Respiratory-Triggered Flow-Independent Noncontrast Non–ECG-Gated MRV (REACT) Versus CE-MRV for Central Venous Evaluation in Children and Young Adults: A Six-Reader Study

Lisa H. Betz, MD[1], Jonathan R. Dillman, MD, MSc[1,2], Alexander J. Towbin, MD[1,2], Christopher G. Anton, MD[1,2], Govind B. Chavhan, MD[3,4], Eric J. Crotty, MD[1,2], Cara E. Morin, MD, PhD[1,2], Erika Pace, MD[5], Gayathri Sreedher, MD[6], Bin Zhang, PhD[7,8], Jean A. Tkach, PhD[1,2]

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BACKGROUND. Contrast-enhanced MRI is commonly used to evaluate thoracic central venous patency in children and young adults. A flow-independent noncontrast non–ECG-gated 3D MRA–MR venography (MRV) technique described in 2019 as "relaxation-enhanced angiography without contrast and triggering (REACT)" may facilitate such evaluation.

OBJECTIVE. The purpose of our study was to compare image quality, diagnostic confidence, and interreader agreement between respiratory-triggered REACT and 3D Dixon-based contrast-enhanced MRV (CE-MRV) for evaluating thoracic central venous patency in children and young adults.

METHODS. This retrospective study included 42 consecutive children and young adults who underwent MRI of the neck and chest to evaluate central venous patency between August 2019 and January 2021 (median age, 5.2 years; IQR, 1.4–15.1 years; 22 female patients and 20 male patients). Examinations included respiratory-triggered REACT and navigator-gated CE-MRV sequences based on the institution's standard-of-care protocol. Six pediatric radiologists from four different institutions independently reviewed REACT and CE-MRV sequences; they assessed overall image quality (scale, 1–5; 5 = excellent), diagnostic confidence (scale, 1–5; 5 = extremely confident), and presence of clinically relevant artifact(s). Readers classified seven major central vessels as normal or abnormal (e.g., narrowing, thrombosis, or occlusion). Analysis used Wilcoxon signed rank and McNemar tests and Fleiss kappa coefficients.

RESULTS. The distribution of overall image quality scores was higher (p = .02) for REACT than for CE-MRV for one reader (both sequences: median score, 5). Image quality scores were not significantly different between the sequences for the remaining five readers (all p > .05). Diagnostic confidence scores and frequency of clinically relevant artifact(s) were not significantly different between sequences for any reader (all p > .05). Interreader agreement for vessel classification as normal or abnormal was similar between sequences for all seven vessels (REACT: κ = 0.37–0.81; CE-MRV: κ = 0.34–0.81). Pooling readers and vessels, 65.4% of vessels were normal by both sequences; 18.7%, abnormal by both sequences; 9.8%, abnormal by REACT only; and 6.1%, abnormal by CE-MRV only.

CONCLUSION. Respiratory-triggered REACT, in comparison with CE-MRV, showed no significant difference in image quality (aside from for one of six readers), diagnostic confidence, or frequency of artifact(s), with similar interreader agreement for vessel classification as normal or abnormal.

CLINICAL IMPACT. High-resolution 3D MRV performed without IV contrast material can be used to assess central venous patency in children and young adults.

MRI, including MR venography (MRV), is commonly used to assess thoracoabdominal venous anatomy and patency in the pediatric population owing to its lack of ionizing radiation and excellent image contrast resolution. Contrast-enhanced MRV (CE-MRV)

[1]Department of Radiology, Cincinnati Children's Hospital Medical Center, 3333 Burnett Ave, Cincinnati, OH 45229. Address correspondence to L. H. Betz (lisa.betz@cchmc.org).

[2]Department of Radiology, University of Cincinnati College of Medicine, Cincinnati, OH.

[3]Department of Diagnostic Imaging, The Hospital for Sick Children, Toronto, ON, Canada.

[4]Department of Medical Imaging, University of Toronto, Toronto, ON, Canada.

[5]Department of Radiology, The Royal Marsden NHS Foundation Trust, London, England.

[6]Department of Radiology, Akron Children's Hospital, Akron, OH.

[7]Division of Biostatistics and Epidemiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH.

[8]Department of Pediatrics, University of Cincinnati College of Medicine, Cincinnati, OH.

is commonly considered a standard-of-care MRV technique and requires the administration of IV gadolinium–based contrast material (GBCM) to promote T1 shortening of blood and thus hyperintense appearance of the vasculature [1, 2]. Concerns about the potential safety of GBCM, including gadolinium retention within the body after even small exposures, have increased interest in noncontrast MRI methods, including unenhanced MRV techniques [3–5]. Additional drawbacks to IV contrast agents for MRI include added cost and the need for adequate vascular access, which can be particularly challenging in some children.

Numerous noncontrast MRV techniques have been described in the literature and used in clinical practice with variable success [6–8]. Individual techniques have different advantages and limitations based on MRI physics and their underlying pulse sequence design. Examples of commonly used unenhanced MRV techniques include time-of-flight, phase-contrast, ECG-gated fast spin-echo (FSE), and balanced SSFP sequences [6]. In general, MRV techniques can be categorized as being blood flow dependent or blood flow dependent [7]. Blood flow–dependent techniques, such as time-of-flight and phase-contrast sequences, have limitations related to in-plane saturation and rate of blood flow, and other blood flow–dependent techniques, such as the ECG-gated FSE subtraction sequence, are subject to motion-related image misregistration [8]. Blood flow–independent techniques, including 2D and 3D SSFP sequences, are relaxation based and create image contrast on the basis of the intrinsic tissue characteristics as opposed to blood flow. Although these latter techniques are commonly used in clinical practice, they can be limited by banding and susceptibility artifacts [9].

