Susceptibility weighted magnetic resonance imaging of cerebral cavernous malformations: prospects, drawbacks, and first experience at ultra–high field strength (7-Tesla) magnetic resonance imaging

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High-resolution susceptibility weighted MR imaging at high field strength provides excellent depiction of venous structures, blood products, and iron deposits, making it a promising complementary imaging modality for cerebral cavernous malformations (CCMs). Although already introduced in 1997 and being constantly improved, susceptibility weighted imaging is not yet routine in clinical neuroimaging protocols for CCMs. In this article, the authors review the recent literature dealing with clinical and scientific susceptibility weighted imaging of CCMs to summarize its prospects and drawbacks and provide their first experience with its use in ultra–high field (7-T) MR imaging. (DOI: 10.3171/2010.6.FOCUS10130)

KEY WORDS • cavernous malformation • venous anomaly • susceptibility weighted imaging • high-field magnetic resonance imaging

Susceptibility weighted imaging is a high-resolution 3D–gradient echo MR imaging sequence that uses both magnitude and filtered phase information, separately or combined, to create an image based on T2*-contrast and phase changes due to magnetic susceptibility. The latter is defined as the magnetic response of a substance when placed in an external magnetic field.9 As most biological tissues are diamagnetic, for example, brain parenchyma,36 phase image contrast is dominated by paramagnetic substances that have a large impact on its surrounding magnetic field, such as deoxygenated blood, hemosiderin, methemoglobin, or ferritin. They produce a strong hypointense signal in the processed susceptibility weighted images and therefore allow high-resolution depiction of venous structures, blood products, and iron deposits (Fig. 1). These principles of susceptibility weighted imaging do not depend on high intravascular flow such as in T2-weighted imaging, time-of-flight angiography, and phase-contrast MR angiography when depicting small vessel structures.38 Among several potential clinical applications in neurosurgery, as already proposed by Mittal et al.,23 susceptibility weighted imaging may therefore be most helpful in imaging CCMs. Occurring as sporadic or hereditary forms,44 these low-flow vascular lesions affect 0.4%–0.9% of the population28 and represent 8%–15% of all cerebrovascular malformations.4 Pathologically, CCMs are characterized by closely packed, thin-walled, enlarged vessels without intervening brain parenchyma43 and are filled with blood at different stages of thrombosis.41 The lesions are accompanied by associated venous malformations in many of the reported cases.24 Recurrent intrallesional microhemorrhages and secondary iron deposit mainly determine the symptoms in patients10 and form the typical appearance of these lesions on conventional MR imaging.17,32

Although the first article on susceptibility weighted imaging was already published in 199731 and sequence software has constantly been improved and is available from all major developers, it has not yet been routinely incorporated into clinical “neuroimaging protocols” for CCM.29 This may be due to the fact that at lower field strength (1.5-T) MR imaging, the full application of sus-
Susceptibility Weighted Imaging in Detection of CCMs

Gradient echo T2*-weighted imaging is currently considered a clinical gold standard in detection of CCM.29,38 The typical signal loss caused by hemosiderin deposits within and around the lesion together with susceptibility changes between deoxygenated blood and the surrounding brain tissue can reveal CCMs that are missed on conventional T1- and T2-weighted images. However, several authors suggested relatively early26,38 that susceptibility weighted imaging should be theoretically superior to conventional T2*-weighted gradient echo imaging in this regard, especially at higher magnetic field strengths. In 1999, Lee et al.29 demonstrated that susceptibility weighted imaging at 1.5-T field strength revealed additional lesions in 2 of 10 patients with CCMs compared with standard T2*-weighted gradient echo imaging. In 2007, Pinker et al.25 reported an improvement in lesion detection using 3-T high-resolution susceptibility weighted imaging compared with T2*-gradient echo imaging at 1.5 T in a series of 17 patients with CCMs. They were able to detect an additional 7 lesions in 6 patients. All of these lesions were very small, on average smaller than 0.33 cm. A study of 15 patients with familial CCMs conducted by de Souza et al.6 compared the sensitivity of lesion detection of susceptibility weighted imaging, T2*-gradient echo imaging, and T2-weighted turbo spin echo sequences at 1.5-T field strength. They found that especially in these patients presenting with multiple lesions, susceptibility weighted imaging has a significantly higher sensitivity than conventional imaging. Recently, Schlamann et al.37 presented a series of 10 patients with CCMs. The authors focused on the comparison of T2*-weighted gradient echo imaging at 1.5-T and 7-T field strength. They detected an additional lesion in 1 patient and numerous new lesions in a patient with a familial CCM using 7-T MR imaging. An additional sensitivity of susceptibility weighted imaging at 7-T fieldstrength imaging compared with T2* gradient echo imaging could not be observed; however, imaging protocols were designed to be comparable to routine 1.5-T MR imaging protocols and not to maximize the detectability of CCM lesions.

