Clinical Value of 3D T2*-weighted Imaging with Multi-echo Acquisition: Comparison with Conventional 2D T2*-weighted Imaging and 3D Phase-sensitive MR Imaging

Akira KUNIMATSU1*, Yuichi SUZUKI2, Kazuchika HAGIWARA1, Hiroki SASAKI3, Harushi MORI1, Masaki KATSURA1, and Kuni OHTOMO1

1Department of Radiology, Graduate School of Medicine, The University of Tokyo
7–3–1, Hongo, Bunkyo-ku, Tokyo 113–8655, Japan
Departments of 2Radiological Technology and 3Radiology, The University of Tokyo Hospital
(Received November 15, 2011; Accepted April 4, 2012)

Susceptibility-weighted angiography (SWAN) is a state-of-the-art 3-dimensional (3D) T2*-weighted imaging (T2*WI) technique with multiple echo acquisitions, but its clinical utility remains to be determined. We compared the utility of susceptibility-weighting sequences among SWAN, 3D phase-sensitive magnetic resonance (MR) imaging (PSI), and conventional 2-dimensional (2D) T2*WI in routine clinical practice. Our results indicate that SWAN can achieve susceptibility weighting more effectively than conventional 2D T2*WI and as effectively as PSI and requires a much shorter scan time than PSI.

Keywords: MRI, susceptibility-weighted imaging, T2*-weighted imaging

Introduction

Susceptibility-weighted magnetic resonance (MR) imaging is widely used to evaluate hemorrhagic foci, iron deposition, or the small venous vasculature of the brain.1 Either 2-dimensional (2D) conventional gradient-recalled echo T2*-weighted or 3-dimensional (3D) susceptibility-weighted MR imaging technique is usually applied for these purposes.

Susceptibility-weighted angiography (SWAN), or T2*-weighted angiography, is a new, commercially available, gradient-recalled echo-based, 3D T2*-weighted imaging (T2*WI) technique with multiple echo acquisitions. Sampling multiple echoes at different echo times (TEs) inherently aims to gain both high signal to noise and high susceptibility weighting at the same time. Higher signals are obtained at shorter TEs, and higher susceptibility effects are achieved at longer TEs.2,3 SWAN uses only magnitude and not phase information of MR signals from the tissues and theoretically offers a different tissue contrast from 3D susceptibility-weighted MR imaging, which utilizes both magnitude and phase information.

SWAN is thus expected to have different imaging characteristics from 2D conventional T2*WI or 3D susceptibility-weighted MR imaging techniques with single echo acquisition at one echo time. However, we believe the paucity of literature means that the diagnostic ability of SWAN has not been determined in comparison with the latter two.4,5 We aimed to investigate diagnostic ability among these 3 imaging techniques with regard to commonly desired aspects of susceptibility-weighted MR imaging—detection of mineralization and cerebral microbleeds, and depiction of small venous vasculature.

Materials and Methods

We retrospectively analyzed SWAN datasets of 32 patients (19 men, 13 women; aged 41.8 years, range 12 to 77) who underwent MR imaging from February to August 2010 at our institution for various medical conditions, including arteriovenous malformation in 16, cavernous malformation in eight, multiple sclerosis in two, and miscellaneous other conditions, including infarction, migraine headache, trauma, and tumor, in six. No study patient had a history of systemic vasculitis. The MR scan techniques performed in our study included 3D susceptibility-weighted MR imaging technique employing magnitude image modulation by phase
information (namely, phase-sensitive MR imaging: PSI) or 2D T$_2^*$WI as a control, in addition to SWAN. Our institutional review board waived informed consent for this retrospective study.

