - \mu_{parenchyma}\right) / SD_{parenchyma}$$

The μ was the average SI of the ROI, and SD was the standard deviation of noise of the respective region. Because noise distribution was inhomogeneous due to parallel imaging techniques[28] and visibility of lesions is dependent on the surrounding contrast, the SI and SD for the calculation of CNR were taken from the adjacent white matter.

For the determination of lesion size, the maximum length of the lesion in either axial, sagittal, or coronar reformation was measured in both sequences in a side-to-side comparison. Moreover, according to the MAGNIMS consensus guidelines, lesion location was recorded as periventricular, cortical/juxtacortical, or infratentorial, respectively.[2]

All images were analyzed on a picture archiving and communication system (Syngo; Siemens AG Healthcare, Erlangen, Germany).

Statistical Analysis

We performed all statistical analyses using SPSS 23 (IBM, Armonk, NY). Metric and normally distributed variables are reported as mean ± SD; nonnormally distributed variables are presented as median with first to third quartiles. Categorical variables are presented as frequency and percentage. The 2-sample *t* test was used for lesion size in MP-RAGE.

The VCE, CNR, number of lesions, localization, and size in T1-mVISTA and T1-mVISTA_1.0 did not display normal distributions; the Wilcoxon test was used for paired samples, and the Mann-Whitney *U* test was used for unpaired samples. Fisher exact test was applied for the detection of differences in localizations of lesions between lesions detected and lesions missed in MP-RAGE.

Two-sided *P* values were determined, and values below 0.05 were considered significant.

RESULTS

Patient Cohort

A total of 22 patients (8 male [36.4%]; age, 31.0 ± 9.2) was included in the study. All patients received a protocol with T1-mVISTA and MP-RAGE; a subgroup of 12 patients additionally received a T1-mVISTA_1.0. Half of the patients (11 of 22) displayed contrast-enhancing lesions. Among the 11 patients with contrast-enhancing lesions, 6 received the T1-mVISTA as the first sequence, whereas 5 received the MP-RAGE as the first sequence. Among patients with missed lesions, there was no significant difference on the order of the sequences ($P > 0.05$). In the substudy for comparison of T1-mVISTA and T1-mVISTA_1.0, 7 of 12 patients showed contrast-enhancing lesions.

MP-RAGE vs T1-mVISTA

When comparing T1-mVISTA and MP-RAGE, 39 lesions were detected with both sequences. The VCE, CNR, and DC were rated significantly higher for T1-mVISTA compared with MP-RAGE (all $P < 0.001$; Table 2; Fig. 1). Lesions detected by T1-mVISTA appeared significantly bigger than lesions detected by MP-RAGE ($P < 0.001$; Table 2). There was no significant difference regarding the image quality for either sequence on a 4-point Likert scale (T1-mVISTA [4–4] vs MP-RAGE [3.75–4], $P = 0.705$).

Total Number of Lesions

Overall, significantly more lesions were detected with T1-mVISTA compared with MP-RAGE (71 vs 39; $P < 0.001$; Fig. 1). Lesions detected only by T1-mVISTA (n = 32) were significantly smaller compared with lesions seen in both sequences (3.0 mm [2.0–6.0 mm] vs 5.0 mm [4.0–8.0 mm], $P = 0.002$). The VCE and CNR were rated significantly lower for lesions detected only by T1-mVISTA ($P < 0.001$; Table 3). Although the DC for lesions only displayed by T1-mVISTA turned out to be significantly lower ($P < 0.001$), median DC was rated with 5.0 (4.0–5.0) on a 5-point Likert scale. No lesion was detected exclusively in MP-RAGE but overseen in T1-mVISTA.

Although failing to be significant, lesions only detected by T1-mVISTA tended to be localized more often in the juxtacortical area, whereas lesions detected with both sequences were more often localized in the periventricular area (62.5% vs 48.7%).

Moreover, in 2 cases, we detected contrast enhancement of the optic nerve in patients with clinically apparent optic neuritis as secondary finding.

