When patients are told that they will undergo an MRI and an EEG to evaluate their epilepsy, I imagine that they think of these studies as standard practice. There will be a "picture of the brain" and a look at the "brain wave activity" to assist with epilepsy diagnosis, classification, and management.

Neurologists know that the product is far from standard. Some aspects of EEG recording are relatively uniform. Development of the International 10-20 system of electrode placement and dissemination of published guidelines have led to the widespread use of standardized electrode placement and a standard number of recording channels at most centers (1). High-density EEG arrays are rarely used, even at specialized epilepsy centers. However, differences in recording quality can result from variability in the training and experience of EEG technologists, and differences in interpretation quality may vary based on the qualifications and experience of the interpreting neurologist. Several reports describe the misdiagnosis of epilepsy based on false-positive findings on EEG interpretations (2, 3). Inter-rater reliability for some EEG features can be poor, and a recent supplement of Neurology (“How not to read an EEG” [4]) was devoted to examining the sources of this variability and potential solutions. The field also lacks a uniform electronic format standard for EEG comparable to the Digital Imaging and Communications in Medicine (DICOM) standard that facilitates sharing of medical images in a common electronic format. Although some “universal EEG reader” programs are available, most clinical neurophysiologists must still cross some technical barriers created by proprietary software to share or review studies recorded elsewhere.

Although the field of MRI has solved some of these data sharing issues (studies can be electronically “pushed” into and reviewed in compatible picture archiving and communication systems (PACS)), MRI for the evaluation of epilepsy is far from a standard product. Von Oertzen and colleagues (5) highlighted this point in their insightful 2002 paper examining factors influencing detection of epileptogenic lesions. A “standard” MRI read by a “nonexpert” radiologist was much less likely to reveal a relevant epileptogenic lesion (39% detection rate) than an “expert” reader reviewing images generated using a dedicated epilepsy protocol (91%). The combination of clinical expertise (people) and optimized protocols (technology) resulted in the best outcomes. Importantly, an experienced reader reviewing

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PURPOSE: Magnetic resonance imaging (MRI) is a key technology in the presurgical evaluation of patients with epilepsy. Already at early outpatient stages it can contribute to the identification of patients who are, in the case of pharmacoresistance, good candidates for epilepsy surgery. Yet, “standard head” MRI examinations often fail to displaying therapeutically relevant epileptogenic lesions. The purpose of this study is to identify an epilepsy-specific MRI protocol, which is likewise sensitive for even small epileptogenic lesions and economical enough to be applied outside specialized epilepsy centers. METHODS: Based on a large European presurgical epilepsy program comprising 2,740 patients we identified the spectrum of common epileptogenic lesions and determine the set of MRI sequences that are required for their reliable detection. Relying on a series of small, therapeutically particularly relevant lesions we determined the required slices thickness, slice angulations, and orientations for an epilepsy-specific MRI protocol. KEY FINDINGS: Indispensable for early outpatient epilepsy specific MRI are fluid attenuated inversion recovery (FLAIR), T2-weighted, T1-weighted, and hemosiderin/calcification-sensitive sequences. Slice thickness for T2 and FLAIR must not exceed 3 mm. The T1 image should be acquired in three-dimensional technique at 1 mmisotropic voxels size. For T2 and FLAIR, at least two slice orientations each must be demanded in hippocampal angulation. We suggest no adaption to a clinical focus hypothesis. The resulting “essential 6” sequence protocol allows the detection of virtually all common epileptogenic lesion entities. SIGNIFICANCE: The creation of a broadly accepted and abundantly applied MRI protocol for epilepsy outpatients can contribute to improved and earlier identification of potential candidates for epilepsy surgery.

Our systematic analysis of MRI requirements for the detection of epileptogenic lesions can serve as basis for protocol negotiations between epileptologists, radiologists, and health care funders.
Proposal for a Magnetic Resonance Imaging Protocol

Poor quality images provided only a small incremental benefit over the inexperienced reader. MRI scans produced using a dedicated epilepsy protocol revealed focal lesions in 85% of patients who previously had “nonlesional” standard MRI. 3 Tesla (3T) MRI scans are superior to 1.5T studies in most cases (6). Thus, the technology is important, but which of the myriad sequences and processing tools are needed to optimally detect epileptogenic lesions? How can the desire to use all of the tools of modern technology be balanced against limitations of the time patients can spend in the scanner?

Wellmer and colleagues took a practical and logical approach to this problem. First, they identified and classified the epileptogenic lesions identified by MRI imaging in 2740 presurgical epilepsy patients over a span of 20 years at their center. Imaging features of the lesions, including size, were catalogued. Next, they set out to describe the sensitivity or “suitability” of each MRI sequence for detection of each of the various classes of lesions. They used a semiquantitative method, rating each sequence as “++” (high suitability, detects the specified lesion even if subtle), “+” (moderate suitability, generally suitable for detecting the given lesion, but might miss some small lesions) or “0” (poor suitability for detecting the lesion). Using this ranking system, they identified the sequence that had “++” ratings for the largest proportion of lesion types: the fluid attenuated inversion recovery (FLAIR) sequence had this rating for 9 of 16 classes of lesions and successfully identified 84.8% of lesions in their large series. Examining each next best sequence in turn using stepwise rank analysis, they arrived at an “essential six” imaging sequences that securely identified 99.4% of epileptogenic lesions (Table).

