3D T1-weighted black-blood magnetic resonance imaging for the diagnosis of giant cell arteritis

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ABSTRACT

Objective. *Imaging techniques have an increasing place in the diagnosis of giant cell arteritis (GCA). Achieving a confident diagnosis of GCA is often challenging and temporal artery biopsy is still considered as the gold standard despite the delayed results. 3T-MRI with 2D sequences has been evaluated for the detection of mural inflammation in extracranial arteries to support the diagnosis of GCA.*

Methods. *We evaluated the diagnostic performance of fat-suppressed 3D T1-weighted black-blood MRI (CUBE T1) with 3D TOF coregistration.*

Results. *Thirty-two patients with clinically suspected GCA were included and 10 had a diagnosis of GCA. Sensitivity and specificity of CUBE T1 were 80% and 100% respectively. Therefore, the positive predictive value of post-contrast CUBE T1 was 100% and the negative predictive value was 92%. Intra- and inter-observer agreement for mural enhancement on CUBE T1 was 1 and 0.83, respectively.*

Conclusion. *We demonstrate that CUBE T1 is accurate for the diagnosis of GCA. The reproducibility and short scan duration of the technique support a wider use of MRI in the diagnosis process.*

Introduction

Giant cell arteritis (GCA) is the most common form of vasculitis of large arteries affecting people older than 50 years. Visual signs are present in 20-30% of patients with GCA. Early diagnosis and treatment are required due to the risk of bilateral involvement. However, achieving a confident diagnosis of GCA is often challenging (1, 2). Indeed, temporal artery biopsy (TAB) has long been considered the gold standard for GCA diagnosis but it is invasive and its sensitivity ranges from 39% to 86% (3). Colour Doppler ultrasonography, the first line imaging exam, and PET scan have been proposed as alternative methods for GCA diagnosis but are not widespread in routine clinical practice (4, 5). Recent recommendations suggest the use of magnetic resonance imaging (MRI) as an alternative method for GCA diagnosis when Colour Doppler ultrasonography is not available (6, 7). 3T-MRI with 2D sequences has been evaluated for the detection of mural inflammation in extracranial arteries to support the diagnosis of GCA (8). Pre- and post-contrast fat-suppressed 3D High-resolution T1-weighted black-blood MRI (CUBE T1) provides a single 3D volume scan with sub-millimeter isotropic data, allowing multiplanar reconstructions of all segments of the external carotid. We decided to evaluate the diagnosis performance of CUBE T1 MRI in patients with a suspected diagnosis of GCA.

Materials and methods

Patients

Between 2014 and 2018, patients with a clinical suspicion of GCA who underwent MRI as part of the diagnosis process were included in this prospective cohort study. Patients originated from an internal medicine department or a neurological intensive care unit. Exclusion criteria were a previous TAB or a glucocorticoid therapy ≥48 hours before the MRI scan. Patients underwent the usual work-up for GCA diagnosis, encompassing TAB, PET scan or CDU, according to medical judgment. The doctor in charge of the patient established the final diagnosis based on the complete work-up and follow-up (except for CUBE T1 MRI). A specialist from the reference centre for vasculitis (AR) retrospectively confirmed the diagnosis.

Ethics statements

This study was conducted in compliance with the Good Clinical Practice protocol and the Declaration of Helsin-

ki principles. The study was approved by local ethics committee, who waived the requirement for informed consent.

MRI acquisition

MRI was performed in one centre on a 3T unit (MR 750, GE Healthcare) with an eight-channel head coil. The protocol included a fat-suppressed 3D High-resolution T1-weighted black-blood MRI sequence (CUBE T1) with the following parameters: sagittal plane acquisition; FOV 23×23×16 cm; TR/TE, 650/14 ms; bandwidth, 62.5 kHz; matrix, 288×288; spatial resolution, 0.9×0.9×1 mm interpolated to 0.45×0.45×0.5 mm^3. Parallel acceleration was applied along the phase direction (Autocalibrating Reconstruction for Cartesian Sampling, factor of 2). The total scanning time was 4 minutes 38 seconds. CUBE T1 was performed before and after injection of gadolinium chelate (0.2 mL/kg of gadoteric acid, DOTAREM®, GUERBET, France). A 3D-TOF was also acquired before gadolinium injection: FOV 22×19×11 cm, TR min TE 2.5ms; bandwidth: 71kHz; matrix 352x246; pixel 0.6×0.9 mm; phase 246; frequency 352, time 4 minutes 43 seconds.

Image analysis

Two neuroradiologists (CRR and WBH with 10 and 6 years of experience in vascular neuroimaging, respectively), blinded to all other data, independently reviewed images on a workstation (AW Workstation; GE Healthcare). In order to differentiate arteries and veins and better analyse vessel wall enhancement, 3D-TOF images were coregistered to pre- and post-contrast CUBE T1 images using an automated 3D rigid registration, visually checked, and manually corrected whenever necessary. A prominent or strong mural enhancement including perivascular enhancement of either frontal or parietal branches of the temporal arteries and/or occipital arteries was classified as positive, as described by Bley *et al*. (9). One reader (CRR) performed another reading session more than one month later, to compute intra-observer agreement. This second reading was used for the final analyses.

