

# 7T Epilepsy Task Force Consensus Recommendations on the Use of 7T MRI in Clinical Practice

Citation for published version (APA):

Opheim, G., van der Kolk, A., Bloch, K. M., Colon, A. J., Davis, K. A., Henry, T. R., Jansen, J. F. A., Jones, S. E., Pan, J. W., Rosler, K., Stein, J. M., Strandberg, M. C., Trattig, S., de Moortele, P. F. V., Vargas, M. I., Wang, I., Bartolomei, F., Bernasconi, N., Bernasconi, A., ... Guye, M. (2021). 7T Epilepsy Task Force Consensus Recommendations on the Use of 7T MRI in Clinical Practice. *Neurology*, 96(7), 327-341. <https://doi.org/10.1212/WNL.0000000000011413>

## Document status and date:

Published: 16/02/2021

## DOI:

[10.1212/WNL.0000000000011413](https://doi.org/10.1212/WNL.0000000000011413)

## Document Version:

Publisher's PDF, also known as Version of record

## Document license:

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# 7T Epilepsy Task Force Consensus Recommendations on the Use of 7T MRI in Clinical Practice

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*Neurology*® 2021;96:327-341. doi:10.1212/WNL.00000000000011413

## Abstract

Identifying a structural brain lesion on MRI has important implications in epilepsy and is the most important factor that correlates with seizure freedom after surgery in patients with drug-resistant focal onset epilepsy. However, at conventional magnetic field strengths (1.5 and 3T), only approximately 60%–85% of MRI examinations reveal such lesions. Over the last decade, studies have demonstrated the added value of 7T MRI in patients with and without known epileptogenic lesions from 1.5 and/or 3T. However, translation of 7T MRI to clinical practice is still challenging, particularly in centers new to 7T, and there is a need for practical recommendations on targeted use of 7T MRI in the clinical management of patients with epilepsy. The 7T Epilepsy Task Force—an international group representing 21 7T MRI centers with experience from scanning over 2,000 patients with epilepsy—would hereby like to share its experience with the neurology community regarding the appropriate clinical indications, patient selection and preparation, acquisition protocols and setup, technical challenges, and radiologic guidelines for 7T MRI in patients with epilepsy. This article mainly addresses structural imaging; in addition, it presents multiple nonstructural MRI techniques that benefit from 7T and hold promise as future directions in epilepsy. Answering to the increased availability of 7T MRI as an approved tool for diagnostic purposes, this article aims to provide guidance on clinical 7T MRI epilepsy management by giving recommendations on referral, suitable 7T MRI protocols, and image interpretation.

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## Glossary

**DNET** = dysembryoplastic neuroepithelial tumor; **DRFE** = drug-resistant focal epilepsy; **FCD** = focal cortical dysplasia; **FLAIR** = fluid-attenuated inversion recovery; **FWMS** = fluid and white matter suppressed; **GRE** = gradient-recalled echo; **HS** = hippocampal sclerosis; **LEAT** = long-term epilepsy-associated tumor; **MCD** = malformations of cortical development; **MPRAGE** = magnetization-prepared rapid acquisition gradient echo; **MRS** = magnetic resonance spectroscopy; **RF** = radiofrequency; **SNR** = signal-to-noise ratio; **SWAN** = susceptibility-weighted angiography; **SWI** = susceptibility-weighted imaging; **TLE** = temporal lobe epilepsy; **TSE** = turbo spin echo; **UHF** = ultrahigh field.

Epilepsy is drug resistant in approximately 30%–40% of patients.<sup>1</sup> In drug-resistant focal epilepsy (DRFE), surgical resection, laser ablation, and disconnection of the epileptogenic zone or network are the only curative options. The chances of successful post-surgical outcome are 2.5–3 times higher if an epileptogenic lesion is identified by MRI.<sup>2</sup> However, precise identification of the resection margin, which is essential for optimizing surgical outcomes, is often difficult using 1.5 or 3T. Moreover, the absence of an MRI-detectable lesion in approximately one-third of patients with DRFE is a major limitation to surgical candidacy. Finally, normal-appearing MRI also hampers targeting for intracranial electrode implantation, which, in addition to seizure onset localization, is also used for chronic brain electrostimulation therapies and targeted laser ablation.

7T MRI, compared with lower field strengths, has increased signal-to-noise ratio (SNR) and susceptibility effects, thereby providing better image contrast, higher spatial resolution, and stronger susceptibility contrast.<sup>3,4</sup> These advantages offered by 7T may address multiple preoperative and postoperative problems in DRFE, including lesion detection (especially malformations of cortical development [MCD]) in 16%–32% of previously MRI-negative patients, and identification of residual epileptogenic tissue after surgical failures.<sup>5–10</sup> Notwithstanding these advantages, technical challenges such as inhomogeneous radiofrequency (RF) distributions present limitations on ultrahigh field systems and add certain challenges for its use in epilepsy. An excellent review article on scientific developments of 7T in epilepsy has recently been published.<sup>11</sup> The present study provides guidance for setting up a 7T epilepsy protocol for clinical use, based on the collective experience of 21 centers in which over 2000 7T MRI epilepsy examinations were performed.

## Clinical Indications, Patient Preparation, and Safety

When operating a non-CE/FDA-approved 7T MRI scanner, clinical patient scanning should be authorized by the local institutional review board (IRB), considering both clinical benefits and possible safety issues.

When planning clinical 7T MRI for an individual with epilepsy, one should pay attention to patient-specific indications for additional enhanced brain imaging, any contraindications to MRI in general and 7T in particular, and other potential issues inherent to the ultrahigh field (UHF) environment. Thorough

evaluation of these 3 factors improves the diagnostic gain of 7T MRI by making optimal use of its advantages—and adapting to its limitations. Given the currently limited availability of clinical 7T MRI platforms, most centers focus on indications for the referral of patients with DRFE for 7T MRI, as opposed to general diagnostic purposes.

### Clinical Indications

The main indications for 7T MRI in epilepsy are to improve imaging to identify a possible morphological lesion responsible for DRFE and to better delineate or classify known lesions. We have identified 4 main indications based on a priori knowledge at the time of 7T MRI referral.

### 3T MRI-Negative Cases

The objective is to detect possible lesions missed by the currently recommended epilepsy-specific 3T MRI protocol.<sup>12,13</sup> The presence of so far undetected lesions can be supported by the clinical history, ictal semiology, interictal and especially ictal scalp EEG, PET, or SPECT.

### Lesion Typing, Delineation, and False Positives

Related to the evaluation of known/suspected lesions, this main indication covers further characterization of known structural abnormalities deemed suitable for resection by improved profiling of the abnormality, including distinction of neoplastic lesions, optimal delineation of MCD and scarring lesions, and distinguishing pathologic lesions from benign or unknown morphological variants. This analysis also includes resolving false-positive 3T MRI (in Radiologic Considerations and Visual Assessment), which may lead to misguided clinical management without the added information from 7T MRI.

