Cerebral venous thrombosis (CVT), including thrombosis of cerebral veins and major dural sinuses, is a relatively uncommon form of stroke that usually affects young individuals. During the past decades, improved diagnosis and treatment have improved the outcome of CVT. However, there is often a diagnostic delay in patients with CVT. This is because the confirmation of the diagnosis always rely on the combination of different imaging modalities, such as computed tomography (CT), magnetic resonance (MR), MR venography (MRV), and conventional x-ray angiography. These methods assess CVT indirectly by imaging venous flow perturbation caused by thrombus. However, given the variation in venous anatomy, it is sometimes difficult to exclude CVT with existing noninvasive imaging studies. The diagnosis dilemma may delay treatment and result in death or permanent disability.

A general solution to these limitations may be the direct visualization of the thrombus itself. Direct thrombus imaging test may be useful to aid in optimizing medical therapy and guiding early invasive management. MR direct thrombus imaging, as a noncontrast-enhanced T1-weighted imaging method, has gained broad interest. Several studies have confirmed a high sensitivity for detecting thrombus in the settings of intracoronary artery, deep vein thrombosis, and pulmonary embolus. By exploiting the short T1 relaxation time of methemoglobin within thrombus, MR direct thrombus imaging depicts subacute thrombus as hyperintense while maintaining background tissues, such as the

**Background and Purpose**—Early diagnosis of cerebral venous thrombosis (CVT) is currently a major clinical challenge. We proposed a novel magnetic resonance black-blood thrombus imaging technique (MRBTI) for detection and quantification of CVT.

**Methods**—MRBTI was performed on 23 patients with proven CVT and 24 patients with negative CVT confirmed by conventional imaging techniques. Patients were divided into 2 groups based on the duration of clinical onset: ≤7 days (group 1) and between 7 and 30 days (group 2). Signal/noise ratio was calculated for the detected thrombus, and contrast/noise ratio was measured between thrombus and lumen and also between thrombus and brain tissue. The feasibility of using MRBTI for thrombus volume measurement was explored, and total thrombus volume was calculated for each patient.

**Results**—In 23 patients with proven CVT, MRBTI correctly identified 113 of 116 segments with a sensitivity of 97.4%. Thrombus signal/noise ratio was 153±57 and 261±95 for group 1 (n=10) and group 2 (n=13), respectively (P<0.01). Thrombus to lumen contrast/noise ratio was 149±57 and 256±94 for group 1 and group 2, respectively. Thrombus to brain tissue contrast/noise ratio was 41±36 and 120±63 (P<0.01), respectively. Quantification of thrombus volume was successfully conducted in all patients with CVT, and mean volume of thrombus was 10.5±6.9 mL.

**Conclusions**—The current findings support that with effectively suppressed blood signal, MRBTI allows selective visualization of thrombus as opposed to indirect detection of venous flow perturbation and can be used as a promising first-line diagnostic imaging tool. (Stroke. 2016;47:404-409. DOI: 10.1161/STROKEAHA.115.011369.)

**Key Words:** magnetic resonance imaging, sinus thrombosis, intracranial, venous thrombosis

---

**Early Detection and Quantification of Cerebral Venous Thrombosis by Magnetic Resonance Black-Blood Thrombus Imaging**

Qi Yang, MD, PhD*; Jiangang Duan, MD, PhD*; Zhaoyang Fan, MD, PhD*; Xiaofeng Qu, MD, PhD; Yibin Xie, PhD; Christopher Nguyen, PhD; Xiangying Du, MD, PhD; Xiaoming Bi, PhD; Kuncheng Li, MD, PhD; Xunming Ji, MD, PhD; Debiao Li, PhD

---

**Background and Purpose**—Early diagnosis of cerebral venous thrombosis (CVT) is currently a major clinical challenge. We proposed a novel magnetic resonance black-blood thrombus imaging technique (MRBTI) for detection and quantification of CVT.

**Methods**—MRBTI was performed on 23 patients with proven CVT and 24 patients with negative CVT confirmed by conventional imaging techniques. Patients were divided into 2 groups based on the duration of clinical onset: ≤7 days (group 1) and between 7 and 30 days (group 2). Signal/noise ratio was calculated for the detected thrombus, and contrast/noise ratio was measured between thrombus and lumen and also between thrombus and brain tissue. The feasibility of using MRBTI for thrombus volume measurement was explored, and total thrombus volume was calculated for each patient.