In summary, these small series show an improved sensitivity of susceptibility weighted imaging in identifying the number of lesions in patients with CCM compared with conventional T2*-weighted gradient echo imaging. Naturally, the effect is suggested to be higher in patients with multiple lesions. Even very small lesions could be detected. These effects might be beneficial for preoperative imaging, screening, and follow-up imaging in patients with familial CCM or multiple CCM after radiation therapy (Fig. 2). In patients with “cryptogenic” epilepsy or atypical intracerebral hemorrhage, susceptibility weighted imaging may also help to confirm the diagnosis of a CCM in cases in which the lesion could not be detected on conventional MR imaging.

Susceptibility Weighted Imaging in Detection of Associated Venous Malformations

The association of CCMs with venous malformations is still controversial. Initially regarded as unusual coincidences,33 several authors reported series with higher numbers of CCMs presenting with associated venous malformations.14,24,28,39,45 Up to now, no consensus has been found regarding whether associated venous malformations are involved in the CCM’s pathogenesis and natural history or how they should be treated.13,24,49 One problem in clarifying this ambiguity is the challenging imaging of associated venous malformations, which are often occult on preoperative MR imaging or digital subtraction angiography.13,28 Recently, Hong et al.11 reported a series of 21 patients who presented with a CCM in the territory of a DVA. They investigated the presence of a curved medullary or draining vein in the distal portion of the CCM, the narrowing of the distal draining vein, and the presence of severe medullary venous tortuosity using contrast-enhanced gradient echo imaging at 3-T field strength. They observed a significantly higher amount of these angiarchitectural findings than in a control group and thus suggested these findings to be key factors in causing concurrent sporadic CCMs. Susceptibility weighted imaging might be a powerful complementary imaging tool in this regard. Although no large clinical series focusing the detection of associated venous malformations in CCMs exist, evidence from single cases is promising (Fig. 3C). Several authors have already reported an excellent depiction of DVAs, demonstrating the supe-
Susceptibility weighted imaging of CCMs

Prior visualization of both medullary and collector veins in non–contrast enhanced susceptibility weighted imaging over conventional MR imaging. However, in the series by Pinker et al., among 17 patients with CCMs, no associated DVAs could be detected using 3-T susceptibility weighted imaging. A correlation with intraoperative findings of associated venous malformations was not possible because most of the patients in this series underwent Gamma Knife surgery rather than surgical removal of the CCM. Hence, the sensitivity of susceptibility weighted imaging in this task has to be investigated in larger series of CCMs undergoing surgical removal.

Susceptibility Weighted Imaging in Preoperative and Postoperative Imaging

Once a neurosurgical treatment decision is made, preoperative MR imaging of the lesion and its surrounding anatomical structures is crucial, especially to identify the optimal surgical approach, estimate the amount of hemosiderin deposit in the adjacent brain tissue, and reveal associated venous malformations. Besides the improved depiction of venous malformations, as mentioned above, susceptibility weighted imaging may foremost be helpful in preoperatively delineating even very small amounts of hemosiderin deposits or residuals of these deposits on postoperative images. Most authors recommend complete removal of the deposits in the adjacent brain to achieve optimal seizure control, and residual hemosiderin deposits have been found to be associated with impaired seizure control, although its complete role in this regard has yet to be discovered. Clearly, susceptibility weighted imaging will be superior in the detection of even the smallest residual CCM postoperatively and has the potential to monitor increase or decrease in lesion vascularity after, for example, Gamma Knife surgery as already mentioned by Pinker et al.