A 3.0-tesla MR scanner was used (Signa HDxt, GE Healthcare, Milwaukee, WI, USA). SWAN was acquired with repetition time (TR), 44 ms; effective TE, 30 ms; flip angle, 20°; field of view (FOV), 210 mm; matrix size, 320×192; slice thickness, 2.0 mm (i.e. voxel size, 0.7×1.1×2.0 mm); and approximate scan time, 3.5 min to cover the entire brain with a parallel imaging technique (parallel imaging acceleration factor of 2). PSI and 2D T$_2^*$WI were performed using our routine clinical parameters. Parameters for PSI were TR/TE, 40/25 ms; flip angle, 30°; FOV, 240 mm; matrix size, 256×192; slice thickness, 2.0 mm, i.e. voxel size, 0.9×1.3×2.0 mm; and approximate scan time, 7 min with maximum scan slab of 120 mm. For 2D T$_2^*$WI, parameters were TR/TE, 560/10 ms; flip angle, 30°; FOV, 210 mm; matrix size, 320×256; slice thickness, 3.0 mm, i.e. voxel size, 0.7×0.8×3.0 mm; and approximate scan time, 4 min to cover the entire brain. Flow compensation was implicitly integrated in SWAN and PSI. No parallel imaging techniques were used in PSI or 2D T$_2^*$WI. All images were acquired in transaxial planes.

Two neuroradiologists (A.K. and K.H.) independently reviewed images of SWAN, PSI, and 2D T$_2^*$WI, and assessed (i) depiction of mineralization of the putamen on SWAN, PSI, and 2D T$_2^*$WI, (ii) depiction of small veins on SWAN and PSI, and (iii) detection of hemosiderin deposition on SWAN and 2D T$_2^*$WI.

**Depiction of mineralization of the putamen**

We scored putaminal mineralization using the 5-point scale reported by Harder and colleagues (Fig. 1).\(^7\) We used source axial images to compare SWAN, PSI, and 2D T$_2^*$WI rather than the minimum intensity projections frequently used for SWAN and PSI. Mineralization was graded according to hypointensity that demonstrated the posterolateral to anteromedial gradient of putaminal mineralization with age. We chose either the right or the left putamen showing hypointensity more evidently. We did not evaluate putamen affected by large infarct or tumor.

**Depiction of small veins**

We scored depiction of small veins using a 5-point scale (Grade 0, none; 1, poor; 2, moderate; 3, good; 4, excellent). We chose medullary veins at the level of the body of the lateral ventricles to the centrum semiovale as small-sized veins and subependymal and cortical veins at the level of the body of the lateral ventricles as small- to medium-sized veins. We carefully excluded draining veins continuous to an arteriovenous malformation from analysis. We defined tubular hypointensity continuously running through neighboring image slices as a vein. We used minimum intensity projections with 10-mm slab thickness for SWAN and PSI.

**Detection of hemosiderin deposition**

We reviewed those radiological reports of the 32 subjects that contained one or more of the words ‘‘microbleed,’’ ‘‘cavernous malformation or angiomata,’’ or ‘‘hemorrhage.’’ Neither acute nor subacute hemorrhage was included in the following analysis. Hemosiderin deposition was defined as a dark spot on the whole brain SWAN or 2D T$_2^*$WI scans. Both observers counted the numbers of dark spots on each type of scan, and the averaged numbers were compared. Source axial images were used for SWAN to compare SWAN with 2D T$_2^*$WI. Because the scan coverage of PSI was limited as described, we did not use PSI to evaluate cerebral microbleeds that could be scattered throughout the brain and did not include PSI in this analysis.

Preliminary to paired comparisons, we used weighted kappa analysis to assess interobserver variability for qualitative grading in (i) and (ii) described above.\(^8\) We averaged measurements by both observers on each subject and used them for the subsequent comparisons. We used paired comparison methods, Wilcoxon’s signed-rank sum test for (i) and (ii), and paired t-test for (iii). The paired t-test was applied to (iii) after we confirmed normal distribution of the numbers of dark spots by Kolmogorov-Smirnov test. Kolmogorov-Smirnov test and all paired comparison tests were performed with standard statistical software (SPSS statistics).
Results

Depiction of mineralization of the putamen

SWAN was acquired in 32 cases. As controls, we used PSI in 16 cases and 2D T2*-WI in the other 16 cases. In 5 of the 16 cases in which PSI was acquired, the putamen was not included in the scan coverage, because of the limitation of the scan slab of 120 mm. These 5 cases were excluded from the paired comparison. Figure 2A shows the results of grading of putaminal mineralization on SWAN and PSI (11 cases) by both observers. Similarly, Figure 2B shows the results of grading on SWAN and 2D T2*-WI (16 cases). Interobserver analysis gave a kappa value of 0.67, and substantial interobserver consistency was found. Both observers gave grades of 3 or 4 more frequently to SWAN than to PSI and 2D T2*-WI (Fig. 3). Statistical analysis confirmed higher scores for SWAN than for PSI ($P = 0.003$) and 2D T2*-WI ($P = 0.001$).