### Electrode Positioning

Improved lesion characterization and visualization of adjacent structures may also augment planning of intracranial electrode positioning for electrophysiologic measurements or electrostimulation therapy. This is facilitated by the increased anatomic details at 7T that enable consideration of fine structures with subtle signal changes, atrophy, or malformations. However, potential increased geometric distortion in some sequences due to stronger magnetic field must be considered.

### Eloquent Areas

Iatrogenic injury to sites of normal cerebral physiology may be avoided by interictal mapping using stimulation or resting-

**Table 1** Summary of the 8 Most Useful Sequences as Identified in a Survey From 19 7T MRI Centers Experienced in Examining Patients With Epilepsy For Research and/or Diagnostic Purposes

Sequence type	Orientation	In-plane spatial resolution in mm, range (median)	Slice thickness in mm, range (median)	Duration in mm:ss, range (median)
<b>Limited coverage</b>				
<b>T<sub>2</sub>w<sup>a</sup></b>				
<b>TSE<sup>1</sup></b>	Coronal	0.25–0.70 (0.30)	1.00–3.00 (1.35)	3:36–8:48 (5:58)
<b>TSE<sup>8</sup></b>	Axial	0.40–0.70 (0.45)	0.75–3.00 (1.55)	3:39–12:00 (6:17)
<b>T<sub>2</sub>*w<sup>6</sup></b>				
<b>GRE</b>	Coronal	0.25–0.38 (0.30)	1.65–2.00 (2.00)	5:22–6:12 (5:58)
<b>Whole-brain coverage</b>				
<b>3D T<sub>1</sub>w</b>				
<b>MPRAGE<sup>4</sup></b>	Sagittal	0.60–0.90 (0.73)	0.60–1.00 (0.73)	6:47–10:12 (8:27)
<b>MP2RAGE<sup>2</sup></b>	Sagittal	0.60–0.80 (0.70)	0.60–0.80 (0.70)	5:20–11:45 (6:21)
<b>3D FLAIR<sup>3</sup></b>	Sagittal	0.70–1.00 (0.80)	0.70–1.40 (0.80)	5:54–10:38 (7:27)
<b>3D T<sub>2</sub>*w<sup>7</sup></b>				
<b>GRE/SWI</b>	Any	0.25–0.80 (0.50)	0.20–2.00 (0.90)	5:17–12:00 (8:27)
<b>3D T<sub>2</sub>w<sup>5</sup></b>				
<b>TSE</b>	Sagittal/ axial	0.50–0.80 (0.70)	0.69–2.40 (0.70)	5:32–10:59 (7:11)

Abbreviations: FLAIR = fluid-attenuated inversion recovery; GRE = gradient-recalled echo; MPRAGE = magnetization-prepared rapid acquisition gradient echo; SWI = susceptibility-weighted imaging; TSE = turbo spin echo; w = weighted.

<sup>a</sup> In a few centers, the multislice T<sub>2</sub>-weighted TSE sequences were reconstructed to an even higher spatial resolution.<sup>1–8</sup> The order of importance as scored by the involved radiologists.

state fMRI. The greater BOLD SNR performance of 7T MRI offers considerable advantages in mapping eloquent cortex over 1.5T and 3T fMRI.<sup>12,14</sup>

### Tolerability Issues at 7T

Although patient motion can be detrimental for image assessment at any field strength, this effect is even more pronounced at 7T. The most efficient way to minimize motion is to prepare patients before the MRI examination. However, even patients who have previously undergone MRI examinations can encounter specific issues or physical sensations at 7T that we recommend addressing during preparation.<sup>13</sup>

### Longer Acquisition Times

To make optimal use of the advantages of UHF MRI, individual 7T sequences (table 1)—and therefore whole MRI protocols—will often take longer to acquire than at 3T. Lying supine inside the MRI scanner for such long times may cause discomfort and musculoskeletal pain in a subset of patients (approximately 25%).<sup>15</sup> Sleepiness is also more likely to occur and might increase the risk of seizures in some patients with DRFE.

### Longer Scanner Bore and Smaller Head Coil

The longer scanner bore may induce claustrophobia. In addition, the most commonly used head coil is smaller than at

lower field strengths; patients with larger heads will therefore receive a thinner pillow under the head, which often leads to numbness in the back of the head (Task Force experience; ~40% feels discomfort during the examination).<sup>15,16</sup> Another consequence of smaller head coils is the lack of space for headphones, which is why most centers use earplugs and/or a soft clay to compensate for the loud noises unavoidable in any MRI scanner.

### Peripheral Nerve Stimulation (PNS)

Some patients have reported mild discomfort or anxiety due to PNS, which can present as tingling or twitches in upper limbs or large muscle groups. Most clinical sequences are designed to have limited PNS. However, sensitivity to these physical sensations differs between patients; reported prevalence varies widely from 23% to 63%.<sup>15–17</sup>

### Dizziness

Dizziness caused by movement in and out of the B<sub>0</sub> field is one of the most frequently reported sensations (25%–80%).<sup>15–17</sup> To suppress this issue, very slow movement of the patient table into the scanner—which may be pre-configured by vendors—is recommended. Usually, dizziness will pass shortly (30–60 seconds) after positioning. During this movement, patients may also sense a metallic taste.

**Table 2** Summary of Sequences of Particular Interest For Certain (Known and/or Suspected) Epileptic Lesion Types; Often Used Acquisition Parameters Can Be Found in the Text and in table 1

Lesion type	Sequences of particular interest
Temporal lobe epilepsy with known or suspected HS	3D T <sub>1</sub> w MPRAGE or MP2RAGE
	3D T <sub>2</sub> w TSE
	2D T <sub>2</sub> w TSE focused on the hippocampus and anterior temporal lobe
Focal cortical dysplasia (type I and II)	3D T <sub>1</sub> w MPRAGE or MP2RAGE (whole-brain)
	3D FLAIR
	3D T <sub>2</sub> *w GRE or SWI
	+/- FWMS sequence
	+/- 2D T <sub>2</sub> w TSE focused on the suspected cortical lesion
LEAT (gangliogliomas, DNET)	3D T <sub>1</sub> w MPRAGE or MP2RAGE
	3D T <sub>2</sub> w TSE
	3D T <sub>2</sub> *w (GRE or SWI)
Polymicrogyria	3D T <sub>1</sub> w MPRAGE or MP2RAGE
	3D T <sub>2</sub> *w (SWI or SWAN)
	+/- FSPGR
Tuberous sclerosis complex	3D T <sub>1</sub> w MPRAGE or MP2RAGE
	3D T <sub>2</sub> *w (SWI or SWAN)
	3D FLAIR
Vascular malformations	3D T <sub>2</sub> *w (SWI)
MRI negative at 3T	3D T <sub>1</sub> w MPRAGE or MP2RAGE
	3D FLAIR
	3D T <sub>2</sub> w TSE
	3D T <sub>2</sub> *w (GRE or SWI)
	+/- FWMS sequence
	+/- 2D T <sub>2</sub> w TSE over regions indicated by, e.g., EEG

Abbreviations: DNET = dysembryoplastic neuroepithelial tumor; FLAIR = fluid-attenuated inversion recovery; FSPGR = fast spoiled gradient echo; FWMS = fluid and white matter suppressed; GRE = gradient-recalled echo; HS = hippocampal sclerosis; LEAT = long-term epilepsy-associated tumor; MPRAGE = magnetization-prepared rapid acquisition gradient echo; SWAN = susceptibility-weighted angiography; SWI = susceptibility-weighted imaging; TSE = turbo spin echo; w = weighted.