Scientific Applications of Susceptibility Weighted Imaging in CCM Research

There are only a few studies that have addressed the application of MR imaging in fundamental CCM research. Shenkar et al. reported the visualization of CCMs in

Fig. 2. Axial slices of susceptibility weighted MR images with MIP in a 34-year-old man with confirmed familial CCM revealing multiple hypointense lesions (several labeled with small white arrows) suggestive of CCM. CP = choroid plexus; GP = globus pallidus; P = putamen; RN = red nucleus; SN = substantia nigra. The small black arrows denote the signal cancellations caused by the adjacent frontal sinus.

Fig. 3. Case 1. Neuroimaging was performed routinely in this 39-year-old man after a car accident. A: On 1.5-T MR imaging, T2*-weighted gradient echo imaging reveals very discreet signal changes in the right parietal white matter (arrows) suggestive of a DVA. B: An additional contrast-enhanced T1-weighted turbo spin echo image (B) confirms that suspicion (arrow). C: Susceptibility weighted imaging at 7 T, using MIP, precisely delineates the DVA (vertical arrow) and reveals 2 hypointense lesions (horizontal arrows) most likely to be associated CCMs.
various states of their development in CCM1 and CCM2 knockout mice using T2*-weighted gradient echo imaging at ultra–high field strength MR imaging. Furthermore, they reported the delineation of intrallesional angioarchitecture in ex vivo MR imaging of excised human CCM lesions and compared their results with histopathological findings.

A variety of animal models of CCM have been recently described to help translate the cellular and biochemical insights into a better understanding of disease mechanism. However, neither CCM1 nor CCM2 heterozygous knockout mice sufficiently develop CNS vascular lesions. The combination of homozygous loss of the tumor suppressor p53 with heterozygous knockout CCM1 sensitizes mice to develop cerebral vascular lesions, but still with an unsatisfactory incidence. These data indicate the requirement of the manipulation of the current animal models to more closely mimic human disease. On the other hand, CCMs in humans can grow for years, whereas the shorter lifespan of mice is likely to limit the size of the lesions that cannot be easily detected using routine histological methods. Applying advanced detection technologies such as susceptibility weighted imaging may largely improve the sensitivity of the visibility of lesions. More importantly, susceptibility weighted imaging is a noninvasive, non–contrast enhanced imaging tool and allows long-term tracking of lesion development. Therefore, susceptibility weighted imaging could be a powerful tool not only in clinical applications but also especially in repetitively monitoring the changes in the venous vascular system of animal models.

**Drawbacks and Pitfalls of Susceptibility Weighted Imaging in Imaging of CCMs**

As mentioned above, susceptibility weighted imaging requires long echo times and high spatial resolution, and therefore leads to an unreasonably long measurement time at lower field strength for covering the whole brain volume. However, this can be compensated by the increased signal-to-noise ratio available at higher field strength MR imaging (B0 ≥ 3 T). The main drawbacks of susceptibility weighted imaging are signal dropouts and phase artifacts especially at the air-tissue boundaries, such as the rostral skull base and the temporal lobe adjacent to the petrosal bone (Fig. 2). In these areas, detection of CCMs might be compromised. Another problem, especially at higher field strengths, could be the increasing “blooming” of susceptibility in the susceptibility weighted imaging data. These circular hypointense artifacts, caused by the strongly paramagnetic blood products within the lesion, can mask venous malformations associated with the CCM or other small CCMs nearby (Figs. 4 and 5). One simple approach to these problems may be the adaptation of the echo time, in-plane resolution and readout bandwidth of the sequence to reduce these artifacts, but also a separate analysis of magnitude, phase, and susceptibility weighted imaging information can be helpful. Further methods to reduce artifacts in susceptibility weighted imaging have been proposed already. Generally, we always have to consider other reasons for hypointense lesions in T2*-weighted gradient echo imaging or susceptibility weight-