Depiction of small veins

SWAN and PSI were both acquired in 16 cases. In PSI, limited scan coverage prevented the scanning of veins as described in 4 cases (medullary veins, 3 cases; cortical and subependymal veins, one case), which we excluded from the paired comparison. Figure 4 shows the results of small vein depiction, 4A, of the medullary veins (SWAN, 16 cases; PSI, 13 cases), and 4B, of the cortical or subependymal veins (SWAN, 16 cases; PSI, 15 cases). The kappa value was calculated at 0.58, and moderate interobserver consistency was found. Both observers graded more than half the cases as 2 (moderate) or higher (Fig. 4). SWAN and PSI did

Fig. 2. Stacked bar chart of grades of mineralization of the putamen. A: Comparison between susceptibility-weighted angiography (SWAN) and phase-sensitive magnetic resonance (MR) imaging (PSI). B: Comparison between SWAN and conventional 2D T2*-weighted imaging (T2*WI).

Fig. 3. Mineralization of the putamen. A: Susceptibility-weighted angiography (SWAN) shows Grade 4 mineralization. B: Phase-sensitive magnetic resonance (MR) imaging (PSI) shows Grade 2 mineralization in a 30-year-old woman with multiple sclerosis.
not differ significantly ($P=0.641$ for depiction of medullary veins and $P=0.564$ for depiction of cortical or subependymal veins) (Fig. 5).

**Detection of hemosiderin deposition**

SWAN and the corresponding 2D T$_2^*$WI of 11 cases fulfilled the inclusion criteria. More dark spots were found in SWAN (32.1 ± 49.0) than in 2D T$_2^*$WI (17.3 ± 31.7) (Fig. 6). The slope of the linear regression analysis shown in Fig. 6 was 1.44, and the results suggested that SWAN could depict dark

![Fig. 4](image1.png)

**Fig. 4.** Stacked bar chart of grades of depiction of medullary veins (A) and cortical or subependymal veins (B). PSI, phase-sensitive magnetic resonance (MR) imaging; SWAN, susceptibility-weighted angiography.

![Fig. 5](image2.png)

**Fig. 5.** Venography with susceptibility-weighted angiography (SWAN) and phase-sensitive magnetic resonance (MR) imaging (PSI). Some medium-sized veins, including the cortical, septal, and thalamostriate veins (arrows), appear more clearly on SWAN (A) than PSI (B) of a 52-year-old woman with an unruptured aneurysm of the internal carotid artery. Depiction of small-sized veins (arrowheads) also seems to be slightly superior on SWAN (A) than PSI (B). However, group comparison showed no statistically significant difference between SWAN and PSI.

![Fig. 6](image3.png)

**Fig. 6.** Scatter plot of the numbers of dark spots between 2-dimensional (2D) T$_2^*$-weighted imaging and susceptibility-weighted angiography (SWAN). Dotted line shows the regression line with a slope of 1.44 and intercept of 8.13.
spots approximately 1.4 times better than 2D T₂*WI (Fig. 7). Paired t-test showed significant difference ($P = 0.040$).

**Discussion**

Our results indicate that SWAN can achieve susceptibility weighting more effectively than 2D T₂*WI and as effectively as PSI. Moreover, SWAN may be more practical for 3D susceptibility-weighted MR imaging because it requires a shorter scanning time than PSI, even with higher spatial resolution. Techniques for magnetic susceptibility-weighted imaging, including 2D T₂*WI and 3D PSI, are now widely used to detect local magnetic inhomogeneities in the brain. The causes of local magnetic susceptibility differences in the brain tissue include mineralization, especially iron deposition, and chemical shift between deoxy- and oxy-hemoglobin. Nowadays, the clinical importance of cerebral microbleeds in cerebrovascular disease is widely accepted. Cerebral microbleeds have been associated with future risk of stroke and are a common MR finding of cerebral amyloid angiopathy. Recent research has also shown that increased venous contrast in ischemic brain tissue can be clearly visualized with PSI.