Missed Lesions in MP-RAGE and T1-mVISTA on First Review Compared With Corresponding Reference Lesions

Ten of 39 reference lesions (25.6%) were missed in MP-RAGE sequences in the initial reading, whereas only 3 of 71 reference lesions (4.2%) were missed in T1-mVISTA (Fig. 2). The 10 lesions missed in MP-RAGE were significantly smaller compared with the lesions that were not overseen (3.0 mm [2.0–4.0 mm] vs 6.0 mm [3.5–9.0 mm]; $P = 0.003$). However, there was no significant difference regarding the VCE and CNR of the 10 lesions missed compared with the VCE and CNR of the lesions detected ($P = 0.52$ and $P = 0.62$, respectively).

T1-mVISTA vs T1-mVISTA_1.0

When comparing T1-mVISTA and T1-mVISTA_1.0 in a substudy for analysis of decreased acquisition time (1:55 vs 4:43 minutes), all lesions detected by T1-mVISTA were also seen in T1-mVISTA_1.0 (n = 40).

TABLE 2. Comparison of Lesions Detected Both in MP-RAGE and VISTA, Both With 0.8 mm Isotropic Resolution

	n	MP-RAGE	T1-mVISTA	*P*
Size, mm	39	5 (3–7)	5 (4–8)	**<0.001***
VCE	39	2.0 (1.0–2.0)	3.0 (3.0–3.0)	**<0.001***
CNR	39	14.6 (7.9–24.3)	29.7 (17.7–45.0)	**<0.001***
DC	39	5 (3–5)	5 (5–5)	**<0.001***

*Wilcoxon test.

CNR indicates contrast-to-noise ratio; DC, diagnostic confidence on a 5-point Likert scale; VCE, visual contrast enhancement on a 3-point Likert scale; MP-RAGE, magnetization-prepared rapid gradient echo; T1-mVISTA, T1-weighted modified volumetric isotropic TSE acquisition.

No significant differences were detected regarding VCE, CNR, DC, and lesion size (Table 4; Fig. 3). However, image quality was rated to be significantly lower in T1-mVISTA_1.0 compared with T1-mVISTA on a 4-point scale due to the decrease of image resolution by increasing voxel size (3.0 [3.0–3.0] vs 4.0 [3.0–4.0], respectively; $P < 0.05$).