## Patient Safety at 7T

Once the clinical indication for 7T imaging has been established, it should be followed by a critical evaluation of possible contraindications. In this regard, it is important to realize that implants that are MR compatible at 3T may be incompatible at 7T, presenting a serious safety hazard. We therefore

recommend thorough safety screening with particular emphasis on potentially hazardous factors that were approved at 3T and might be overlooked on referral to 7T.

There is no whole-body RF coil in a 7T scanner; brain imaging is obtained with the combined transmit/receive coil, which limits the RF field to the head (plus a safety margin). Generally, for implants, displacement force and torque due to B<sub>0</sub> are higher, and for both implants and tattoos, the risk of RF heating is increased because of the shorter RF wavelength. Despite initiatives on harmonizing approaches,<sup>18</sup> there is no global consensus regarding implant safety at 7T yet, and centers differ in their approach to contraindications. Some centers have dedicated safety committees that have scanned phantoms and/or obtained electromagnetic field numerical simulations to assess safety margins of common implants and might therefore practice less conservative safety margins relative to the head coil. Until official 7T MRI safety guidelines that cover both implant types and safety margins are in place, implants within the RF coil volume should be locally approved at 7T based on literature or local testing.<sup>18</sup> Further statements regarding these and other safety aspects at 7T would in the near future complement already existing recommendations.<sup>19</sup>

## Acquisition Protocol and Recommended Setup

Among other topics, the survey answered by centers in our Task Force contained questions on which sequences they use in patients with epilepsy and to what degree they are useful for radiologic evaluation. When comparing protocols, the majority included a subset of structural sequences, which although differed in parameter settings served the same purpose. The contrast weightings in the protocols mirrored those included in the most recent recommendations for 3T MRI of patients with epilepsy,<sup>12</sup> taking advantage of the increased magnetic field mainly by increasing spatial resolution. Based on frequency of use and radiologic rating of importance, 8 sequences across 4 different contrast weightings scored highest and were presented to the Task Force for consensus voting. These 8 sequences will be discussed in detail in the following paragraphs, whereas major acquisition parameters can be found in table 1. Specific sequence recommendations based on clinical indication are given in table 2; a general protocol takes approximately 50 minutes to acquire.

## Most Valued Sequences in (Clinical) Practice

### 3D T<sub>1</sub>-Weighted Sequences

Because of the significantly longer acquisition times of spin echo-based sequences, gradient echo (GRE)-based MPRAGE<sup>20</sup> or MP2RAGE<sup>21,22</sup> is the mainstay for T<sub>1</sub>-weighted imaging at 7T, with isotropic voxel sizes ranging from 0.6 to 0.9 mm. The main advantage of using MP2RAGE over MPRAGE is its better resistance to RF field inhomogeneity; MP2RAGE can therefore

**Figure 1** Use of Dielectric Pads

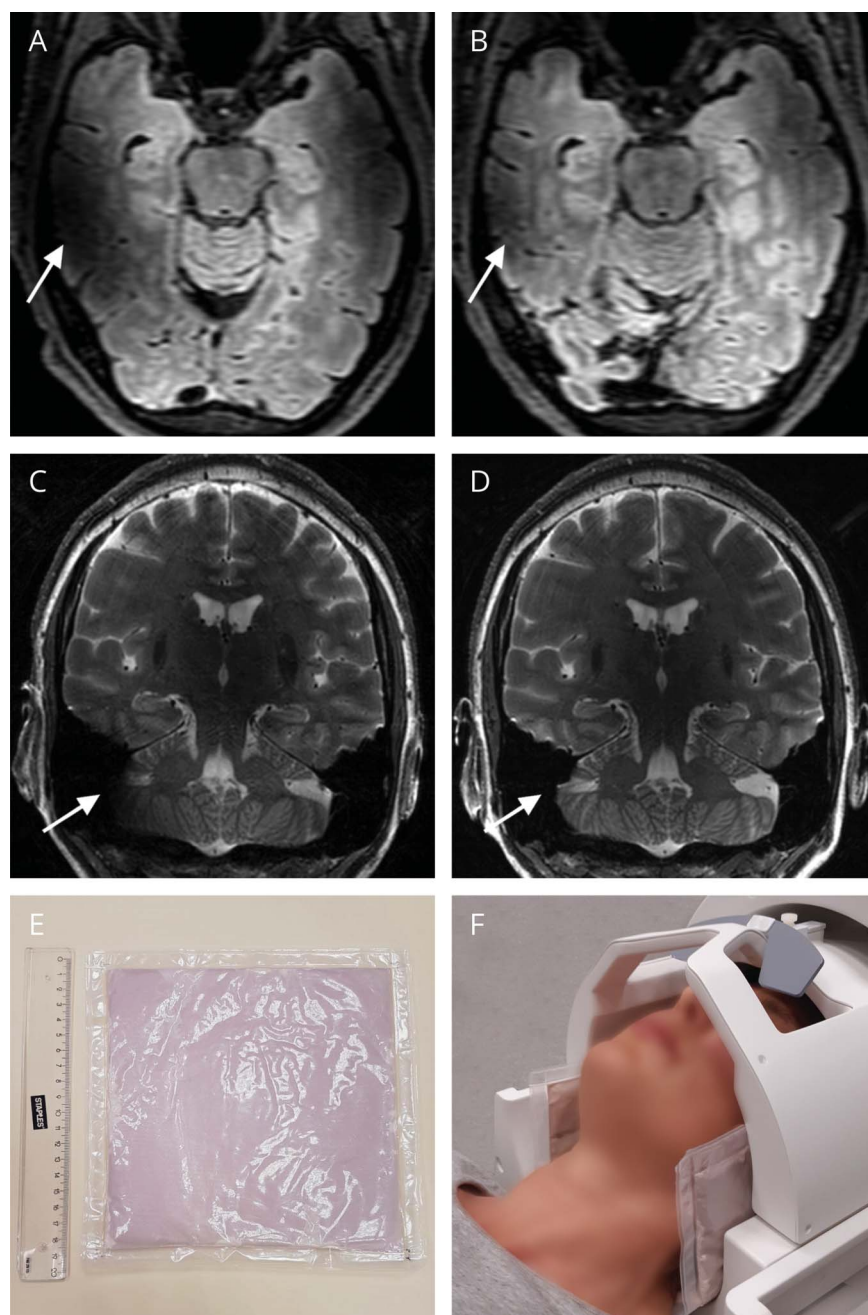


Illustration of the effect of dielectric pads on (A and B) 3D fluid-attenuated inversion recovery (FLAIR, 0.7 mm isotropic resolution) and (C and D) T<sub>2</sub>-weighted sequences (0.3 × 0.3 × 1.5 mm resolution). In (A and C), no pads are used, whereas in (B and D) they are. Arrows indicate corresponding areas before and after signal improvement (A versus B, C versus D). The dielectric pads used in this case are 19 × 19 cm (E); pad placement for obtaining images (B and D) is demonstrated in image (F). Of note, optimal pad placement depends on the head size and shape.