Absent from the “essential six” are contrast enhanced scans, and the authors recognized that this is an area open for debate. In their experience, contrast enhanced images did not improve the detection rate for epileptogenic lesions, but did help characterize vascular lesions and grade tumors.

Wellmer and colleagues also examined imaging parameters other than choice of pulse sequence, including slice thickness, orientation, and angulation. Epileptogenic lesions as small as 5 to 7 mm in diameter were described in their series. Small lesions, if identified, may be eminently resectable. Knowledge that that the lesion should be at least 2 to 3 voxels in one direction to be detectable led to the slice thickness recommendations in the Table, using a 1.5T scanner. Scanners with magnetic field strength <1.5T are unable to maintain adequate signal to noise ratio in thin sections; thus, the authors felt that these scanners should be considered obsolete for the evaluation of epilepsy. Higher field strength scanners, with improved signal to noise ratio, have opened additional opportunities for detection of epileptogenic lesions. The authors recommended that each sequence be performed in two planes unless it was a three dimensional (3D) sequence that could be reformatted, or unless a lesion could be validated in another orientation on a different suitable sequence. The main goal was to distinguish partial volume effects from pathology. Angulation of most scans perpendicular to the long axis of the hippocampus was found to be optimal for detecting medial temporal lesions as well as for limiting the number of voxels lost to susceptibility artifact in areas near air–tissue interfaces.

The challenge is to capture most epileptogenic lesions in a practical and time efficient manner, and Wellmer and colleagues make a compelling case for the “essential six.” This six sequence protocol does not supplant the need for the epileptologist, with knowledge of the clinical case, and the neuroradiologist, with expertise in neuroimaging, to jointly scrutinize reconstructed 3D thin slices or computer post processed images to bring an occult epileptogenic lesion to light in an individual surgical case. Nor should it arrest the progress of innovation in imaging techniques and post processing tools that facilitate identification of subtle lesions. But the work of Wellmer and colleagues makes the case for the additional scan time needed to produce sufficiently high yield imaging in all epilepsy patients undergoing MRI, and adoption of the protocol would produce images suitable for later expert review while reducing the need for repeat imaging.

by David Spencer, MD, FAAN

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**TABLE 1. Epilepsy Outpatient Specific MRI Protocol: The “Essential Six”**

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Slice Thickness</th>
<th>Cut-Plane Orientation</th>
<th>Cut-Plane Angulation</th>
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<tr>
<td>3D-T1</td>
<td>1-mm isotropic</td>
<td>3D</td>
<td>ac-pc</td>
</tr>
<tr>
<td>T2/STIR</td>
<td>≤3 mm</td>
<td>Axial</td>
<td>hc</td>
</tr>
<tr>
<td>T2/STIR</td>
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<td>Coronal</td>
<td>hc</td>
</tr>
<tr>
<td>FLAIR</td>
<td>≤3 mm</td>
<td>Axial</td>
<td>hc</td>
</tr>
<tr>
<td>FLAIR</td>
<td>≤3 mm</td>
<td>Coronal</td>
<td>hc</td>
</tr>
<tr>
<td>Hemosiderin/calcium sensitive sequence</td>
<td>≤3 mm Axial</td>
<td>hc</td>
<td></td>
</tr>
</tbody>
</table>

Above protocol is for 1.5T scanner. On 3T scanner, slice thickness can be further decreased.

Abbreviations: ac-pc, anterior commissure to posterior commissure; STIR, short T1 inversion recovery; hc, hippocampus; FLAIR, fluid attenuated inversion recovery.
References

Instructions
The purpose of this form is to provide readers of your manuscript with information about your other interests that could influence how they receive and understand your work. Each author should submit a separate form and is responsible for the accuracy and completeness of the submitted information. The form is in four parts.

1. Identifying information.
   Enter your full name. If you are NOT the main contributing author, please check the box “no” and enter the name of the main contributing author in the space that appears. Provide the requested manuscript information.

2. The work under consideration for publication.
   This section asks for information about the work that you have submitted for publication. The time frame for this reporting is that of the work itself, from the initial conception and planning to the present. The requested information is about resources that you received, either directly or indirectly (via your institution), to enable you to complete the work. Checking “No” means that you did the work without receiving any financial support from any third party – that is, the work was supported by funds from the same institution that pays your salary and that institution did not receive third-party funds with which to pay you. If you or your institution received funds from a third party to support the work, such as a government granting agency, charitable foundation or commercial sponsor, check “Yes”. Then complete the appropriate boxes to indicate the type of support and whether the payment went to you, or to your institution, or both.

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<th>Money to Your Institution*</th>
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** Use this section to provide any needed explanation.
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Place a check in the appropriate boxes in the table to indicate whether you have financial relationships (regardless of amount of compensation) with entities as described in the instructions. Use one line for each entity; add as many lines as you need by clicking the “Add” box. You should report relationships that were present during the 36 months prior to submission.

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<td>no</td>
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<td>PI for studies sponsored by NeuroPace and Upsher-Smith Laboratories. Neither I nor my institution receive direct compensation</td>
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<td>6. Payment for lectures including service on speakers bureaus</td>
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<td>13. Other (err on the side of full)</td>
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<td>editor for</td>
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</table>
No other relationships/conditions/circumstances that present a potential conflict of interest.

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David Spencer, MD

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