**Results**—In 23 patients with proven CVT, MRBTI correctly identified 113 of 116 segments with a sensitivity of 97.4%. Thrombus signal/noise ratio was 153±57 and 261±95 for group 1 (n=10) and group 2 (n=13), respectively (P<0.01). Thrombus to lumen contrast/noise ratio was 149±57 and 256±94 for group 1 and group 2, respectively. Thrombus to brain tissue contrast/noise ratio was 41±36 and 120±63 (P<0.01), respectively. Quantification of thrombus volume was successfully conducted in all patients with CVT, and mean volume of thrombus was 10.5±6.9 mL.

**Conclusions**—The current findings support that with effectively suppressed blood signal, MRBTI allows selective visualization of thrombus as opposed to indirect detection of venous flow perturbation and can be used as a promising first-line diagnostic imaging tool. (Stroke. 2016;47:404-409. DOI: 10.1161/STROKEAHA.115.011369.)

**Key Words:** magnetic resonance imaging, sinus thrombosis, intracranial, venous thrombosis

---

Cerebral venous thrombosis (CVT), including thrombosis of cerebral veins and major dural sinuses, is a relatively uncommon form of stroke that usually affects young individuals. During the past decades, improved diagnosis and treatment have improved the outcome of CVT. However, there is often a diagnostic delay in patients with CVT. This is because the confirmation of the diagnosis always rely on the combination of different imaging modalities, such as computed tomography (CT), magnetic resonance (MR), MR venography (MRV), and conventional x-ray angiography. These methods assess CVT indirectly by imaging venous flow perturbation caused by thrombus. However, given the variation in venous anatomy, it is sometimes difficult to exclude CVT with existing noninvasive imaging studies. The diagnosis dilemma may delay treatment and result in death or permanent disability.

A general solution to these limitations may be the direct visualization of the thrombus itself. Direct thrombus imaging test may be useful to aid in optimizing medical therapy and guiding early invasive management. MR direct thrombus imaging, as a noncontrast-enhanced T1-weighted imaging method, has gained broad interest. Several studies have confirmed a high sensitivity for detecting thrombus in the settings of intracoronary artery, deep vein thrombosis, and pulmonary embolus. By exploiting the short T1 relaxation time of methemoglobin within thrombus, MR direct thrombus imaging depicts subacute thrombus as hyperintense while maintaining background tissues, such as the
blood, vessel wall, and surrounding brain tissues as relatively low, isointense signal. However, the signal intensity of evolving thrombus may be complicated by coexisting more acute and older thrombus components, which may appear isointense as well. As a result, part of thrombus could be mistaken as venous blood or surrounding brain tissues. This would be more challenging when using MR direct thrombus imaging in the cerebral venous system where anatomic variants, including sinus atresia/hypoplasia asymmetrical sinus drainage is commonly present.

To address this limitation, we hypothesize that the thrombus can be well isolated from the surrounding tissues, including lumen and wall, by using so-called black-blood MR techniques. In this study, we proposed to use a magnetic resonance black-blood thrombus imaging (MRBTI) technique, namely 3-dimensional (3D) variable flip angle turbo spin echo, to achieve accurate detection of thrombus in the cerebral venous system. The diagnostic performance of MRBTI was assessed in patients with or without CVT.

**Subjects and Methods**

**Patients**

Between February 2014 and May 2015, consecutive patients with signs and symptoms suspected of CVT within the past 30 days were prospectively recruited in this study. Exclusion criteria included general contraindications to MR examination and patients with incomplete conventional imaging examinations (CT, MR, and MRV). Informed consent was obtained from all participants, and all protocols were approved by the Institutional Review Board.

**Conventional Imaging Evaluation**

Thrombi were defined as intraluminal filling defects detected by conventional imaging techniques. Two readers (J.D. and X.J.) performed a consensus reading of all conventional imaging studies for each patient, including CT, MR, and MRV, with full clinical and outcome information on the patient to obtain a reference standard. The following 14 venous segments were included in evaluations: superior sagittal sinus, inferior sagittal sinus, right transverse sinus, right sigmoid sinus, left transverse sinus, left sigmoid sinus, straight sinus, confluence of sinuses, veins of galen, internal cerebral veins, basal veins of Rosenthal, veins of Labbé, right cortical veins, and left cortical veins.