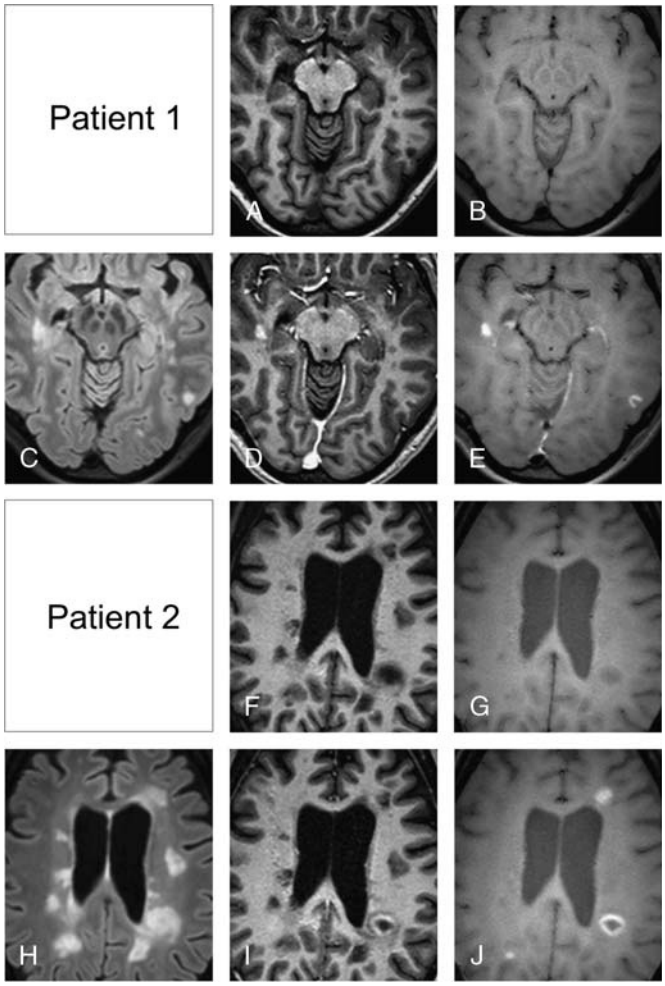

FIGURE 1. Scans in axial reconstruction of 2 different patients are displayed in this figure: T2 FLAIR (C and H), precontrast MP-RAGE (A and F), precontrast T1-mVISTA (B and G), contrast-enhanced MP-RAGE (D and I), and contrast-enhanced T1-mVISTA (E and J). All scans were acquired at 0.8 mm isotropic resolution. After contrast agent application, T1-mVISTA was acquired before MP-RAGE in patient 1 and vice versa in patient 2. In patient 1, 2 contrast-enhancing lesions are displayed: 1 lesion in the white matter of the right temporal lobe adjacent to the temporal horn and another lesion in the left temporal lobe in cortical/juxtacortical localization. Both lesions appear hypointense in precontrast MP-RAGE and hypointense to cortex isointense in precontrast T1-mVISTA. Both lesions display a contrast enhancement; however, the signal intensities of lesions displayed by T1-mVISTA are increased and lesions appear brighter compared with the MP-RAGE sequence. Especially, the lesion in the cortical/juxtacortical localization displays a low contrast compared with the adjacent white matter. In patient 2, an annular-enhancing lesion is seen in the left periventricular white matter both in contrast-enhanced MP-RAGE (I) and in contrast-enhanced T1-mVISTA (J). However, 2 additional lesions can be clearly depicted in the white matter of the right posterior and the left frontal lobe in contrast-enhanced T1-mVISTA (J), whereas at best faint and no contrast agent uptake is seen in the corresponding MP-RAGE (I), respectively. MP-RAGE indicates magnetization-prepared rapid gradient echo; T1-mVISTA, T1-weighted modified volumetric isotropic TSE acquisition; T2 FLAIR, T2-weighted fluid attenuation inversion recovery.

TABLE 3. Comparison of Lesions Detected Only in T1-mVISTA (n = 32) vs Lesions Seen in MP-RAGE, Both With 0.8 mm Isotropic Resolution

	Detected Lesions in MP-RAGE (n = 39)	Lesions Seen Only in T1-mVISTA (n = 32)	*P*
Size,* mm	5.0 (4.0–8.0)	3.0 (2.0–6.0)	**0.002†**
VCE*	3.0 (3.0–3.0)	2.0 (2.0–2.0)	**<0.001†**
CNR*	29.7 (17.3–45.0)	17.5 (11.8–24.6)	**<0.001†**
DC*	5.0 (5.0–5.0)	5.0 (4.0–5.0)	**<0.001†**

*As measured in VISTA 0.8. †Mann-Whitney *U* test.

CNR indicates contrast-to-noise ratio; DC, diagnostic confidence on a 5-point Likert scale; VCE, visual contrast enhancement on a 3-point Likert scale; MP-RAGE, magnetization-prepared rapid gradient echo; T1-mVISTA, T1-weighted modified volumetric isotropic TSE acquisition.

DISCUSSION

The results of this single-center study show that 3D T1-mVISTA improves the detectability of contrast-enhancing cerebral MS lesions by almost doubling the detection rate (54.9%) due to increasing the CNR of the lesions significantly. Further, significantly fewer lesions were missed in T1-mVISTA compared with the standard MP-RAGE sequence (4.2 vs 25.6%, respectively).

Because 2 or more contrast-enhancing lesions have reported to be associated with a worse clinical outcome and therapeutic aims have shifted to no evident disease activity, which is defined by clinical and MRI parameters,[14] the total number of active lesions is of high clinical relevance.

When comparing postcontrast MP-RAGE and T1-mVISTA, we noticed differences in contrast agent behavior: there were some T2 FLAIR hyperintense lesions, which were enhancing on T1-mVISTA but seemed hypointense on contrast-enhanced MP-RAGE. On the corresponding non–contrast-enhanced T1-mVISTA, these lesions were either slightly hypointense or isointense to the white matter.