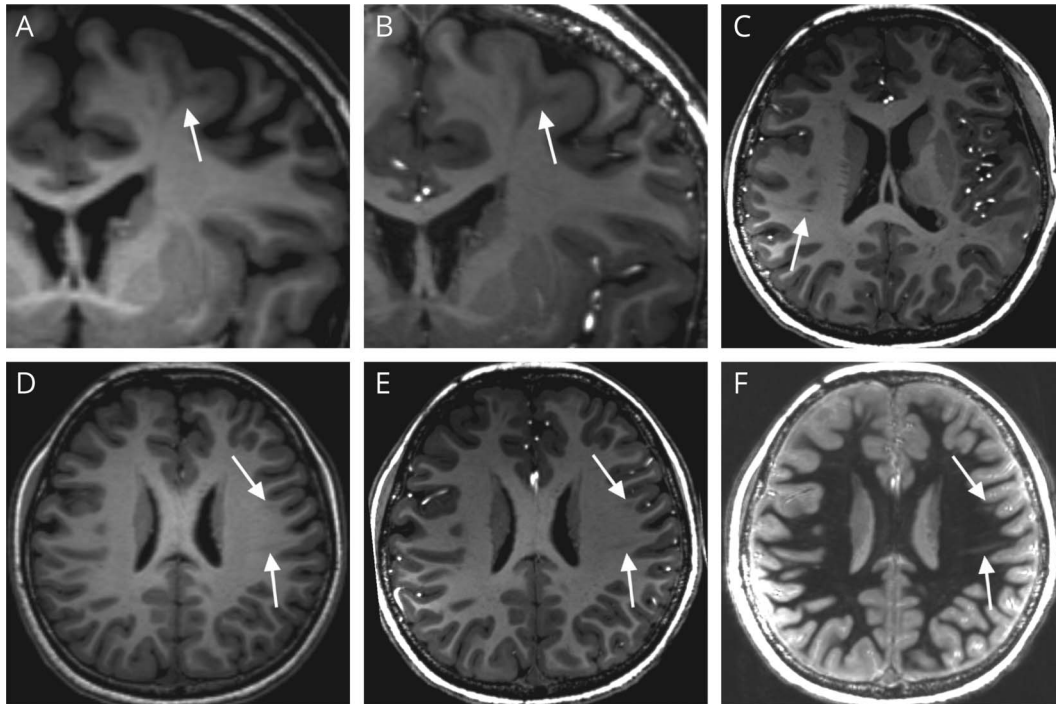
also be useful in quantitative techniques. However, some 7T platforms are not equipped with an embedded pipeline to process MP2RAGE data and output DICOM images, in which case offline processing is required, which hampers clinical workflow with PACS export.

### 3D Fluid Attenuation Inversion Recovery (FLAIR) Sequence

A 3D FLAIR with isotropic reconstructed spatial resolutions of 0.7–0.8 mm and whole-brain coverage is preferred because it can be reformatted in any orientation. Implementation of FLAIR at

7T is not trivial for several reasons.<sup>23</sup> From a technical point of view, RF-pulses at 7T have to be insensitive to the inhomogeneities of the B<sub>0</sub> and RF field over the brain, while also complying with the restrictions on specific absorption rate (SAR). 3D FLAIR sequences are very sensitive to flip angle (FA) calibrations; if the true FA deviates too much from the set FA—which is spatially different at 7T because of RF field inhomogeneity—signal dropouts will occur and may hamper image assessment. As a consequence, finding the balance between signal intensities across the brain may be subject to radiologic priorities, that is, whether a radiologist wants to focus on medial

**Figure 2** Example of Tuberos Sclerosis Complex at 7T



3T T<sub>1</sub>-weighted 0.9 mm isotropic MPRAGE (A and D), 7T T<sub>1</sub>-weighted 0.6 mm isotropic MPRAGE (B–D), and 0.8 mm isotropic white matter-suppressed T<sub>1</sub>-weighted images (F) in an 11-year-old girl diagnosed with tuberous sclerosis complex (TSC). Cortical tubers were found throughout the brain both at 3T and 7T MRI (arrow in A and B). Radial migration bands, however, were much more difficult to visualize; subtle radial bands could be identified at 7T in the left frontal and parietal lobe (arrows in E and F), which were only retrospectively seen at 3T (D). In addition, more detailed structures surrounding both tubers and radial bands, as well as previously unidentified subtle TSC abnormalities such as a small cyst associated with a radial band in the right parietal lobe (C), were seen only at 7T images. This detailed delineation of TSC abnormalities may improve surgical resection, thereby increasing the likelihood of a seizure-free postoperative outcome. *Courtesy of Kaibao Sun, PhD, Center for MR Research, University of Illinois at Chicago, Chicago, IL, USA. Data were acquired during his employment at the State Key Lab. of Brain and Cognitive Science, Beijing MRI Center for Brain Research, Institute of Biophysics, Chinese Academy of Sciences, Beijing, China.*

(prioritize low FA) or lateral (prioritize high FA) structures. These difficulties have led to research into new types of RF pulse strategies and sequence designs<sup>24,25</sup> to mitigate these problems.

### T<sub>2</sub>-Weighted Sequences

The obtainable in-plane spatial resolution of T<sub>2</sub>-weighted sequences depends on the requested coverage and is limited by SNR, acquisition time, and patient motion. For instance, to cover the hippocampus with a coronal T<sub>2</sub>-weighted sequence within a reasonable time, in-plane acquisition resolutions of 0.25–0.50 mm are used, with slice thicknesses of 1–2 mm. However, this will increase sensitivity to patient motion because of the long acquisition times (table 1). These sequences are therefore natural targets for motion correction techniques. The 3D T<sub>2</sub>-weighted TSE sequence has less obvious motion artifacts than the multislice T<sub>2</sub>-weighted sequences, however at the expense of a less pronounced image contrast and higher sensitivity to RF field inhomogeneity. For this 3D sequence, an isotropic spatial resolution of 0.5–0.8 mm and whole-brain coverage is recommended.