CE-MRV remains an essential technique for assessing the vasculature owing to its relatively short acquisition times, excellent anatomic coverage, and decreased vulnerability to flow and non–flow-related artifacts compared with historic noncontrast techniques [10, 11]. In 2019, a noncontrast 3D MRA-MRV technique referred to as "relaxation-enhanced angiography without contrast and triggering" (REACT) was described [12]. This blood flow–independent technique uses a dual-echo 3D Dixon-based water-fat separation pulse sequence with nonbalanced gradient-echo readouts as well as T2 preparation and inversion recovery pulses. This sequence design provides intravascular signal hyperintensity and uniform fat and soft-tissue suppression across a large volume of tissue and with high spatial resolution. In addition, the technique does not use image subtraction or cardiac gating. The sequence's initial description described its use while patients were breathing freely; the additional use of respiratory triggering for respiratory compensation is considered optional. Multiplanar reformations and 3D reconstructions (e.g., maximum intensity projections and volume renderings) also can be obtained from the acquired 3D volumetric dataset [12].

A paucity of studies have directly compared the REACT sequence with a conventional CE-MRV sequence. The purpose of this study was to compare image quality, diagnostic confidence, and interreader agreement between a respiratory-triggered flow-independent noncontrast non–ECG-gated MRV sequence (i.e., the REACT sequence) and a conventional 3D Dixon-based CE-MRV sequence for evaluating thoracic central venous patency in children and young adults, using a multireader approach.

Highlights

Key Finding

- *Respiratory-triggered REACT and CE-MRV showed no significant difference in overall image quality (except for one reader who rated REACT more highly), diagnostic confidence, or frequency of clinically relevant artifact(s) ($p > .05$). They showed similar interreader agreement across seven major central vessels (REACT, $\kappa = 0.37–0.81$; CE-MRV, $\kappa = 0.34–0.81$).*

Importance

- *Respiratory-triggered REACT provides an alternative to CE-MRV for evaluating central venous patency in children and young adults, potentially eliminating the need for intravascular contrast material.*

Methods

This retrospective HIPAA-compliant study was approved by the institutional review board at Cincinnati Children's Hospital Medical Center. The requirement for written informed consent was waived.

Study Sample

The EMR of the Cincinnati Children's Hospital Medical Center was searched to identify consecutive pediatric and young adult patients (age range, 0–21 years old) who underwent MRI of the neck and chest for evaluation of central venous anatomy and patency, performed between August 2019 and January 2021. Such MRI examinations were typically performed for venous mapping before central venous catheter placement or before small-bowel or multivisceral transplantation. Patients 21 years old or younger were included because this age range is representative of the patient population that commonly undergoes imaging for these indications. Because the standard-of-care protocol for MRI examinations performed for the previously noted indications at the institution during the study period included both the respiratory-triggered REACT and CE-MRV sequences, all identified examinations included both MRV techniques. MRI examinations were performed with the patient under anesthesia or sedation in some patients (typically those < 8 years old).

MR Venography Techniques

MRI examinations were performed using either a 1.5- or 3-T clinical scanner (Ingenia, Philips Healthcare). The REACT sequence used in this study was a magnetization-prepared 3D nonbalanced steady-state gradient-recalled echo (GRE) two-point Dixon-based sequence with magnetization parameters optimized to take advantage of the long T1 and T2 relaxation times of unenhanced blood, thereby providing blood flow–independent noncontrast images of the vasculature without ECG gating. Background fat suppression and soft-tissue suppression were achieved through the combined use of Dixon-based fat-water separation (mDixon XD, Philips Healthcare) and STIR techniques. T2 preparation with four refocusing pulses (i.e., T2 preparation pulse) was used to further increase the image contrast between the blood pool and background tissues (e.g., muscle) as well as to provide slight differentiation between arteries and veins based

on signal intensity, with the arteries generally appearing slightly more hyperintense than the veins. A T2 preparation time of 50 ms was chosen on the basis of the work of Toyonari et al. [13], who showed that longer T2 preparation times are associated with a failure of fat-water separation. Finally, the acquisition was respiratory triggered using a bellows (belt) to monitor the respiratory signal to minimize breathing-related artifacts. Respiratory triggering was incorporated on the basis of the authors' earlier anecdotal experience that imaging exclusively during the time period between breaths yields improved overall image quality for this sequence, including sharper delineation of vessel walls and better visualization of small vessels. The scanning time for the REACT sequence was 2 minutes 30 seconds, excluding the time required for respiratory triggering.

CE-MRV of the neck and chest was performed using a 3D turbo GRE two-point Dixon-based sequence (mDixon XD), incorporating respiratory navigator gating. After completion of the REACT sequence, patients were administered a standard dose of IV GBCM (gadoterate meglumine, 0.1 mmol/kg; maximum dose, 15 mL). Patients then underwent conventional dynamic breath-hold contrast-enhanced first-pass MRA of the neck and chest, which was followed immediately by the CE-MRV sequence. The scanning time for the CE-MRV sequence was 2 minutes 0 seconds, excluding the time required for navigator gating.

Detailed parameters for both the respiratory-triggered REACT and CE-MRV sequences are reported in Table S1 (available in the online supplement).