Gradient-recalled-based 2D T₂*WI is a conventional and traditional technique for susceptibility-weighted imaging that has been widely utilized to detect hemosiderin deposition resulting from intracerebral hemorrhage. The common cause of intracerebral hemorrhage includes asymptomatic cerebral microbleeds in the elderly, cavernous malformation, and intratumoral hemorrhage. Our results indicate that SWAN may more effectively detect hemosiderin deposition and display mineralization of the basal ganglia earlier than 2D T₂*WI. The scanning time required to cover the entire brain is not longer with SWAN than 2D T₂*WI, which may be another clinical advantage of SWAN.

Compared with PSI, SWAN may have an equivalent ability to depict venous vasculature and a superior ability to detect mineralization of the basal ganglia. Since the advent of 3D susceptibility-weighted MR imaging, including PSI, clinical attention has been directed at detecting further subtle differences in local magnetic susceptibility of the brain. Another target for detection by 3D susceptibility-weighted MR imaging is the chemical shift between deoxy- and oxy-hemoglobin, which results in signal loss of deoxygenated venous blood and an increase in contrast between veins and surrounding tissue. Therefore, clinicians have been demanding improved detection of iron or hemosiderin deposition and enhanced venous vessel depiction based on the new, highly susceptibility-weighted imaging techniques. Though its constructs of image contrast are different from those of PSI, SWAN may be able to detect very subtle magnetic inhomogeneities. However, 2 major differences noted between PSI and SWAN are the number of times of echo acquisition and the presence or absence of image modulation with a series of phase-masking processes. In PSI, magnitude images are acquired at a single TE and then multiplied by the phase mask, whereas
SWAN uses only magnitude images acquired at multiple TEs to accomplish the final images without modulation by the phase mask. Thus, use of the SWAN approach might result in a loss of information because phase information is not taken into account, but the loss of phase information could result in robust depiction of veins independent of vessel orientation. So, this may be another advantage of SWAN. Moreover, by saving the post-processing required for PSI, SWAN may have an added value as a clinical routine in a limited scan time.

The advantages of SWAN may be mostly ascribed to multiple echo acquisitions at different TEs, which inherently provide both high signal to noise and high susceptibility weighting simultaneously. Higher signals are obtained at shorter TEs, and higher susceptibility effects are achieved at longer TEs. In addition, multiple acquisitions result in an increased number of signals averaged and thus a decrease in random noise effects. Use of single-echo-long TE scans to achieve a strong susceptibility effect lead to geometric distortion and chemical shift artifacts. However, SWAN addresses this drawback by using a series of magnitude images with different TEs and calculating a weighted sum of these multiple echoes. Collection of multiple echoes within a single TR acquisition does not prolong scan time compared to the time needed to acquire a single echo. Further, SWAN can acquires thin slice 3D images and, as a result, is expected to reduce partial volume averaging. The SWAN approach may be especially useful in evaluating brain tissue likely exposed to large susceptibility differences at air-to-soft tissue or bone-to-soft tissue interfaces of the skull base.

The user can manipulate only the first TE and effective TE; then, the total number of TEs and sampling time points for the second to the last echoes are implicitly assigned depending on the effective TE. We chose the first TE of 25 ms and a relatively short effective TE of 30 ms to achieve higher signal to noise and obtained satisfactory susceptibility weighting. The manufacturer recommends an effective TE of 30 to 40 ms, which results in 3 or 4 echo acquisitions. The user can finely adjust the effective TE depending on the purpose of the scan; it involves a trade-off between much higher susceptibility weighting and sufficient signal to noise.