### T<sub>2</sub>\*-Weighted Sequences

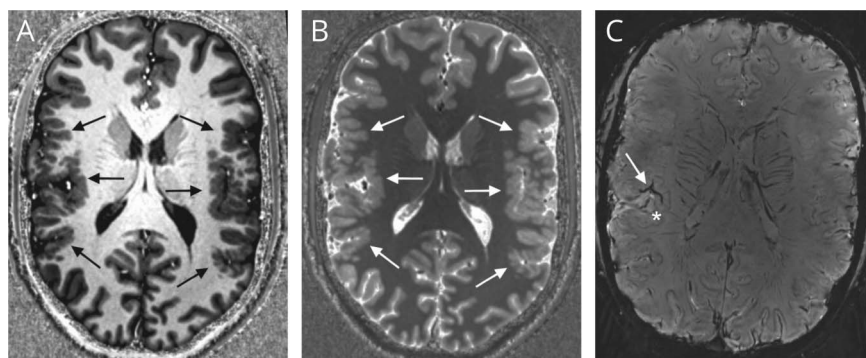
Because of more pronounced susceptibility effects at 7T, image contrast in T<sub>2</sub>\*-weighted sequences increases. Many centers use 3D T<sub>2</sub>\*-weighted sequences (GRE or

susceptibility-weighted imaging [SWI]) complementary to other images to assess vascular pathologies and vascularity in given structures. A faster, thus less motion-sensitive, alternative to 3D sequences, is to choose 2D T<sub>2</sub>\*-weighted sequences that cover specific regions with the same spatial resolution as 3D sequences.

### Use of Dielectric Pads

The inhomogeneous RF field often manifests as contrast changes or signal losses in the temporal lobes and cerebellum, an effect that is most pronounced on FLAIR images (figure 1, A and B) but also apparent on T<sub>2</sub>-weighted images (figure 1, C and D). One straightforward way to increase RF field homogeneity is to apply dielectric pads (<1 cm thick) on each side of the head,<sup>26</sup> which is followed by two-thirds of the centers with sizes varying from 10 × 10 cm<sup>2</sup> to 19 × 19 cm<sup>2</sup> (figure 1E). The pads are placed as shown in figure 1F. To ensure that the contents are always well mixed and to verify cracks/dryness in the compound, we recommend to gently massage pads before each scan. Renewing the pads annually/biannually prevents suboptimal effects due to degradation of the material over time (depending on the type). Of note, by introducing dielectric pads into the transmit coil, SAR estimations produced by the scanner are no longer valid. It is therefore

**Figure 3** Example of Polymicrogyria at 7T



7T T<sub>1</sub>-weighted MP2RAGE (A) and MP2RAGE T<sub>1</sub>-map (B) images illustrate thickening of the perisylvian cortex (arrows in A and B) in an 18-year-old patient who had known polymicrogyria as already visualized at 3T MRI; clinical indication for 7T imaging was better lesion delineation. An additional 7T T<sub>2</sub>\*-weighted (SWI) sequence (C) shows a hyperintense cortex associated with veins perpendicular to the cortex (\* in C) and a tree-like distribution of vessels (arrow in C).

important that simulations of pad placements are made to ensure patient safety. Such simulations have been made and published for the standard NOVA head coil (1- and 2-channel transmit, NOVA Medical, Wilmington, MA, USA),<sup>27</sup> which is used in most 7T centers worldwide. When using other coils, new simulations should be performed, and the pads should not be used if transmission settings are varied between patients unless on-the-fly SAR calculations including the pads are done.

### Deciding on the Imaging Protocol

The individual patient-specific indications for 7T imaging (in Clinical indications) will drive the selection of sequences, which should be performed in the order of priority to preempt motion artifacts from hampering assessment of the most important sequences. Recommendations for a minimum scan protocol can be found in table 2.

## Radiologic Considerations and Visual Assessment

Moving to 7T requires adaptation of the observer's blueprint of what healthy tissue and pathology looks like. The changes in image quality aspects at 7T can be perceived as an improvement, or sometimes the contrary. For virtually all 7T images, contrast between tissues will be much higher. For instance, the cortex will be more discernible from white matter, basal ganglia will have more heterogeneous signal intensity reflective of substructures that can now be discriminated, and very small vessels, perivascular spaces, and u-fibers are clearly identifiable. Although the amount of perivascular spaces has been suggested to correlate with seizure laterality,<sup>28</sup> these findings are normal and should not be interpreted as pathology; on the contrary, they can be used for resolving false-positive blurring and transmante signs at 3T. Another characteristic 7T finding (caused by RF transmit head coils) on T<sub>1</sub>-weighted (MPRAGE/MP2RAGE) images is that arteries appear bright even without contrast administration.

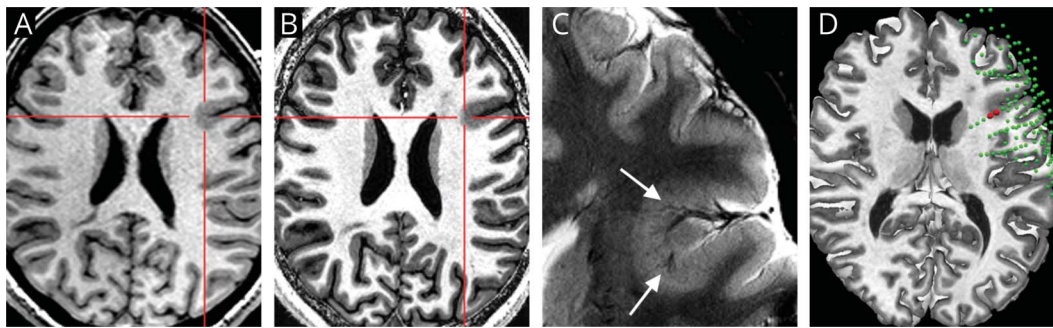
RF field inhomogeneity effects (in Acquisition protocol and recommended setup) are substantial and remain one of the most significant artifacts at 7T. These effects, however, can be partially suppressed by RF shimming, for example, through the use of dielectric pads (figure 1). Furthermore, susceptibility artifacts will be more pronounced, particularly in areas close to air-containing structures, which may overlap with those affected by RF field inhomogeneities. An additional strategy is to adapt the window width and level, depending on which part of the brain is of interest; this will improve image contrast in, for example, the temporal lobes, whereas the center of the brain will be less assessable with those same settings. Flow artifacts in and from large vessels are also present, and in cases in which such artifacts extend across gray and white matter, care should be taken not to mistake these for pathology. Because there currently does not exist any uniform 7T-specific training material, we recommend surveying several 7T MRI scans, preferably of healthy volunteers, to get acquainted with these characteristics and thus avoid mistaking them for 7T false positives in the epilepsy examination routine. The following section provides detailed imaging findings and sequence considerations for selected lesions for which our collective experiences consider 7T MRI particularly helpful.