MR Venography Image Review

Six fellowship-trained pediatric radiologists (A.J.T., C.G.A., G.B.C, E.J.C, C.E.M., and G.S.; participating in this study through a collaboration with the Society for Pediatric Radiology's MRI Committee) with varying clinical practice experience (2–23 postfellowship years) independently assessed the REACT and CE-MRV sequences in all patients; the first-pass MRA sequence was not evaluated. At the time of image review, three radiologists were from the institution where the MRI examinations were performed, and three radiologists were from three distinct other institutions; thus, the radiologists were from a total of four different institutions. Before the image review, each reader completed a 30-minute training session led by the senior investigator (J.R.D., a fellowship-trained pediatric radiologist with 13 years of postfellowship clinical experience) who presented examples of normal and abnormal images for both MRV sequences. For the purposes of the image review, the MRV sequences were deidentified and transferred to a secure HIPAA-compliant cloud-based research PACS platform (Ambra Research, Intelerad). The REACT and CE-MRV sequences were randomly assigned to one of two groups (group 1 or group 2). Group 1 contained the REACT sequences from 21 patients and the CE-MRV sequences from the other 21 patients, whereas group 2 contained the REACT and CE-MRV sequences not contained in group 1. The radiologists completed the review of cases in group 1 before imitating the review of cases in group 2; the reviews of the two groups were separated by a washout period of at least 4 weeks. The sequences were reviewed in a random order within each group. For each sequence, radiologists had access to coronal source images as well as to maximum-intensity-projection reconstructions. The radiologists were blinded to the sequence being reviewed (REACT vs CE-MRV), one another's assessments, all clinical data, and the clinical radiology reports.

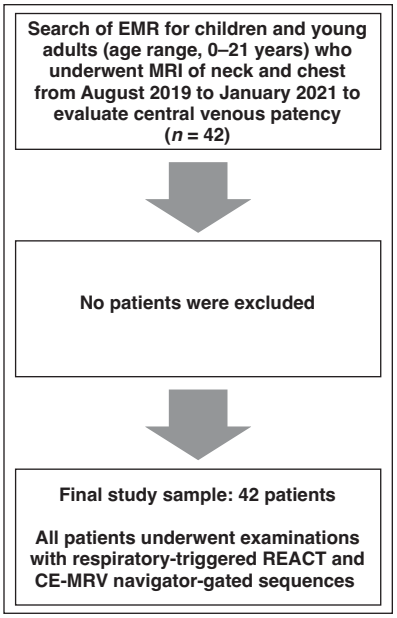

Fig. 1—Flowchart shows patient selection process. REACT = relaxation-enhanced angiography without contrast and triggering, CE-MRV = contrast-enhanced MR venography.

TABLE 1: Comparison of Overall Image Quality Scores Between REACT Sequence and CE-MRV Sequence for Six Independent Readers

Reader	Overall Image Quality Score[a]		p[b]
	REACT	CE-MRV	
1	3 (3.0–4.0) [1–5]	3 (2.0–4.0) [1–5]	.67
2	5 (4.0–5.0) [2–5]	5 (4.0–5.0) [1–5]	.02
3	3 (3.0–4.0) [1–5]	4 (2.0–4.0) [1–5]	.25
4	4 (3.0–4.0) [1–5]	4 (3.0–4.3) [1–5]	.87
5	4 (4.0–5.0) [1–5]	4 (3.5–5.0) [1–5]	.41
6	5 (3.0–5.0) [1–5]	4 (3.0–5.0) [1–5]	.09

Note—Data are expressed as median with IQR in parentheses and range in brackets. REACT = relaxation-enhanced angiography without contrast and triggering, CE-MRV = contrast-enhanced MR venography.

[a]Image quality scores are defined as follows: 1 = nondiagnostic, 3 = average clinical quality, and 5 = excellent.

[b]Wilcoxon signed rank test.

The readers assessed features for each reviewed sequence using an electronic case report form. The readers scored the sequence's overall image quality using a 5-point Likert scale (1 = nondiagnostic, 3 = average quality as encountered in clinical practice, and 5 = excellent quality) as well as the sequence's diagnostic confidence using a 5-point Likert scale (1 = not confident, 3 = average confidence, and 5 = extremely confident). The readers also recorded the presence of clinically relevant artifact(s) (i.e., an artifact or artifacts resulting in a nondiagnostic assessment of one or more vessels) in a binary fashion (present vs absent). If a clinically relevant artifact(s) was present, then the reader recorded a free-text description of the type of artifact present. In addition, the readers classified seven major central vessels (superior vena cava, left brachiocephalic vein, right brachiocephalic vein, left subclavian vein, right subclavian vein, left internal jugular vein, and right internal jugular vein) as normal or abnormal in a binary manner. They deemed vessels abnormal if showing stenosis (vessel narrowing without thrombus), thrombosis (occlusive or nonocclusive filling defect within the vessel), or chronic occlusion (nonvisualization of a vessel, with or without collaterals); the specific findings resulting in vessel categorization as abnormal were not recorded. Readers could choose to not classify an individual vessel if the vessel was obscured by artifact.

Statistical Analysis

Continuous data were summarized as medians and IQR, whereas categoric data were summarized as counts and percentages. Readers' free-text assessments of types of artifacts present were summarized in a binary fashion in terms of whether or not relating to motion.

The Wilcoxon signed rank test was used to compare scores for overall image quality and diagnostic confidence between REACT and CE-MRV sequences for each reader. The McNemar test was used to compare the frequency of artifacts between the two sequences for each reader. Fleiss kappa coefficients were used to evaluate agreement among the six readers for the classification of each of the seven assessed vessels as normal or abnormal, and this evaluation was performed separately for the two sequences. The level of agreement was classified as almost perfect (κ = 0.81–1.00), substantial (κ = 0.61–0.80), moderate (κ = 0.41–0.60), fair (κ = 0.21–0.40), or none to slight (κ = 0.01–0.20) [14]. Finally, pooling all six readers' assessments and all seven assessed vessels, the following percentages were calculated: percentage of vessels classified as abnormal by both sequences, percentage of vessels classified as normal by both sequences, percentage of vessels classified as abnormal by only REACT sequence, and percentage of vessels classified as abnormal by only CE-MRV sequence. These percentages were also calculated for the seven vessels individually. If a reader did not classify a vessel on either sequence owing to artifact, then the vessel was excluded from the pooled percentages.