**Magnetic Resonance Black-Blood Thrombus Imaging**

3D variable flip angle turbo spin echo has an inherent black-blood effect and has recently been proposed for arterial vessel wall imaging. To exploit the short T1 property of acute thrombus, the sequence was used for MRBTI with a T1-weighted acquisition mode.

All MR studies were conducted on a 3.0-T system (Magnetom Verio, Siemens Healthcare, Erlangen, Germany) using a 32-channel coil. Repetition time was 800 ms, echo time, variable flip angle turbo spin echo, to achieve accurate detection of thrombus in the cerebral venous system. The diagnostic performance of MRBTI was assessed in patients with or without CVT.

**MRBTI Image Evaluation**

All MRBTI images were randomized and presented to 2 independent readers with 10 years (Q.Y.) and 8 years (X.Q.) of experience in reading. The readers were not involved with the diagnostic or therapeutic management of the patients and were blinded to clinical information and conventional imaging data on which the diagnosis of CVT was based. Source images, free mode multiplanar reformations, and minimum intensity projection images were used by readers. A third reader with 15 years of experience of reading (K.L.) was involved to resolve any disputes.

Image quality was first rated for each segment using a 4-point scale as follows: 4=excellent, no relevant artifacts; 3=good, minimal inhomogeneity, only minor flow artifacts; 2=adequate, delineated lumen, major flow artifacts; and 1=nondiagnostic.

Thrombus was visually assessed in each segment based on its characteristic hyperintense signals relative to the luminal blood and surrounding brain tissues. The presence or absence of thrombus was recorded for each segment. Patients with CVT detected by MRBTI were divided into 2 groups based on the duration of clinical onset: ≤7 days (group 1) and between 7 and 30 days (group 2). Signal intensity was measured from thrombus, luminal blood, and gray matter. Signal/noise ratio was calculated for the detected thrombus and was defined as the ratio of the thrombus signal intensity and SD of the background noise measured in an area outside of the head free of tissue structure and artifact. Contrast/noise ratio (CNR) was measured between thrombus and lumen and also between thrombus and gray matter. CNR was calculated as signal intensity difference between the thrombus and lumen/gray matter divided by the SD of background noise.

In addition, the feasibility of using MRBTI for thrombus volume measurement was explored. Specifically, thrombi in each patient were segmented in a semiautomatic fashion using commercial software (Object Research System, Montreal, Quebec, Canada), and total thrombus volume was reported for each patient.

**Statistical Analysis**

Differences in signal/noise ratio and CNRs between group 1 and group 2 were tested with 2-tailed independent t-test. A value of P<0.05 was considered to indicate statistical significance. The level of agreement in thrombus detection between the 2 readers was evaluated by the κ value on a per-segment basis. The consensus reading of conventional imaging techniques was used as the reference standard for assessing the sensitivity, specificity, and negative and positive predictive values of MRBTI. For the patient level analysis, each patient was categorized as correctly diagnosed if at least 1 venous segment was judged as positive CVT. All statistical analysis was performed using statistical software (SAS version 9.1, SAS Institute Inc, Cary, NC).

**Results**

**Patients Characteristics**

Sixty-two consecutive patients met the eligibility criteria, and 15 patients were excluded because of incomplete imaging at baseline. Thus, 47 patients were enrolled in the MRBTI

| Table 1. Baseline Study Population Characteristics |
|---------------------------------|---------------------------------|
| Demographics                   | n/N (%)                         |
| Mean age, y (SD)               | 34±13                           |
| Sex, female (%)                | 28/47 (60)                      |
| Clinical characteristics (%)   |                                 |
| Headache                       | 27/47 (57)                      |
| Papilledema                    | 12/47 (26)                      |
| Focal neurological deficit     | 5/47 (11)                       |
| Comatose                       | 1/47 (2)                        |
| Duration from onset to MRBTI, d |                                 |
| 0–7                            | 19/47 (40)                      |
| 7–30                           | 28/47 (60)                      |
| Risk factors                   |                                 |
| Pregnancy or puerperium (%)    | 6/47 (13)                       |
| Oral contraceptives (%)        | 8/47 (17)                       |
| Infection (%)                  | 7/47 (15)                       |

MRBTI indicates magnetic resonance black-blood thrombus imaging.
examination. MRBTI was successfully performed in all 47 patients without complications. The mean age of the patients in the study was 34 years (range, 5–84 years), and 28 (60%) were women. Study population characteristics are listed in Table 1.