Table I. Main clinical and biological characteristics of patients undergoing MRI.

	Patients with GCA final diagnosis	Patients without GCA final diagnosis	Total population
Male/Female (%)	2/8	5/17	7/25 (22/78)
Mean age (year) ± SD	69 ± 13	71 ± 12	70 ± 12
Mean C-reactive protein (mg/dL) ± SD	148 ± 150	23 ± 40	59 ± 98
Clinical symptoms:			
• *Headaches* (%)	9 (90)	15 (68)	24 (75)
• *Acute neurological deficit* (%)	0	15 (68)	15 (47)
Visual palsy or loss of vision		8 (36)	8 (25)
Other acute neurological deficiency		7 (32)	7 (22)

GCA: giant cell arteritis; SD: standard deviation.

Inter- and intra-reader agreement for presence or absence or arterial wall enhancement was assessed with Cohen's kappa statistic.

Results

Thirty-two patients (25 women, 7 men mean±SD age 70.2±12.1 years) were included. Main clinical and biological characteristics of patients at the time of inclusion are summarised in Table I. Ten of these patients had a final diagnosis of GCA. Another diagnosis was obtained for 21 patients. Interestingly, among diagnosis, 2 patients had a primary central nervous system vasculitis, 1 patient had an ANCA associated vasculitis, 1 had a polymyalgia rheumatica without evidence of GCA and another patient had a temporal cellulitis. Thirteen patients had non-arteritis vascular event. No diagnosis was obtained despite extensive workup for 1 patient.

3D CUBE T1 displayed the arteries wall clearly, allowing an easy identification of parietal enhancement, and the 3D TOF coregistration was helpful in image analysis (Fig. 1). Indeed, intra- and inter-observer agreement for mural enhancement on CUBE T1 was 1 and 0.83, respectively.

Eight of the 10 patients with GCA had a strong mural enhancement in post-contrast CUBE T1 (Fig. 1), while none of the 22 patients without GCA had mural enhancement on MR images: sensitivity was therefore 80% and specificity 100%. Regarding the 2 patients with GCA and no mural enhancement on MRI, both had normal TAB and the diagnosis was obtained on an aortic FDG uptake with PET scan in one case and on clinical symptoms only in the other case. Therefore, the positive predictive value of post-contrast CUBE T1 was 100% and the negative predictive value was 92%. In our cohort, only 6 of the 10 GCA patients had a positive TAB (length of TAB ranging from 5 to 20 mm) (10). Therefore, the sensitivity of TAB was 60%. If TAB was used as the reference standard, MRI yielded a sensitivity of 100%. Despite normal TAB, two patients with a final diagnosis of GCA had arteritis on MRI after analysis of CUBE T1 images; in one of them, vessel enhancement was observed only in occipital artery.

Among the patients with another diagnosis than GCA, post-contrast CUBE T1 would have been contributive in the diagnosis of primary isolated central nervous vasculitis (2 patients); indeed, a strong mural enhancement was observed in intracranial internal carotid arteries in post-contrast CUBE T1, sparing extra-cranial vessels. Another patient had temporal cellulitis with a clear MR enhancement of subcutaneous fat, without mural enhancement of extracranial arteries. Interestingly, another patient had a diagnosis of small vessel vasculitis and no mural artery enhancement was observed.

Discussion

We here demonstrate the feasibility and accuracy of a 3D post-contrast CUBE T1 in the diagnosis of GCA. Indeed, we observed a sensitivity of 80%, which is higher than the 64.1% sensitivity observed by Rhéaume *et al*. with 2D sequences in their series of 171 patients (8). We cannot exclude that the higher sensitivity we observed was due to a shorter duration of glucocorticoid ther-