For all inference testing, a p value of less than .05 was considered statistically significant. Corresponding 95% CIs were calculated, as appropriate. All statistical analyses were performed using SAS software (version 9.4, SAS Institute).

Results

Patient Sample

The search identified 42 patients who underwent MRI of the neck and chest for evaluation of central venous anatomy and patency performed during the study period. No patient identified by the initial search was excluded. Thus, the final sample comprised these 42 patients (Fig. 1). The median patient age was 5.2 years (IQR, 1.4–15.1 years; age range, 3 months–21 years). Twenty-two (52%) patients were female, and 20 (48%) were male. Clinical indications for thoracic vascular imaging included evaluation of vascular anatomy not otherwise specified (n = 14), evaluation of vascular anatomy as part of the imaging protocol for small-bowel or multivisceral transplant (n = 11), superior vena cava syndrome (n = 6), venous mapping before central line placement (n = 7), central line malfunction (n = 1), central line infection (n = 1), chronic central venous thrombosis (n = 1), and assessment of vascular anatomy after initiation of extracorporeal membrane oxygenation (n = 1). Twenty-two patients were imaged at 1.5 T, and 20 patients were imaged at 3 T. A total of 25 (59.5%) examinations were performed with the patient under anesthesia or sedation.

Overall Image Quality, Diagnostic Confidence, and Artifacts

The distribution of overall image quality scores was significantly higher for REACT than for CE-MRV for one reader (median score = 5 for both sequences for this reader; p = .02). Overall image quality was not significantly different between the two MRV sequences for the other five readers (all p > .05) (Table 1).

TABLE 2: Comparison of Diagnostic Confidence Scores Between REACT Sequence and CE-MRV Sequence for Six Independent Readers

Reader	Diagnostic Confidence Score[a]		p[b]
	REACT	CE-MRV	
1	4 (2.3–4.8) [1–5]	3 (2.0–4.0) [1–5]	.67
2	5 (4.0–5.0) [1–5]	4 (4.0–5.0) [1–5]	.06
3	4 (3.0–4.0) [1–5]	4 (2.0–4.0) [1–5]	.36
4	4 (3.0–4.0) [1–5]	4 (3.0–5.0) [1–5]	.28
5	4 (4.0–5.0) [1–5]	4 (3.0–4.0) [1–5]	.15
6	5 (4.0–5.0) [1–5]	5 (4.0–5.0) [1–5]	.23

Note—Data are expressed as median with IQR in parentheses and range in brackets. REACT = relaxation-enhanced angiography without contrast and triggering, CE-MRV = contrast-enhanced MR venography.

[a]Diagnostic confidence scores are defined as follows: 1 = not confident, 3 = average confidence, and 5 = extremely confident.

[b]Wilcoxon signed rank test.

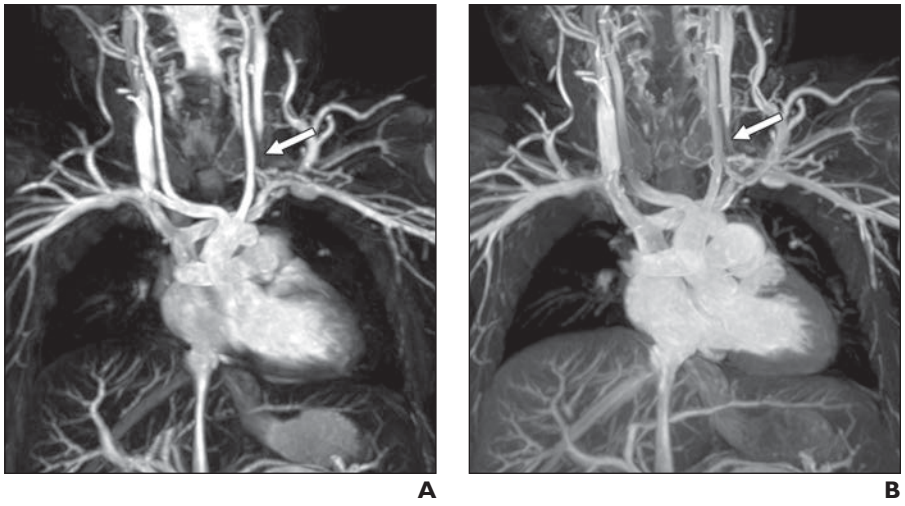

Fig. 2—8-year-old patient with hemophagocytic lymphohistiocytosis. MRI was performed to evaluate for central venous patency.
A, Coronal maximum-intensity-projection image of neck and chest from respiratory-triggered flow-independent noncontrast non–ECG-gated MR venography (MRV) sequence (relaxation-enhanced angiography without contrast and triggering) shows narrowing of left internal jugular vein (*arrow*) and dilatation of left external jugular vein. Major thoracic venous structures are otherwise patent. Median image quality score was 5.0; median diagnostic confidence score was 4.5.
B, Coronal maximum-intensity-projection image from contrast-enhanced MRV, performed during same examination as **A**, shows similar findings, including left internal jugular vein stenosis (*arrow*). Median image quality score was 4.5; median diagnostic confidence score was 4.0.

Diagnostic confidence was not significantly different between the two sequences for any reader (all $p > .05$) (Table 2).

The frequency of clinically relevant image artifact(s) was not significantly different between the two sequences for any reader (all $p > .05$) (Table 3). Pooling assessments by all six readers, clinically relevant artifact(s) related to motion was present in 6.0% (15/252) for REACT and in 15.1% (38/252) for CE-MRV.