Distribution of Venous Thrombosis by Conventional Imaging Techniques

All 47 patients have CT, MR, and time-of-flight MRV; 5 of 47 patients have contrast-enhanced CT venography. A total of 116 thrombosed venous segments were identified in 23 patients. Thrombosed segments included superior sagittal sinus (14), right transverse sinus (16), right sigmoid sinus (17), left transverse sinus (11), left sigmoid sinus (9), straight sinus (8), confluence of sinuses (12), veins of galen (4), internal cerebral veins (2), veins of Labbé (1), right cortical veins (11), and left cortical veins (11).

MRBTI Image Quality

Figure 1 shows a typical example of thrombosis case acquired with conventional time-of-flight technique and the propose MRBTI method. Blood signal was effectively suppressed using MRBTI, and thrombi were depicted as hyperintense with excellent contrast relative to surrounding tissues (Figure 1B and 1D). In comparison, some flow dephasing–related signal loss was observed in time-of-flight images (Figure 1A, arrowheads). The overall image quality score was 3.5±0.6. Among 658 segments, 647 (98%) were diagnostic (score, ≥2). Among the nondiagnostic segments, 7 were due to limited spatial coverage and 4 were due to flow artifacts. These 11 segments were excluded in the following diagnostic performance analyses.

Thrombus Signal Intensity

All thrombi were depicted as hyperintense relative to surrounding tissues, as demonstrated in Figure 1D (arrow). Thrombus signal/noise ratio was 153±57 and 261±95 for group 1 (n=10) and group 2 (n=13), respectively. Thrombus-to-lumen CNR was 149±57 and 256±94 for group 1 and group 2. Thrombus to brain tissue CNR was 41±36 and 120±63 (P<0.01), respectively. The difference between the 2 groups were significant in all above signal measurements (Figure 2).

Diagnostic Performance of MRBTI

MRBTI correctly identified 113 of 116 segments with CVT with a sensitivity of 97.4%. In 527 of 531 segments, CVT was ruled out correctly with a specificity of 99.3%. A detailed overview of the diagnostic performance of MRDTI compared with standard of reference is summarized in Table 2.

MRBTI was able to detect hyperintense thrombi in different segments. Figure 3 demonstrates detection of thrombi in the superior sagittal sinus, the right transverse and sigmoid sinuses, and the cortical veins.
Quantification of Thrombus Volume

Quantification of thrombus volume was successfully conducted in all patients with CVT. Mean volume of thrombus was 10.5±6.9 mL. There was no significant difference between the 2 groups (8.6±7.2 versus 11.9±6.5 mL; \( P = 0.28 \)). Figure 4 demonstrates thrombus volume quantification in 1 patient who underwent series scans on day 7 and day 14 (22.4 versus 12.5 mL). The complicated signal intensity pattern of evolving thrombus was also revealed.

Discussion

The presented results demonstrated that MRBTI can early detect CVT with a high diagnostic accuracy. This study was, to the best of our knowledge, the first evaluation of MRBTI for direct visualization of CVT.

Neuroimaging plays a key role in the diagnosis of CVT. CT venography and MRV have been widely used for detecting cerebral venous changes that may be related to thrombosis. Instead of directly imaging thrombus, most of these techniques rely on visualization of altered blood flow in the veins resulting from thrombotic vessel lumen. Anatomic variants of normal venous anatomy, including sinus atresia/hypoplasia, asymmetrical sinus drainage, and normal sinus filling defects, may mimic sinus thrombosis and compromise the diagnostic confidence using these methods. For example, arachnoid granulations protruding into the sinus lumen may produce a focal filling defect on MRV that can simulate focal thrombosis. Contrast-enhanced MRV with elliptic centric ordering has been widely used as a venographic method, which may assist in distinguishing anatomic variants from CVT. However, it has limited utility
in patients with renal impairment because of the requirement of gadolinium.