### Malformations of Cortical Development (Excluding Focal Cortical Dysplasia)

#### Tuberous Sclerosis Complex (TSC) and Long-Term Epilepsy-Associated Tumors (LEATS: Gangliogliomas and Dysembryoplastic Neuroepithelial Tumors [DNET]) (Barkovich Group I)

The increased spatial resolution and image contrast at 7T improves detection and delineation of cerebral lesions in TSC such as cortical and subependymal tubers,<sup>29</sup> cortical dysplasia, and white matter abnormalities.<sup>30</sup> Also, a new finding first identified at 7T is the presence of tortuous veins associated with subependymal tubers.<sup>30,31</sup> Next to T<sub>2</sub>-weighted/FLAIR imaging for visualization of cortical tubers and white matter abnormalities, and 3D T<sub>1</sub>-weighted (MP2RAGE or MPRAGE) imaging for cortical and subependymal tubers (figure 2), we particularly recommend a 3D SWI or GRE T<sub>2</sub>\*-weighted





Axial 3T  $T_1$ -weighted MPRAGE (A), axial 7T  $T_1$ -weighted MP2RAGE (B), and zoomed in axial 7T  $T_2^*$ -weighted GRE (C) images of a patient for whom visual review of 7T MRI yielded previously unappreciated subtle findings. The red crosshairs/arrows pinpoint the location of an area of focal cortical dysplasia (FCD), which was detected by visual analysis of 7T images. The vascular changes associated with the FCD can be well appreciated on the  $T_2^*$ -weighted GRE images in panel C (arrows). Detection of this subtle lesion guided subsequent placement of intracranial-EEG (icEEG) with subdural grids and depth electrodes. The icEEG implantation was devised to confirm the epileptogenicity of the subtle lesion and map out the lesion extent and its proximity to eloquent cortex with language function. The subtle lesion location was concordant with ictal onset on the icEEG as shown in the 3D reconstruction of electrode location and 7T MRI, with a 2D axial cut-plane (D). In panel D, green spheres indicate all implanted electrodes and red spheres indicate ictal onset.

sequence because the increased sensitivity to susceptibility effects enables better visualization of (frequently encountered) tuber calcification. Image characteristics at 7T are consistent with those seen at lower field strengths; the main advantage is the higher lesion conspicuity leading to both detection of more lesions and better delineation for surgical planning. LEATS (gangliogliomas and DNET) are low-grade tumors that consist of a composition of mature neuronal cells and glial cells.<sup>32</sup> Imaging characteristics include a solid and/or cystic component, and sometimes edema. At 7T, a 3D  $T_1$ -weighted (MP2RAGE or MPRAGE) image will better delineate the solid component because of increased image contrast. In addition, 3D  $T_2$ -weighted sequences excel at both showing the septa (walls) between and around the solid/cystic components and more precisely delineating the extent of any associated edema. Both factors are important when planning the resection margin for surgical intervention. 3D SWI or GRE  $T_2^*$ -weighted images can additionally evaluate the degree of calcification, which is another common feature of gangliogliomas.

### Polymicrogyria (Barkovich Group III)

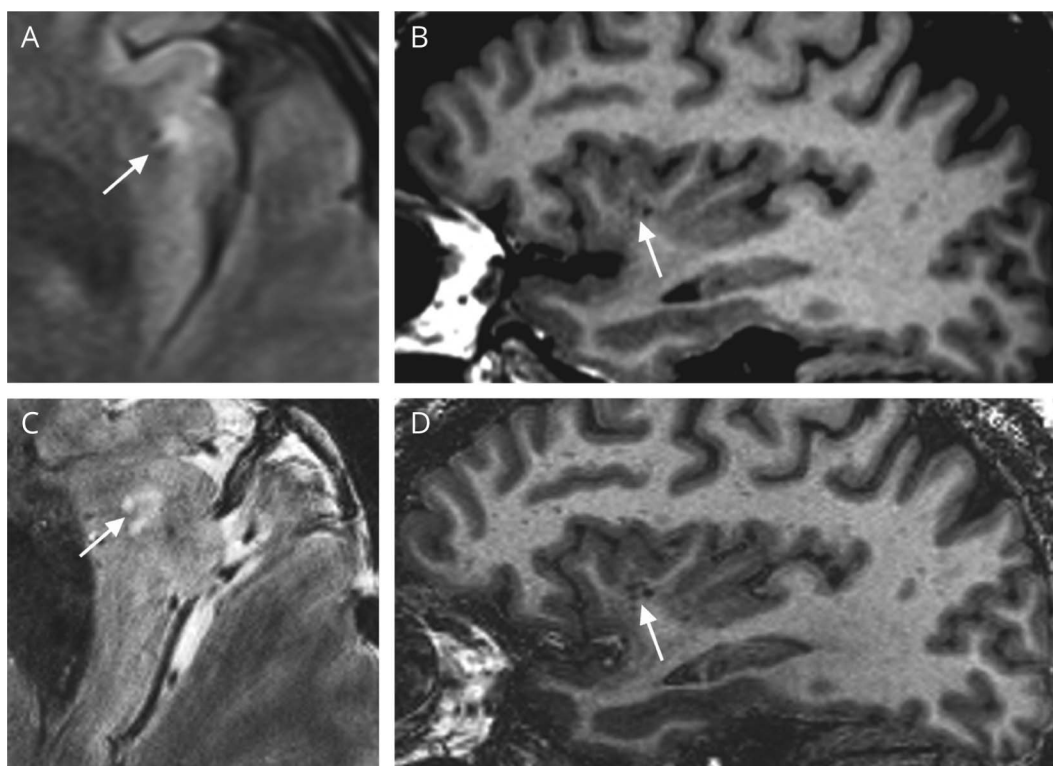
Polymicrogyria is characterized by fused small gyri separated by shallow sulci, with cortical thickness varying from thin to thick, and can be unilateral or bilateral, often with perisylvian predominance.<sup>29</sup> 3D  $T_1$ -weighted sequences (MP2RAGE or MPRAGE) are essential for assessing this type of pathology<sup>30</sup> because they permit clear delineation of lesion extent, which can guide surgical resection (figure 3). On these images, the cortex will appear hypointense and wavy at the gray and white matter interface. 3D sequences can be used to screen the whole brain for polymicrogyria, whereas 2D sequences with ultrahigh resolution can be an alternative when delineation of a known lesion is requested. In addition, 3D SWI, SWAN, and/or GRE  $T_2^*$ -weighted images enable visualization of small pial vessels, seen as thin hypointense lines in the malformed cortex and sulci with an arboriform distribution as an additional identifying feature; the cortex itself appears extra hyperintense in these sequences.<sup>6,33</sup>

### Focal Cortical Dysplasias

Typical MRI findings of focal cortical dysplasia (FCD) include blurring of the gray-white junction with or without increased cortical thickness and cortical and subcortical signal abnormality on both  $T_2$ -weighted/FLAIR and  $T_1$ -weighted sequences. Detection of FCD is generally more difficult than with other types of lesions because the above-mentioned features can be subtle and inconspicuous given the complex convexities of the neocortex. Compared with 3T, lesion conspicuity and boundaries for FCD are typically better visualized at 7T (figure 4).<sup>34</sup> 3D SWI or GRE  $T_2^*$ -weighted sequences allow visualization of intracortical signal changes (black line sign), which can improve subtyping of FCD type II.<sup>10,35</sup> Most centers rate 3D  $T_1$ -weighted and FLAIR sequences as most helpful for visualizing and diagnosing FCD because of their high image contrast at 7T; reconstructions in all 3 planes are recommended. Fluid and white matter suppression (FWMS) sequences have also been proposed to detect the transmantle sign in FCD type II.<sup>36</sup> Detection of FCDs at 7T that are completely invisible at lower field strengths seems infrequent<sup>5,6,8,13</sup>; typically, the FCD is significantly less conspicuous at 3T and therefore easily missed. In other words, 7T images make it easier for the human eye to detect these subtle signal changes. Occasionally, de novo appearance of new lesions at 7T can be seen, although often in cases of very small lesions not optimally captured by the thicker 3T slices.<sup>13</sup> We suggest scrolling carefully through slices that cover regions where a suspected FCD lesion might be located, as they might still be subtle on 7T images. Finally, 7T can be helpful in ruling out FCD-appearing normal cortex because of, among other factors, reduced partial volume effects compared with 3T (figure 5).<sup>13</sup>