Examples of REACT and CE-MRV sequences, along with median image quality and diagnostic confidence scores, are presented in Figures 2–6.

Interreader Agreement

Kappa coefficients with 95% CIs for agreement among the six readers for the classification of each of the seven vessels as normal or abnormal are presented for the REACT and CE-MRV sequences in Table 4. Interreader agreement for this classification was qualitatively similar between the two sequences. Agreement for classification of a vessel as normal or abnormal by REACT ranged from fair (left subclavian vein, $\kappa = 0.37$) to almost perfect (left brachiocephalic vein, $\kappa = 0.81$) and by CE-MRV ranged from fair (left subclavian vein, $\kappa = 0.34$) to almost perfect (superior vena cava, $\kappa = 0.81$).

Frequencies of Normal and Abnormal Vessels

After excluding 69 vessels that a reader did not classify as normal or abnormal on either sequence owing to artifact, the six readers classified a total of 1695 vessels as normal or abnormal on both sequences. Pooling the six readers' assessments and all seven evaluated vessels, a total of 65.4% (1109/1695) of the vessels were normal by both MRV sequences, 18.7% (317/1695) were abnormal by both sequences, 9.8% (166/1695) were abnormal by REACT but normal by CE-MRV, and 6.1% (103/1695) were abnormal by CE-MRV but normal by REACT. These classifications, stratified by individual vessel, are presented in Table 5. The percentage of vessels classified as abnormal only by REACT versus only by CE-MRV for the right internal

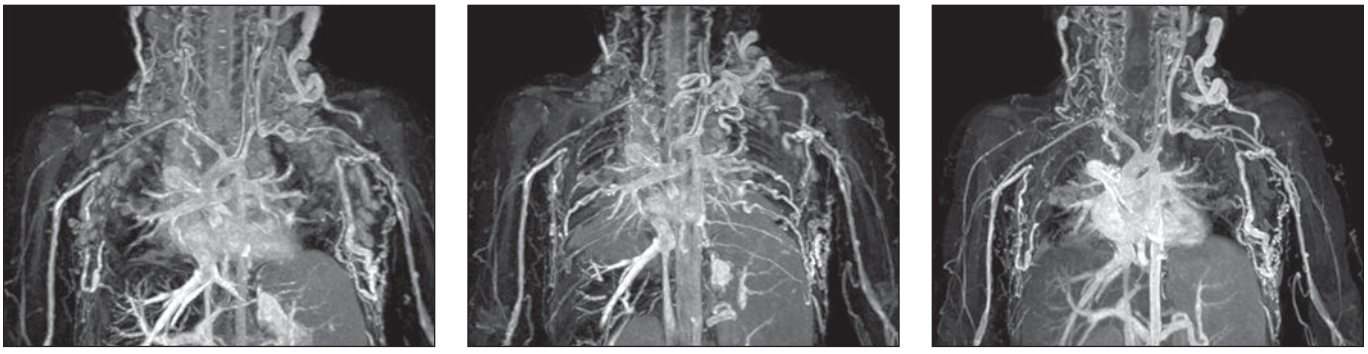

Fig. 3—4-year-old patient with gastroschisis. MRI was performed to evaluate for central venous patency.
A, Coronal maximum-intensity-projection image of neck and chest from respiratory-triggered flow-independent noncontrast non–ECG-gated MR venography (MRV) sequence (relaxation-enhanced angiography without contrast and triggering [REACT]) shows nonvisualization of superior vena cava, right and left brachiocephalic veins, right and left subclavian veins, and right internal jugular vein owing to chronic vessel occlusions. Left internal jugular vein and left subclavian vein are also narrowed. Extensive venous collaterals are present. Median image quality score was 4.0; median diagnostic confidence score was 4.0.
B, Coronal maximum-intensity-projection REACT image, obtained posterior in position to **A**, shows additional collateral pathways involving left arm, body wall, and intercostal veins.
C, Coronal maximum-intensity-projection image from contrast-enhanced MRV from same examination as **A** and **B** shows similar findings. Median image quality score was 4.5; median diagnostic confidence score was 5.

TABLE 3: Comparison of Frequency of Clinically Relevant Artifact(s) Between REACT Sequence and CE-MRV Sequence for Six Independent Readers

Reader	REACT	CE-MRV	*p*[a]
1	11.9 (5/42)	9.5 (4/42)	> .99
2	11.9 (5/42)	14.3 (6/42)	> .99
3	16.7 (7/42)	23.8 (10/42)	.55
4	14.3 (6/42)	11.9 (5/42)	> .99
5	14.3 (6/42)	19.0 (8/42)	.69
6	7.1 (3/42)	19.0 (8/42)	.06

Note—Data are expressed as percentage with numerator and denominator in parentheses. Clinically relevant artifact(s) is defined as artifact(s) causing evaluation of one or more vessels to be nondiagnostic. REACT = relaxation-enhanced angiography without contrast and triggering, CE-MRV = contrast-enhanced MR venography.
[a]McNemar test.

jugular vein was 5.0% versus 4.1%; for the left internal jugular vein, 9.5% versus 6.6%; for the right brachiocephalic vein, 7.1% versus 5.0%; for the left brachiocephalic vein, 7.0% versus 5.3%; for the right subclavian vein, 15.7% versus 5.4%; for the left subclavian vein, 17.4% versus 12.8%; and for the superior vena cava, 7.0% versus 3.3%.