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**Fig. 4.** Case 2. Preoperative 7-T MR images of a pontine CCM in a 29-year-old woman. The patient presented with a hemihypesthesia of the left half of the face and the right half of the body, and a mild motor weakness. The CCM was fully removed using a left subtemporal transtentorial approach. Comparison of T2-weighted turbo spin echo (A), T2*-weighted gradient echo (B), and susceptibility weighted imaging at the same brain level. In the phase image (D) and in the processed susceptibility weighted image (E), a curved draining vein can be seen (white arrows), which was identified intraoperatively (F). In the T2*-weighted gradient echo (B) and in the magnitude (C) images, as well as in the routine preoperative contrast-enhanced T1-weighted turbo spin echo, this vessel structure could not be delineated. The T2-weighted turbo spin echo (A) is showing the typical popcorn-like aspect of the CCM, representing different stages of microhemorrhage. The rather acute hemorrhages lead to stronger intrallesional signal cancellations in the T2*-weighted gradient echo and susceptibility weighted images. TN = trochlear nerve. Small black arrows denote the incised tentorium.
ed imaging, even in patients with multiple CCMs. In this regard, especially calcifications of a different origin or microangiopathic lesions have to be taken into account. Schlamann et al. also observed differences in lesion size between 1.5-T and 7-T MR imaging in T2*-weighted gradient echo imaging up to 11%, which might also account for susceptibility weighted imaging. It will be difficult to investigate whether this increase in lesion size is caused by higher sensitivity to adjacent hemosiderin deposits or an artifact of the increased susceptibility at higher magnetic field strength MR imaging.

First Experience With Susceptibility Weighted Imaging of CCM at 7-T Field Strength

The local ethics committee authorized the patient examinations as part of fundamental research on high-field MR imaging. Written consent was obtained from all patients before imaging.

Susceptibility weighted imaging was performed using a 7-T MR imaging system (Magnetom 7T, Siemens Healthcare) equipped with a gradient coil (coil length 125 cm) capable of 45 mT/m maximum amplitude and a slew rate of 220 mT/m/msec. We used a custom-built 8-channel transmit/receive (Tx/Rx) head coil, which was previously characterized in simulations and benchmark measurements, and a commercially available 1-channel Tx and 32-channel Rx (Nova Medical) head coil. The standard susceptibility weighted imaging sequence parameters are as follows: TE 15 msec, TR 27 msec, flip angle 14°, in-plane resolution 250 × 250 μm², slice thickness 2 mm, bandwidth 140 Hz/pixel. Note that the flip angle was chosen to maximize the vessel/brain contrast leading to a decreased CSF signal. Recommended sequence parameters for different magnetic field strength can be found elsewhere. After image acquisition magnitude, phase, susceptibility weighted imaging, and MIP, susceptibility weighted imaging data were analyzed separately. Minimum intensity projection is a postprocessing tool to accumulate image information from multiple slices into a single plane of projection, thereby creating a 3D impression. Patients undergoing 7-T MR imaging were rather admitted to the department of neurosurgery for treatment of a CCM or included in follow-up or screening MR imaging examinations at the department of radiology. Figures 3–5 display the different findings in a group of selected patients.

Conclusions

Susceptibility weighted imaging is a very helpful complementary MR imaging sequence for CCMs. It has proven to be superior to conventional MR imaging in the detection of these lesions, and the data available from single case reports suggest that the modality has further applications, especially in imaging of the associated venous structures. Now that higher field strength (≥ 3-T) MR imaging becomes more and more available, the technical limitations of susceptibility weighted imaging can be overcome and its integration into standard neuroimaging protocols for CCM may expand.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following: Conception and design: Dammann. Acquisition of data: Dammann. Analysis and interpretation of data: Dammann. Drafting the article: Dammann, Sure. Critically revising the article: Barth, Zhu, Maderwald, Schlamann, Ladd, Sure. Reviewed final version of the manuscript and approved it for submission: Ladd, Sure. Administrative/technical/material support: Barth, Zhu, Maderwald, Schlamann.
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