Unlike conventional imaging techniques, MRBTI directly targets the thrombus itself and depicts thrombus as hyperintense and other tissues as isointense based on strong T1 contrast weighting. Despite the sufficient contrast for thrombus detection with conventional thrombus imaging technique, the volume of thrombus could be underestimated due to sometimes heterogeneous appearance in acute or subacute thrombus. To overcome the limitation, we proposed to apply T1-weighted variable flip angle turbo spin echo to CVT detection by using its intrinsic blood nulling capability. Our results demonstrated that CVT was well isolated from the surrounding tissues, including lumen and wall with this MRBTI method, and the entire thrombus volume is readily appreciated. In addition, sinus anatomy structures, such as sinus wall, arachnoid granulations, and surrounding tissues, can be well visualized. On the other hand, the black-blood contrast helps reduce the false-positive diagnosis because of flow artifacts commonly observed on time-of-flight, as shown in Figure 1. This suggests that the black-blood feature was a major contributor to the high detection accuracy of CVT in this study.

The feasibility of quantifying thrombus volume was demonstrated in this work. Because of the high signal contrast of thrombus and clear spatial depiction of venous structure as mentioned above, the volume of CVT can be quantified with the aid of software in a semiautomatic fashion. Such a quantitative method may make MRBTI as a robust technique for monitoring thrombus progression.

The noncontrast nature of MRBTI is highly relevant to clinics. The technique is free of the risk for allergic reactions and can be used for repeated follow-up examination if necessary. A substantial patient population, including pregnant and postpartum women and the elderly with severe kidney insufficiency, will greatly benefit from such a radiation free, noncontrast imaging technique. The MRBTI technique can potentially serve as a first-line diagnostic imaging test.

There are several limitations in this study. First, because of the relatively small numbers of patients included in this single-center study, the sensitivity and specificity of the MRBTI technique need to be fully investigated before it is accepted as standard imaging technique for CVT detection. However, CVT is a rare disease, thus rendering the recruitment of large patient cohort difficult. Thus, a multicenter evaluation of the performance of this MRBTI technique is desirable. Second, hyperacute or chronic thrombosis does not have a short T1 relaxation time and exhibits isointense signal on T1-weighted images. However, with the blood signal adequately suppressed on MRBTI, normal venous anatomy was depicted as hypointense black area. Therefore, thrombus with isointense signal can still be readily detected. In addition, the presence of high signal intensity in chronic CVT patients could potentially be used as a conclusive sign of a recurrent CVT. Third, despite using highly efficient variable flip angle turbo spin echo technique for data acquisition, the imaging time of the current protocol is still long (6–8 minutes), and further acceleration of data acquisition is highly desirable. Finally, the reference gold standard used in this study was a combination of conventional imaging techniques (CT, MR, and MRV) with clinical information. The combined use of these imaging techniques gave a more comprehensive reference that mitigates known deficiencies found in any single technique. Despite this comprehensive gold standard, it is difficult to generalize our sensitivity and specificity findings because we relied on the interpretation of these images by 2 readers at a single center. Follow-up studies designed as larger clinical trials can aid in determining a more general sensitivity and specificity. Furthermore, the ease of directly imaging the thrombus with the proposed MRBTI technique may simplify the evaluation and diagnosis of CVT.

In conclusion, the current findings support that MRBTI allows selective visualization of thrombus with high accuracy and holds promise to provide a valuable alternative to current techniques, opening a new place for MRBTI in CVT diagnostics.
Sources of Funding
The study was partially supported by National Institutes of Health grant number (2R01HL096119), American Heart Association (15SDG25710441), National Science Foundation of China (no. 81322022, 81325007, and 81120108012), Program for New Century Excellent Talents in University (no. 13–0918), and Cheung Kong Scholars Programme(T2014251).

Disclosures
D. Li reports receiving research support from Siemens Medical Solutions. X. Bi is an employee of Siemens AG Healthcare. The other authors report no conflicts.

References