Discussion

In this study, we have shown that a noncontrast relaxation-based blood flow–independent noncontrast non–ECG-gated MRV pulse sequence (i.e., the REACT sequence), introduced in 2019 and subsequently implemented at the study institution using respiratory triggering, can be used to evaluate central venous anatomy and patency in a sample of children and young adults. When compared with a conventional CE-MRV sequence, REACT showed no significant difference in overall image quality for five of six readers or in diagnostic confidence for all six readers. In addition, the frequency of clinically relevant artifact(s) was not significantly different between the two sequences for any reader.

In a pilot study of 10 healthy adults and 12 patients with vascular abnormalities, Yoneyama et al. [12] found REACT to have good image quality and high vessel conspicuity. Quantitative assessments of REACT images and contrast-enhanced MRA-MRV images showed no significant difference in CNR between blood and background tissues, although the REACT sequence had a slightly higher overall mean CNR. Isaak et al. [15] evaluated the thoracic vasculature of 70 pediatric and adult patients with congenital heart disease using REACT and compared REACT to nongated multiphase first-pass cardiovascular MRA and respiratory- and ECG-gated 3D SSFP imaging. In their study, the image quality of REACT was found to be higher than that of first-pass MRA and did not differ from SSFP imaging, and REACT had lower frequencies of nondiagnostic image quality than the other sequences. In addition, agreement for vessel diameter measurements between REACT and contrast-enhanced MRA-MRV was excellent, with minimal bias. Other studies have shown that REACT allows reliable imaging of the pulmonary arteries and veins [16], thoracic aorta [17], extracranial arteries in acute stroke [18, 19], and pelvic veins [20]. The current study is the first to our knowledge to compare image quality and diagnostic performance between REACT and CE-MRV for evaluation of central venous patency in a primarily pediatric cohort.

The REACT sequence showed slightly higher frequencies of abnormality for all assessed vessels compared with the CE-MRV sequence. The reason for this discordance between sequences is unknown from the present work. One possible explanation is that REACT may be more sensitive for vessel abnormalities owing to its blood flow independence and excellent image contrast resolution, in turn resulting from the sequence's superior background tissue suppression (e.g., Dixon and inversion recovery techniques). Alternatively, REACT may yield a greater frequency of false-positive abnormal findings for some vessels in some

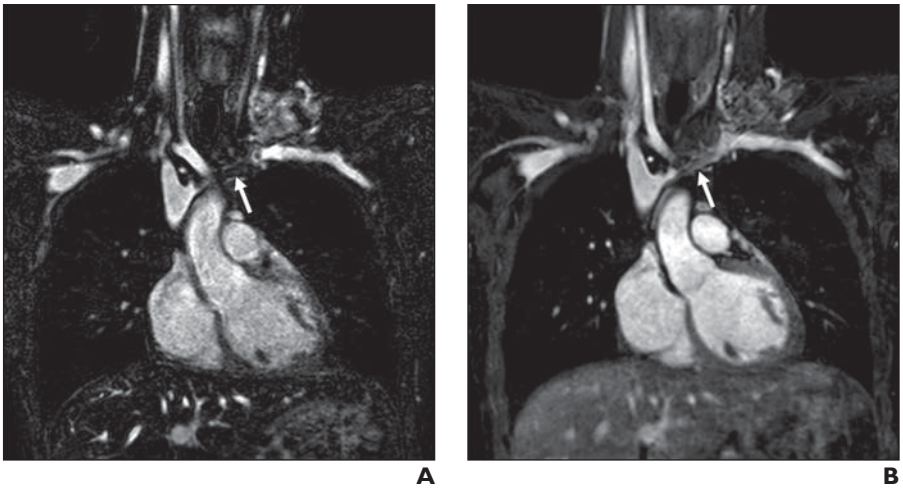

Fig. 4—20-year-old patient with cytotoxic T lymphocyte antigen 4 deficiency. MRI was performed to evaluate for central venous patency.
A, Coronal source image of neck and chest from respiratory-triggered flow-independent noncontrast non–ECG-gated MR venography (MRV) sequence (relaxation-enhanced angiography without contrast and triggering [REACT]) shows nonvisualization of left brachiocephalic vein owing to chronic occlusion (*arrow*). Collateral vessels (not shown) were present in mediastinum and neck. Median image quality score was 5.0; median diagnostic confidence score was 4.5.
B, Coronal source image from contrast-enhanced MRV shows no enhancement within left brachiocephalic vein (*arrow*). Median image quality score was 4.5; median diagnostic confidence score was 4.0.

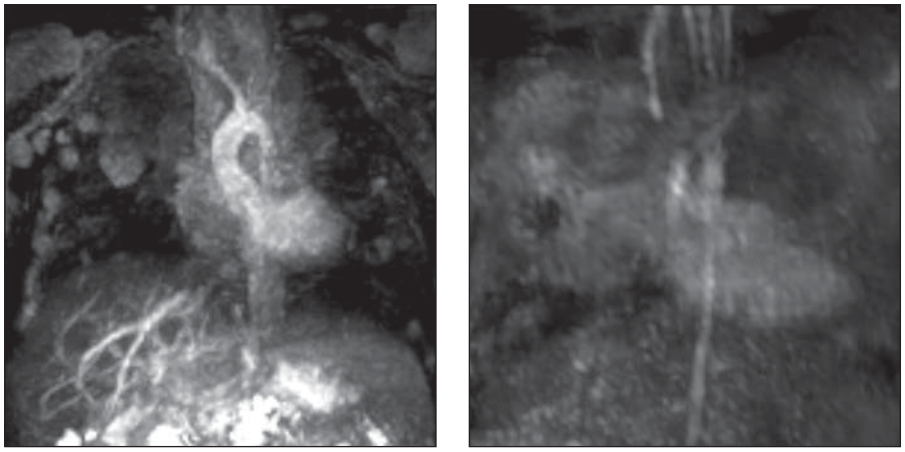

Fig. 5—5-month-old patient with chronic lung disease related to prematurity. MRI was performed to evaluate for central venous patency. **A** and **B,** Coronal maximum-intensity-projection image from respiratory-triggered flow-independent noncontrast non–ECG-gated MR venography (MRV) sequence (relaxation-enhanced angiography without contrast and triggering [REACT]) (**A**) and coronal maximum-intensity-projection image from contrast-enhanced MRV (CE-MRV) (**B**) of both neck and chest. Five of six readers assigned image quality score of 1 (nondiagnostic) for both sequences. Remaining reader assigned image quality score of 2 for REACT and 1 for CE-MRV.

patients, resulting in diminished specificity. In the absence of a reference standard (e.g., catheter-based venography), it is challenging to know in the current study which sequence was correct when REACT and CE-MRV yielded discrepant assessments.