Nonenhancing T1 hypointense lesions, in the literature also known as black holes, were reported to be areas of edema or chronic lesions representing severe axonal damage.[29–31] Black holes begin as a contrast-enhancing lesion and evolve differently over time: they can shrink, enlarge, or become permanent.[32] Acute black holes display contrast enhancement, whereas persistent black holes lose contrast agent uptake.[30,32] These permanent black holes were observed to be associated with a worse long-term outcome and disease progression.[33,34] Bagnato et al[32] showed in their monthly follow-up of 9 untreated RRMS patients over 4 years that 55.7% of acute black holes developed into persisting black holes and that the likeliness of the formation of a persisting black hole correlated with the duration of contrast enhancement. Our results suggest that residual contrast enhancement of black holes, as defined by Bagnato et al, can be detected with T1-mVISTA due to the increased CNR, whereas this can partially be masked in MPRAGE sequences. Because duration of contrast enhancement seems to be a key factor in pathogenesis of RRMS and long-term outcome, further studies are needed to investigate the consequence of the additional contrast-enhancing lesions displayed by T1-mVISTA.

In general, lesions appeared bigger in the T1-mVISTA images, a phenomenon we already encountered in our previous study on brain metastases.[25] Kato et al[20] also described that finding when comparing T1-SPACE and MP-RAGE in brain metastases, a congeneric sequence to T1-mVISTA. In accordance to Kato et al, we also assume that the increase of CNR might have lead to an increase in lesion size.

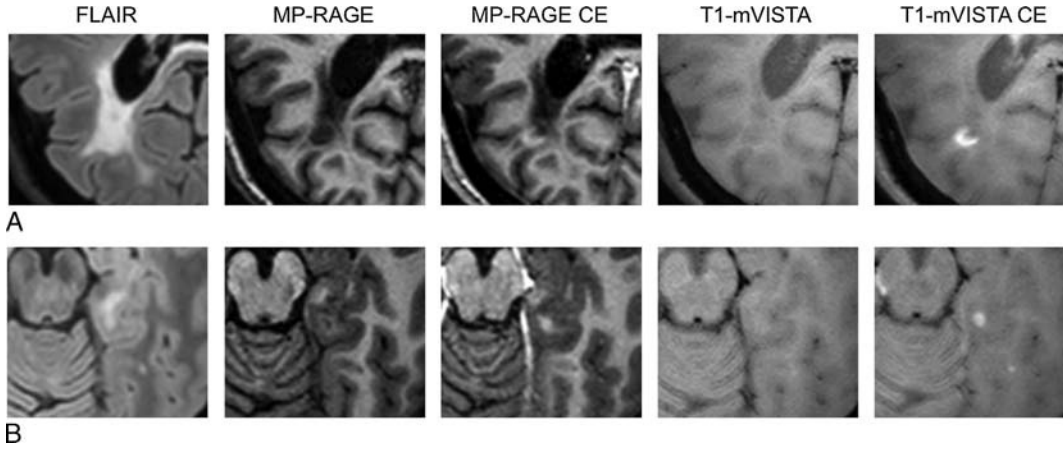

FIGURE 2. The figure displays examples of missed lesions by contrast-enhanced MP-RAGE in 2 different patients (A and B). The first lesion in patient A was located in the white matter of the right posterior lobe adjacent to the cortex; the second lesion and third lesion in patient B were located in cortical/juxtacortical localization in the left mesial temporal lobe and in the white matter of the left posterior lobe, respectively. All lesions were missed in contrast-enhanced MP-RAGE due to the lower contrast-to-noise ratio compared with T1-mVISTA. In both patients, T1-mVISTA was acquired before MP-RAGE. CE indicates contrast-enhanced; MP-RAGE, magnetization-prepared rapid gradient echo; T1-mVISTA, T1-weighted modified volumetric isotropic TSE acquisition; T2 FLAIR, T2-weighted fluid attenuation inversion recovery.

Furthermore, significantly more lesions were overlooked in MP-RAGE compared with T1-mVISTA: with 3D MP-RAGE, 25.6% (10/39) of the reference lesions were missed in the initial reading, whereas only 4.2% (3/71) of the reference lesions were missed with T1-mVISTA. This finding is consistent with a study of Reichert et al[35] on brain metastases; the authors also reported that lesion detection was significantly improved when using T1-SPACE (99.1% of lesions for reader 1 and 96.3% of lesions for reader 2) compared with MP-RAGE (73.6% of lesions for reader 1 and 68.5% of lesions for reader 2).