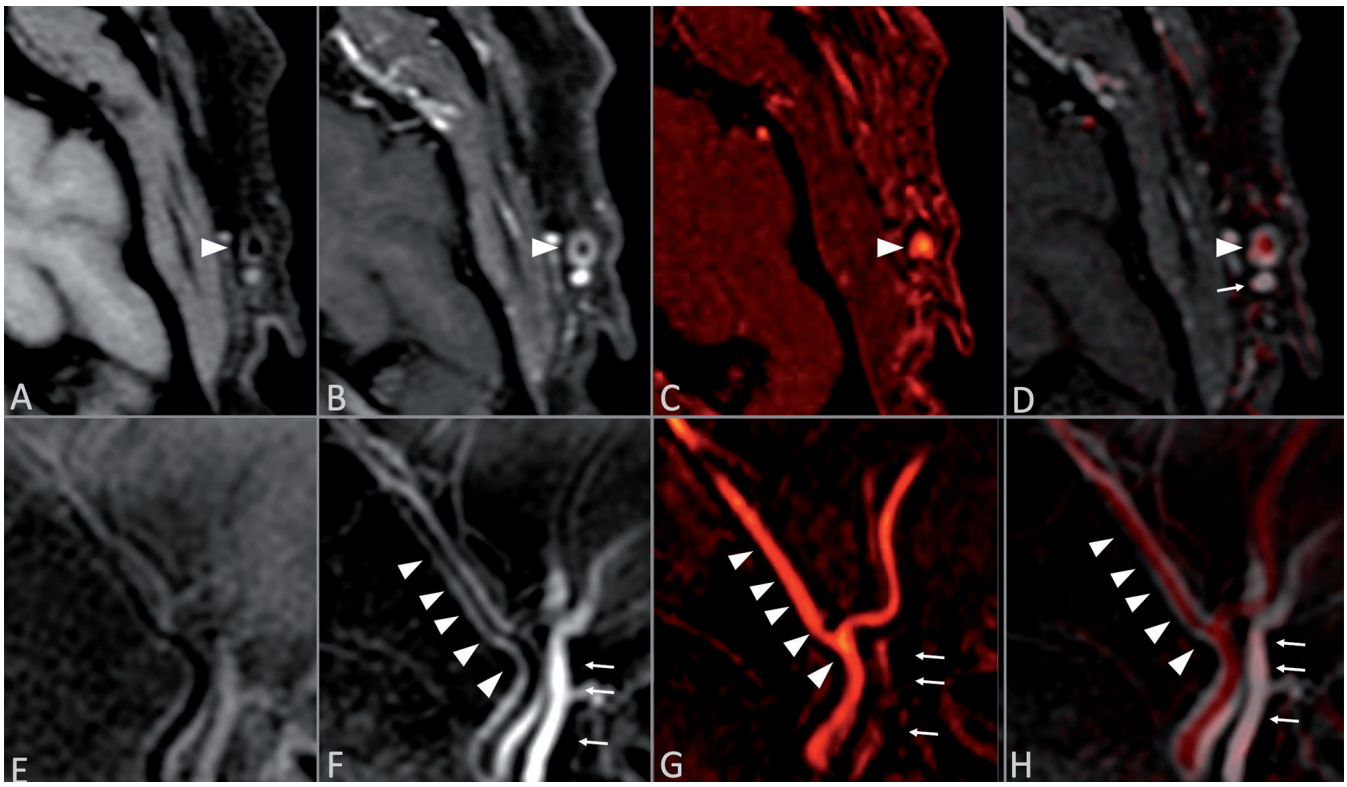

Fig. 1. Mural enhancement of the left temporal artery in giant cell arteritis.
Axial and sagittal reconstructions of CUBE T1 sequence before (**A** and **E**, respectively) and after contrast injection (**B** and **F**, respectively). 3D TOF sequence in axial and sagittal plane (**C** and **G**, respectively) coregistered with post-contrast CUBE T1 sequence (**D** and **H**, respectively), allowing differentiation between the temporal artery in red (arrowhead) (**C**, **G**) and the temporal vein (arrows) (**D**, **H**). Strong mural enhancement of the temporal artery (arrowhead) (**B**, **D**, **F**, **H**).

apy received by our patients (<2 days in our study compared to 8.5±8.2 days in the Rhéaume study). Indeed, sensitivity was decreased in patients who received more than 5 days of glucocorticoid before MRI (11). However, it seems more likely, that the 3D MRI acquisition, allowing multiplanar reconstructions, together with the 3D TOF coregistration could account for the higher sensitivity and the excellent reproducibility. In our study, we had similar sensitivity and specificity as compared to a previous study focusing on superficial cranial arteries (11). Post-contrast CUBE T1 enables all branches of external carotid arteries to be evaluated and was superior to TAB in 2 patients of our cohort by identifying another site of parietal inflammation in occipital arteries, missed by TAB (12). In addition, this increased sensitivity was obtained with a very high specificity (100%). Our results support the view that MRI might become a major examination for the diagnosis of GCA, as recently proposed by the EULAR recommendations and previous studies (6-9, 11). One patient had a diagnosis of GCA based on the high 18-FDG uptake in aorta on PET scan. Further studies are needed to confirm that combining imaging of proximal arteries with that of distal branches of external arteries increases the sensitivity of MRI. MRI could also provide additional help in the diagnosis process, as it would have been informative for differential diagnosis in 3 patients.

Finally, the inter-reader and intra-reader agreement for the detection of mural enhancement were excellent. The reproducibility and short scan duration are clearly an advantage of the CUBE T1 sequence with sub-millimetric voxels acquisition.

Our study has several limitations. First, patients included in the study underwent MRI as part of the clinical work-up based on clinical GCA suspicion. Although patients came from two different hospitals, our population might not be representative of all patients with a GCA clinical suspicion. In addition, the small size of our cohort does not allow definitive conclusion. Last, MRI was performed with a 3T single imager. Although 3D fat-suppressed T1-weighted black blood MRI sequences are available from all manufacturers, larger studies are required to confirm our preliminary results and evaluate our technique with 1.5T imager.

Conclusion

We have demonstrated the feasibility of 3D fat-suppressed T1-weighted black blood sequence for the diagnosis of GCA. We also propose 3D TOF coregistration in order to improve image analysis. Further studies are required to confirm our preliminary results.

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