REACT has advantages compared with conventional noncontrast and contrast-enhanced MRI techniques used to evaluate the vasculature. First, REACT eliminates issues related to the timing of imaging with respect to contrast material administration, which is critical to successful first-pass MRA-MRV. Although REACT provides a static anatomic assessment, its excellent spatial resolution and contrast resolution facilitate differentiation of arteries and veins. Second, the lack of IV contrast material may eliminate the need for peripheral IV catheter placement when not otherwise needed. The need for such catheters negatively impacts patient experience and can be particularly challenging in children with venous patency issues. Third, as REACT generates image contrast on the basis of the relaxation properties of blood, the sequence is expected to exhibit fewer artifacts in comparison with flow-dependent noncontrast MRV sequences in the settings of abnormally increased or decreased blood flow or of in-plane blood flow. Fourth, based on its pulse sequence design, REACT allows acquisition of large FOVs with robust fat and soft-tissue background signal suppression. Fifth, unlike conventional SSFP-based methods, REACT allows the acquisition of a 3D dataset without banding artifacts. Sixth, whereas conventional contrast-enhanced first-pass MRA-MRV requires breath-holding, the free-breathing nature of REACT (with optional respiratory triggering) eliminates the need for breath-holding and thus decreases the likelihood of artifacts resulting from inadequate and/or failed breath-holding. Finally, the high spatial resolution and 3D nature of REACT allow the creation of diagnostic-quality 2D reformations and 3D reconstructions; however, the value of such additional images was not specifically evaluated in the current study.

Although the initial description of REACT used free breathing, the version used in clinical practice at the study institution and that was used in the patients in the present sample incorporated respiratory triggering (using bellows) to limit data acquisition to the quiescent period of end-expiration. The current study did not assess the impact of respiratory triggering on the sequence's image quality. Additional research is needed to confirm the advantages of the addition of respiratory compensation to the originally described REACT technique given that this addition increases the acquisition time.

This study had limitations. First, although the six readers were from four different institutions, all examinations were performed at a single institution using that institution's standard-of-care clinical protocols. Second, REACT was compared to only a static CE-MRV sequence. Its performance versus the performance of other noncontrast and contrast-enhanced MRV techniques remains un-

TABLE 4: Interreader Agreement Among Six Pediatric Radiologists for Classification of Blood Vessel as Normal or Abnormal, Assessed Separately for REACT Sequence and CE-MRV Sequence

Vessel	REACT	CE-MRV
Right IJV	0.78 (0.63–0.94)	0.70 (0.52–0.88)
Left IJV	0.52 (0.34–0.71)	0.58 (0.37–0.78)
Right BCV	0.60 (0.32–0.88)	0.67 (0.40–0.95)
Left BCV	0.81 (0.68–0.94)	0.74 (0.61–0.87)
Right SCV	0.51 (0.36–0.67)	0.52 (0.35–0.69)
Left SCV	0.37 (0.21–0.53)	0.34 (0.22–0.46)
SVC	0.69 (0.49–0.89)	0.81 (0.61–1.00)

Note—Data are expressed as Fleiss kappa coefficient with 95% CI in parentheses. REACT = relaxation-enhanced angiography without contrast and triggering, CE-MRV = contrast-enhanced MR venography, IJV = internal jugular vein, BCV = brachiocephalic vein, SCV = subclavian vein, SVC = superior vena cava.

TABLE 5: Distribution of Classifications of Vessels as Normal or Abnormal for REACT Sequence and CE-MRV Sequence, Pooling Assessments by Six Independent Readers

Vessel	Normal by Both Sequences	Abnormal by Both Sequences	Abnormal by REACT Only	Abnormal by CE-MRV Only
Right IJV	76.0 (184/242)	14.9 (36/242)	5.0 (12/242)	4.1 (10/242)
Left IJV	66.5 (161/242)	17.4 (42/242)	9.5 (23/242)	6.6 (16/242)
Right BCV	82.2 (198/241)	5.8 (14/241)	7.0 (17/241)	5.0 (12/241)
Left BCV	55.3 (135/244)	32.4 (79/244)	7.1 (17/244)	5.3 (13/244)
Right SCV	53.3 (129/242)	25.6 (62/242)	15.7 (38/242)	5.4 (13/242)
Left SCV	46.3 (112/242)	23.6 (57/242)	17.4 (42/242)	12.8 (31/242)
SVC	78.5 (190/242)	11.2 (27/242)	7.0 (17/242)	3.3 (8/242)
All vessels	65.4 (1109/1695)	18.7 (317/1695)	9.8 (166/1695)	6.1 (103/1695)

Note—Data are expressed as percentage with numerator and denominator in parentheses. Calculations exclude vessels not scored by reader on either sequence because of artifact obscuring the vessel. REACT = relaxation-enhanced angiography without contrast and triggering, CE-MRV = contrast-enhanced MR venography, IJV = internal jugular vein, BCV = brachiocephalic vein, SCV = subclavian vein, SVC = superior vena cava.