Our study was limited because it was relatively small and retrospective. Results would be more robust with more cases. Second, susceptibility weighting depends on the choice of parameter settings; choices of different parameters might have yielded different results. Longer TEs yield greater susceptibility weighting, and theoretically, the signal-to-noise ratio would worsen with longer TEs. It is a trade-off, and imaging parameters may need to be optimized according to clinical experience at each institution. Third, we did not investigate the cause of susceptibility effect in the putamen. Mineralization of the putamen includes deposition of iron, calcium, and other metals, all of which could cause local magnetic susceptibility. We attempted to compare sensitivity to local magnetic susceptibility among SWAN, PSI, and $T_2^*$WI, so differentiating the cause of susceptibility was not our study purpose. Finally, because histological confirmation of each lesion was unavailable and impractical, we based diagnosis of cavernous malformation and cerebral microbleed on clinical imaging findings. So, even with great care, we may have mistakenly counted small veins in tiny cavernous malformations or cerebral microbleeds and thereby included some false positive lesions.

Though based on limited samples, our study results indicate sufficient susceptibility weighting by SWAN in approximately half the scan time of PSI, a feature that will encourage the use of SWAN rather than PSI for routine susceptibility-weighted MR imaging.

**Conclusion**

SWAN is considered a highly efficient 3D susceptibility-weighted MR imaging technique for cerebral regions, and its shorter scan time is a further benefit for the application of SWAN in clinical use.

**Acknowledgements**

We thank Dr. Hiroyuki Kabasawa (GE Healthcare) for technical advice.

**References**

1. Thomas B, Somasundaram S, Thamburaj K, et al. Clinical applications of susceptibility weighted MR imaging of the brain—a pictorial review. Neuro-radiology 2008; 50:105–116.
2. Brainovich V, Sabatini U, Hagberg GE. Advantages of using multiple-echo image combination and asymmetric triangular phase masking in magnetic resonance venography at 3T. Magn Reson Imaging 2009; 27:23–37.
3. Du YP, Jin Z, Hu Y, Tanabe J. Multi-echo acquisition of MR angiography and venography of the brain at 3 Tesla. J Magn Reson Imaging 2009; 30: 449–454.
4. Boekh-Behrens T, Lutz J, Lummel N, et al. Susceptibility-weighted angiography (SWAN) of cer-
ebral veins and arteries compared to TOF-MRA. Eur J Radiol 2012; 81:1238–1245.
5. Lummel N, Boeckh-Behrens T, Schoepf V, Burke M, Brückmann H, Linn J. Presence of a central vein within white matter lesions on susceptibility weighted imaging: a specific finding for multiple sclerosis? Neuroradiology 2011; 53:311–317.
6. Haacke EM, Xu Y, Cheng YC, Reichenbach JR. Susceptibility weighted imaging (SWI). Magn Reson Med 2004; 52:612–618.
7. Harder SL, Hopp KM, Ward H, Neglio H, Gitlin J, Kido D. Mineralization of the deep gray matter with age: a retrospective review with susceptibility-weighted MR imaging. AJNR Am J Neuroradiol 2008; 29:176–183.
8. Armitage P, Berry G, Matthews JNS. Kappa measurement of agreement. In: Armitage P, Berry G, Matthews JNS, eds. Statistical methods in medical science. 4th ed. Oxford: Blackwell Science, 2002; 698–704.
9. Hermier M, Nighoghossian N. Contribution of susceptibility-weighted imaging to acute stroke assessment. Stroke 2004; 35:1989–1994.
10. Greenberg SM, Vernooij MW, Cordonnier C, et al. Cerebral microbleeds: a guide to detection and interpretation. Lancet Neurol 2009; 8:165–174.
11. Yamashita E, Kanasaki Y, Fujii S, Tanaka T, Hirata Y, Ogawa T. Comparison of increased venous contrast in ischemic stroke using phase-sensitive MR imaging with perfusion changes on flow-sensitive alternating inversion recovery at 3 Tesla. Acta Radiol 2011; 52:905–910.
12. Zhang J, Zhang Y, Wang J, et al. Characterizing iron deposition in Parkinson’s disease using susceptibility-weighted imaging: an in vivo MR study. Brain Res 2010; 1330:124–130.