The reasons for the impaired lesion detection with MP-RAGE are probably the combination of the decreased CNR of the contrast-enhancing lesion to the adjacent parenchyma and the increase of CNR between white and gray matter as displayed in Figure 2 and already observed in our study comparing T1-mVISTA and MP-RAGE in patients with brain metastases.[25] Moreover, because contrast between gray and white matter is decreased[25] as well as the signal of blood vessels is suppressed, T1-mVISTA creates a more homogeneous image background without distracting signals from enhanced vessels, such as in MP-RAGE.[20] Therefore, small, low contrast-enhancing lesions are not masked in T1-mVISTA compared with MP-RAGE.

Moreover, significantly more lesions were detected by T1-mVISTA compared with MP-RAGE (71 vs 39 lesions, 54.9%). Lesions only detected by T1-mVISTA were significantly smaller (<5 mm). Although the VCE and CNR of smaller lesions detected only by T1-mVISTA were significantly decreased, DC was still high, with a median of 5 on a 5-point scale compared with lesions detected in both sequences.

TABLE 4. Comparison of Lesions Detected in T1-mVISTA_1.0 (1.0 mm^3 resolution) and T1-mVISTA (0.8 mm^3 Resolution)

	n	T1-mVISTA_1.0	T1-mVISTA	*P*
Size, mm	40	5.5 (3.0–7.75)	5.5 (3.0–7.0)	1.0*
VCE	40	2.0 (2.0–3.0)	2.0 (2.0–3.0)	0.083*
CNR	40	18.4 (11.5–32.8)	18.2 (13.1–28.1)	0.677*
DC	40	5.0 (4.0–5.0)	5.0 (4.0–5.0)	0.157*

*Wilcoxon test.

CNR indicates contrast-to-noise ratio; DC, diagnostic confidence on a 5-point Likert scale; VCE, visual contrast enhancement on a 3-point Likert scale; MP-RAGE, magnetization-prepared rapid gradient echo; T1-mVISTA, T1-weighted modified volumetric isotropic TSE acquisition.

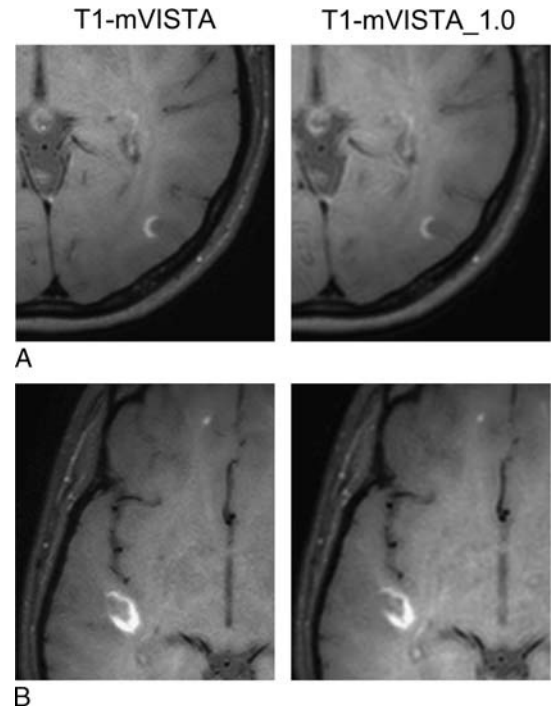

FIGURE 3. The left vertical row shows contrast-enhanced T1-mVISTA at 0.8 mm isotropic resolution (T1-mVISTA), the right vertical row displays contrast-enhanced T1-mVISTA at 1.0 mm isotropic resolution (T1-mVISTA_1.0) of 2 different patients (A and B). In general, all 3 contrast-enhancing lesions are depicted with comparable signal intensities by T1-mVISTA and T1-mVISTA_1.0, respectively. However, due to the lower resolution, the image quality of T1-mVISTA_1.0 is slightly impaired because the margins of the lesions, the vessel contours, and the general image impression seem a little more blurred. In both patients, T1-mVISTA_1.0 was acquired before T1-mVISTA. T1-mVISTA indicates T1-weighted modified volumetric isotropic TSE acquisition.