### Hippocampal Sclerosis

Classic MRI features of HS are hippocampal atrophy, increased  $T_2$ -weighted/FLAIR signal intensity, and loss of normal morphology. 7T MRI excels in showing hippocampal morphology, including internal structure and surface features; 2D coronal TSE  $T_2$ -weighted and 3D  $T_1$ -weighted/FLAIR



Example of a lesion suspected to be FCD at 3T but concluded to be vascular changes after reviewing 7T images. The 3T axial FLAIR (A) and 3T sagittal T<sub>1</sub>-weighted images (B) suggested subcortical FLAIR hyperintensity (arrow on A) and gray-white matter blurring (arrow on B) of the left insular cortex, suspicious for FCD. The patient had an SEEG evaluation to explore the suspected area and other possible areas for seizure generation. The suspected area in the left insula was not involved in seizure onset. 7T T<sub>2</sub>\*-weighted GRE (C) and 7T sagittal T<sub>1</sub>-weighted images (D) revealed the lesion to be a vascular abnormality causing adjacent gliosis that mimicked the appearance of FCD, as indicated by arrows. Because of convincing evidence from the 7T images, the patient's surgical plan did not include the left insula.

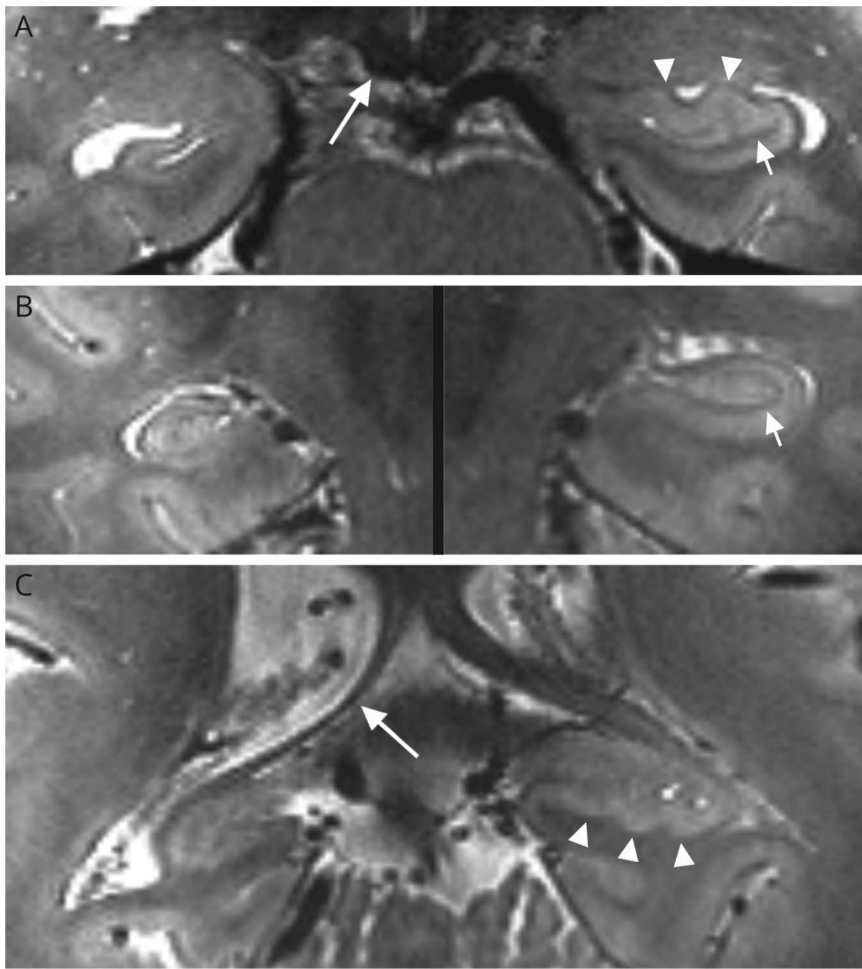
sequences are particularly suitable for this.<sup>37–39</sup> Hippocampal subfields can be more precisely delineated with training based on landmarks and surface features at 7T, including by automated segmentation methods.<sup>40–42</sup> Although evident at lower field strengths, the stratum radiatum lacunosum moleculare is more consistently identified on 7T T<sub>2</sub>-weighted images as a continuous dark band running at the internal aspect of the cornu ammonis in normal hippocampi and variably absent or indistinct in HS (figure 6). Prominent infolding can cause the dark band to appear obscured on coronal 3T images because of partial volume effects, and high-resolution images at 7T help to avoid this pitfall. The absence of digitations along the hippocampal head is another sensitive and specific finding for HS that is considerably more apparent on 7T images,<sup>43</sup> as is loss of surface undulations along the inferior aspect of the hippocampal body, which is best assessed in the sagittal plane. In addition, although subclassification of HS is not currently used for presurgical assessment, pathologic examination of subfields in postoperative tissue has been shown to provide prognostic information regarding expected surgical outcomes.<sup>44</sup> Overall, these findings suggest that preoperative detailed imaging of the entire hippocampal axis could have a significant impact on both detection and postsurgical outcome prediction.

### Vascular Malformations

The most frequent findings with 7T MRI include a higher number of small vascular malformations, particularly venous malformations, and improved visualization and characterization of cavernomas. Some lesions not visible at 1.5 or 3T can be observed with 7T, and the angioarchitecture shown with 7T is close to histopathologic findings.<sup>45,46</sup> Sequences taking advantage of the increased spatial resolution and susceptibility (SWI/SWAN) are particularly helpful in detecting these lesions and any associated (micro) hemorrhage. SWI sequences at 7T can also clearly delineate the iron-containing gliotic rim, which is important when planning sufficient surgical resection. Care must be taken, however, not to overestimate lesion size; because of the increased susceptibility effects at 7T, cavernomas and other iron-containing structures will appear larger than they really are.<sup>47</sup>

### Technical Issues Relevant For Clinical Practice

Although 7T MRI is already beneficial because of increased image contrast and spatial resolution, it is expected that its utility in epilepsy will be further expanded and optimized. Such progress, however, requires substantial engineering and



Coronal T<sub>2</sub>-weighted images at the level of the hippocampal head (A), body (B), and tail (C) show normal appearance of the left hippocampus including a continuous dark band reflecting the stratum radiatum lacunosum moleculare (arrows) and normal digitations along the head and tail (arrowheads). In contrast, the right hippocampus shows features of HS, including decreased volume, smooth outer contours, and indistinct internal architecture. Note also atrophy of the right mammillary body (long arrow in A) and fornix (long arrow in C).

scientific development to account for challenges posed by working on a UHF platform. Some of these technical challenges and possible solutions will be discussed here.