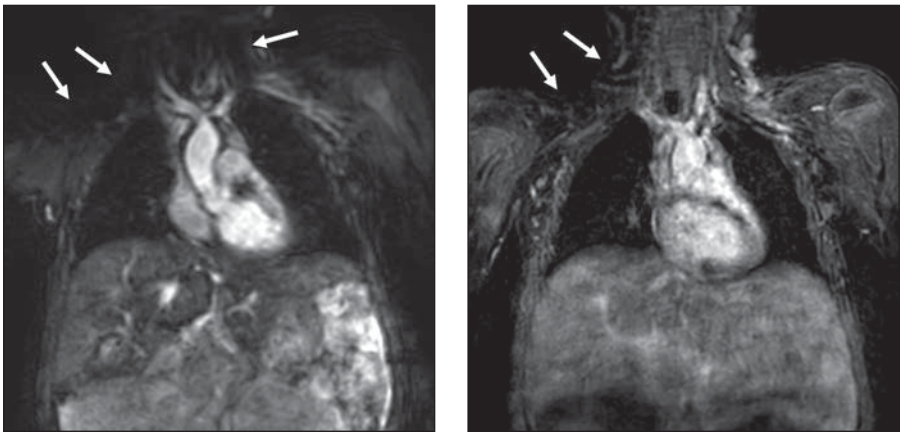

Fig. 6—9-year-old patient with gastroschisis. MRI was performed to evaluate for central venous patency.
A and **B,** Coronal source image from respiratory-triggered flow-independent noncontrast non–ECG-gated MR venography (MRV) sequence (relaxation-enhanced angiography without contrast and triggering [REACT]) (**A**) and coronal source image from contrast-enhanced MRV (CE-MRV) (**B**) of both neck and chest. All six readers documented presence of clinically relevant artifact(s), which was defined as artifact(s) resulting in nondiagnostic assessment of one or more vessels, for both sequences. REACT image shows areas of susceptibility artifact (*arrows*, **A**) in lower neck and right shoulder regions; CE-MRV image shows similar artifacts (*arrows*, **B**) involving right neck and neck base. CE-MRV also shows motion artifacts.

known. Third, the study was designed to evaluate central venous anatomy and patency specifically in the neck and chest; the performance of REACT was not evaluated for veins in other areas of the body or for arteries. Fourth, approximately half of the MRI examinations were performed at 1.5 T, and the remaining examinations were performed at 3 T. The impact of field strength on overall image quality, diagnostic confidence, frequency of artifacts, or frequency of abnormal vessels was not evaluated. Fifth, given the nature of the study design and the lack of a reference standard for vessel abnormalities, diagnostic performances could not be determined for REACT and CE-MRV and could not be compared. Finally, REACT was developed by and is currently available from only a single MRI scanner manufacturer, thus impacting availability of this emerging vascular imaging technique.

In conclusion, a respiratory-triggered high-resolution flow-independent noncontrast non–ECG-gated 3D MRV pulse sequence (REACT), in comparison with a conventional CE-MRV sequence, yielded no significant difference in image quality (aside from in one of six readers) or diagnostic confidence and yielded similar interreader agreement for classification of vessels as normal or abnormal. However, REACT yielded slightly higher frequencies of abnormal vessels compared with CE-MRV; the explanation and significance of this finding are uncertain from the current study and require further investigation. Nonetheless, the results suggest that REACT may be an alternative to CE-MRV for evaluating thoracic central venous anatomy and patency in children and young adults, potentially eliminating the need for intravascular contrast material administration in this setting.

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Editorial Comment: High-Resolution Noncontrast MRA Technique Shows Utility in Pediatric Imaging

Relaxation-enhanced angiography without contrast and triggering (REACT), first described in 2019, is a 3D blood flow–independent noncontrast MRA–MR venography (MRV) sequence that provides excellent contrast and spatial resolution of blood vessels with fast data acquisition. The sequence uses a combination of inversion recovery and dual gradient-echo Dixon-based techniques to generate robust background suppression over a large FOV without vulnerability to the signal loss or field inhomogeneity artifacts encountered in other blood flow–independent noncontrast sequences [1]. Experience with REACT in adults has supported its use for varied applications, including evaluation of peripheral vascular malformations, suspected renal artery stenosis, and the extracranial arteries in the setting of acute stroke [1, 2].

The benefits of the REACT sequence present substantial advantages when imaging children. Obviating gadolinium-based contrast material resolves the potential logistical complexities of obtaining IV access in children and also decreases cost and scanner time. As this study shows, data acquisition time with REACT (2 minutes 30 seconds) was comparable to that of the counterpart 3D two-point Dixon-based gradient-echo contrast-enhanced MRV sequence (2 minutes 0 seconds). Gadolinium deposition in the brain may be of particular concern in children [3], as the agent's long-term effects over the course of the child's future lifetime remain uncertain.

In this work evaluating MRI for assessment of central venous patency in 42 children and young adults, the authors found that REACT performed at least as well as the contrast-enhanced sequence with regard to image quality, motion-related artifacts, and confidence in determination of vessel patency. The REACT sequence is currently available on only a limited number of MRI platforms. Nonetheless, this work—the first, according to the authors, to evaluate REACT in a primarily pediatric sample—provides a foundation for the technique's application for the imaging of many other vascular disorders in children. Just as night follows day, the inevitable advancements in MRI continue.

Abhay S. Srinivasan, MD
Children's Hospital of Philadelphia
Perelman School of Medicine at the University of Pennsylvania
Philadelphia, PA
srinivasaa@chop.edu

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