The increase of detected contrast-enhancing MS lesions is in line with a previous study of Hodel et al[36]; the authors detected 40.6% more contrast-enhancing lesions (90 vs 64) in 19 MS patients using a 3D T1w TSE sequence (Brain View; Philips, a congeneric sequence to T1-mVISTA) in 4-mm-thick axial reformats compared with a standard 2D T1w SE sequence with 4-mm slice thickness and even 65.5% more lesions (106 vs 64) when using multiplanar reconstructions with 1.2-mm resolution.[36] They also reported a significantly higher contrast rate for the 3D T1w TSE than for the 2D SE sequence.

In a previously published study of our group on the detection of brain metastases, we reported an increased detection rate of 59.0% for contrast-enhancing metastases (61 vs 36) and a significantly increased CNR comparing 3D T1-mVISTA to conventional 3D MP-RAGE.[25] Two other studies using 3D BB T1w TSE sequences also reported higher detection rates for brain metastasis, especially for small lesions < 5 mm.[19,20]

Compared with the commercially available sequence used by Hodel et al[36] and the studies on brain metastases of Kato et al[20] and Park et al,[19] scan times of our protocol were considerably shorter at comparable image resolutions (1.0 mm isotropic) without impairment of lesion detectability and image quality (1:55 vs 4:42 minutes in the study by Kato et al, 5:30 minutes in the study by Hodel et al, and 9:00 minutes in the study by Park et al).

The reasons for the higher detectability with T1-mVISTA were probably multifactorial. First, in conventional 3D T1w TSE BB sequences, after an initial decrease, the refocusing angle reaches a plateau, which results in a fast signal loss. The refocusing angle in T1-mVISTA continually increases afterward, resulting in a slower signal loss.[25] The use of a long echo train in T1-mVISTA compared with other studies[19,20,36] might further contributes to scan efficiency and allows for a high resolution in a shorter scan time. Moreover, the entire *k*-space is used in T1-mVISTA, therefore, no information regarding image contrast and image sharpness is lost.[25]

Although not investigated in this study, our initial experience demonstrates that the orbital cavity could also be assessed with high-resolution, fat-saturated T1-mVISTA, with the same sequence to diagnose or exclude optic neuritis, a common primary symptom in MS patients and recently recommended to be included to the McDonald criteria in the consensus paper of the European collaborative for MR studies in MS of 2016.[2] Therefore, application of T1-mVISTA could be timesaving in the clinical routine, as a conventional 2D T1w SE sequence in axial and coronal slicing would result in longer scan times.

There are several limitations in our study. First, the small number of patients is a substantial limitation of our study. As only 11 of 22 patients displayed contrast-enhancing lesions, our results can only be interpreted as an indication for a superiority of T1-mVISTA. Second, blinding to sequence type was not possible due to the characteristic appearance of T1-mVISTA. Third, we did not compare T1-mVISTA to 2D T1w SE sequences. However, Hodel et al[36] had already showed that 3D T1w TSE was superior in the detection of contrast-enhancing lesions and displayed less pulsation artifacts compared with 2D T1w SE sequence. Moreover, we did not compare T1-mVISTA to a spoiled gradient recalled echo sequence, which might have performed better than MP-RAGE. Because it is not used in our clinical routine, we did not apply subtraction techniques, which could have probably led to an increase of detection rate in contrast-enhanced MP-RAGE as reported by Dodo et al[37] in a comparison of contrast-enhanced MP-RAGE and 2D SE in patients with glioma. Further, we only measured the length of the lesions, but not the volume, which would have been more precise.

In a future study, we aim to explore, whether the increase of CNR in T1-mVISTA can be used to reduce the gadolinium dose, as reduction of gadolinium dose is of utmost clinical importance to keep the chance of gadolinium deposition as low as possible, especially in patients with MS due to patients' age and the repetitive MRI scans.

Moreover, the combination of a gadolinium decreased protocol with a 32-channel head coil might lead to a further increase of the detection rate and a decrease in scan time.

In conclusion, our findings suggest that 3D T1-mVISTA seems to be superior to conventional 3D MP-RAGE for the detection of contrast-enhancing cerebral lesions in MS patients. Higher detectability of active lesions might improve the early diagnosis of MS, the diagnostic performance and might, therefore, be supportive in future studies and therapeutic management of MS patients. However, further studies with a larger patient cohort should be performed to confirm these initial findings.

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