### RF Coils, RF Shimming, and Multitransmit (pTx) Systems

Transmit RF fields represent one of the predominant challenges at 7T. Higher <sup>1</sup>H Larmor frequency implies shorter RF wavelengths, translating into strong tissue contrast and signal variations. This may also lead to an increase of SAR for a given target flip angle, with a tendency to form spatially localized hot spots presenting a safety hazard. Proposed solutions can be stratified into a) existing techniques applicable to any 7T platform with single/dual transmit coils; and b) techniques relying on more advanced resources, useable only in specialized research centers with pTx systems. The use of dielectric pads, described in Use of dielectric pads, perfectly illustrates an existing technique for portable RF shimming. Other existing solutions include specialized sequence designs, for example, adiabatic pulses that are relatively insensitive to RF field variations.<sup>48,49</sup> Among advanced solutions, strategies that

use expensive amplifiers and multitransmit coils are, for example, higher-order shimming and calibration-less Universal Pulse models for pTx.<sup>50</sup> The use of the latter methods in clinical settings is pending CE/FDA approval of pTx 7T systems.

### Motion Correction

As described in Acquisition protocol and recommended setup, the high-resolution 7T MRI sequences are particularly sensitive to motion.<sup>51</sup> Even small movements or breathing will create artifacts in susceptibility sensitive techniques such as T<sub>2</sub>\*-weighted sequences or echo planar imaging (EPI).<sup>52</sup> Several retrospective and prospective correction methods have been suggested, and although promising, tracking of optical markers<sup>53</sup> or NMR-active probes<sup>54</sup> can be challenging because of the tight space in standard head coils and require a workflow impractical for clinical use. Alternatively, methods based on embedding fat-selective navigators<sup>55</sup> or phase navigators<sup>56</sup> into sequence designs have been successfully used in a variety of applications. To correct for B<sub>0</sub> variation induced by motion, a prospective correction technique that

dynamically updates shimming parameters in addition to the imaging geometry will be necessary.<sup>57</sup>

## Susceptibility Effects and Artifacts

Different tissue types cause variations in susceptibility contrast and local field inhomogeneity. Because this property scales with field strength, tissue components exhibiting increased susceptibility—such as deoxyhemoglobin, ferritin, and hemosiderin—can be more readily visualized by 7T  $T_2^*$ -weighted sequences (including SWI, quantitative susceptibility mapping, and BOLD imaging).<sup>58</sup> However, tissues with different susceptibility characteristics can also cause undesirable local inhomogeneity. To minimize these undesired effects at 7T, advanced methods for  $B_0$  shimming (including higher-order shims) are needed. As a result, on the majority of new 7T platforms, additional automated  $B_0$  shimming techniques are used; however, novel methods continue to be developed.

## Future Directions and Concluding Remarks

The increased SNR and susceptibility effects at 7T not only improve spatial resolution and image contrast but also facilitate more detailed analysis of functional and molecular aspects of tissues. Several MRI techniques that particularly benefit from these advantages, and have the potential to affect epilepsy MRI, are described below.

### Functional MRI

Functional connectivity studies using 7T fMRI have been conducted to assess network alterations, for example, by probing the fine-grained function and microstructure of hippocampal subfields in patients with temporal lobe epilepsy (TLE). Significantly different patterns of functional network asymmetry in the hippocampus and its subfield CA1 have been found between patients with TLE with and without HS using resting-state fMRI, possibly improving preoperative lesion localization.<sup>40</sup> In addition, task-related fMRI mapping, which is often used for pre-surgical planning, benefits from the increased sensitivity to the BOLD effect, improved localization, and decreased acquisition time at 7T compared with 3T.<sup>12</sup> Simultaneous EEG/fMRI recordings<sup>59</sup> and laminar fMRI using UHF<sup>60</sup> could also improve the delineation of (intra)cortical hemodynamic correlates of epileptic activity and laminar-specific brain rhythm alterations.

### MR Spectroscopy (MRS) and GluCEST

Molecular imaging at 7T takes advantage of not only the increased spatial resolution but also the increased spectral resolution of UHF. Both improve sensitivity and specificity of MRS by enabling detection of molecules that are difficult to resolve at lower field strengths, including neurotransmitters such as GABA and glutamate. Previous studies have shown that an abnormal metabolism in the surgical resection region was related to the outcome after surgery,<sup>61</sup> and although MRS could not demonstrate that metabolic characteristics can consistently lateralize the epileptogenic hippocampus, glutamine

concentrations were found to correlate with verbal memory performance in patients with TLE.<sup>62</sup> Exploring the concept of neurotransmitter brain networks using 7T MRS, another study investigated interregional GABA and glutamate associations and found that MRI-negative patients displayed an increased number of glutamate and GABA connections and increased average strength of the GABA network.<sup>63</sup> As a whole-brain alternative to MRS, CEST primed to glutamate (GluCEST) has also been used in epilepsy. One study identified increases in the glutamate concentration in the ipsilateral hippocampus in a small case series of patients with MRI-negative TLE.<sup>64</sup>

### X-Nuclei MRI

Increased sensitivity of UHF is particularly valuable for nuclei with lower abundance and SNR compared with  $^1\text{H}$ -protons. X-nuclei MRI could provide new insights into molecular and cellular dysfunctions beyond the visible lesions. For instance, sodium ( $^{23}\text{Na}$ ) MRI, with which ionic homeostasis and cell viability can be assessed in the human brain, would be a good candidate for epilepsy imaging; a previous study has shown that  $^{23}\text{Na}$  MRI is sensitive to pathologic processes related to epileptic activity.<sup>65</sup>

## Concluding Remarks

In this article, we have presented recommendations on how to set up and evaluate a 7T MRI epilepsy protocol, based on both literature and cumulative experience of the 7T Epilepsy Task Force in clinical practice and research. There are still significant technical challenges to be solved, and the field could profit from more clinical studies comparing specifically optimized (instead of clinically used) 3T protocols with 7T sequences. Nevertheless, comparative studies of epileptogenic lesions between 7T and lower fields have shown better lesion conspicuity and delineation as well as less ambiguous findings at a higher field in a clinical setting.<sup>66,67</sup> Thus, several clinical indications clearly exist for patients with epilepsy in whom a lesion is suspected and not convincingly seen at 3T or requires better characterization. Promising future directions of 7T MRI in epilepsy also include MR techniques beyond structural imaging although such novel functional and molecular methods need further clinical validation. At a time when approval for use of 7T MRI for diagnostic purposes is becoming a reality on a global level, we hope that this article provided useful guidance when setting up a 7T MRI epilepsy protocol in the clinic.

### Study Funding

No targeted funding reported.

### Disclosures

S. Jones receives travel and speaker fees from SIEMENS Healthineers. All other authors report no disclosures relevant to the manuscript. Go to [Neurology.org/N](http://Neurology.org/N) for full disclosures.

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Received by *Neurology* June 2, 2020. Accepted in final form October 29, 2020.

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