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Clinical Assessment of MR of the Brain in Nonsurgical Inpatients

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PURPOSE: To evaluate the effect of MR imaging of the brain on four domains of patient care: diagnosis, diagnostic workup, therapy, and prognosis. **METHODS:** Pre- and post-MR written questionnaires and oral interviews were administered to the referring clinicians of 103 medical and neurologic inpatients at a tertiary care institution. Additional information was obtained from radiologic reports and records. **RESULTS:** The study population had a diverse array of signs and symptoms and of presumptive clinical diagnoses, reflecting the breadth of disease seen at our institution. The vast majority of physicians (89%) reported that MR imaging added significant diagnostic information, playing an important role in guiding diagnostic workup (24%), planning treatment (34%), and estimating prognosis (47%). MR imaging was significantly more likely to decrease than to increase confidence in the presumptive clinical diagnosis. Thus, MR imaging may be most useful in the setting of diagnostic uncertainty. **CONCLUSION:** Our results show that MR imaging of the brain has important effects on each of the four domains of care for medical inpatients.

Index terms: Brain, magnetic resonance; Efficacy studies; Magnetic resonance, in treatment planning

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Magnetic resonance (MR) imaging is an established and accurate method for evaluating suspected abnormalities of the central nervous system (CNS). For example, MR imaging is highly accurate in detecting and evaluating congenital malformations (1, 2), metastatic disease (3, 4), primary brain tumors (5, 6), abscesses (7), hemorrhagic lesions (8, 9), vascular anomalies (10), and meningeal disease (11).

Rapid acceptance and proliferation of this new imaging technique in the early 1980s often preceded rigorous statistical evaluations of its clinical usefulness (12). While the sensitivity of brain MR imaging has been assessed for specific medical issues (as described above), its ultimate effect on decisions regarding patient care for the broad spectrum of problems to which it is currently applied has not been fully explored. In this era of capitation and prospective payment, questions will increasingly be raised regarding the effect of MR technology on the diagnosis, workup, and ultimately the outcome of patients for whom it is used. Accordingly, a study was designed to address these issues and to assess the effect of MR imaging on the clinical care of patients (J. Lee, C. Tanio, C. Langlotz, B. Landon, C. Russo, K. Schulman, "The Clinical Utility of Magnetic Resonance Imaging of the Head: A Prospective Study," *Clin Res* 1993;41:543A, abstract). Specifically, we assessed the impact of MR imaging on four domains of patient care: diagnosis, diagnostic workup, therapeutic management, and prognosis. We report results that estimate the impact of MR imaging on the reasoning of referring clinicians regarding suspected disease of the CNS.

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Subjects and Methods

Our study population consisted of medical and neurologic inpatients who were scheduled to undergo MR imaging of the brain at a tertiary-care university-affiliated institution. Patients were excluded if they had contraindications to MR imaging, if they did not complete a diagnostic MR study, if they were not cared for primarily by the medicine or neurologic service at the time the study was performed, or if their referring physician was unwilling to participate in the study. Approximately 10% of potential study patients were excluded by these criteria. Because we wanted to focus our analysis on a patient population with a high prevalence of disease, outpatients were not considered for our sample.

A part-time research assistant was able prospectively to identify and accrue 113 inpatients (after exclusions) over a period of 9 months. This 9-month period was preset as the duration of a pilot study for a larger, multiinstitutional study currently underway. Post-MR interviews could not be completed for 10 patients, yielding a study sample of 103 patients. All MR examinations were performed at 1.5 T and were monitored by a neuroradiology fellow. At our institution, an MR examination of the brain is routinely allocated 50 minutes of magnet time. Our standard MR protocol includes sagittal T1-weighted images and axial fast spin-echo proton density–weighted and T2-weighted images, followed by axial contrast-enhanced T1-weighted images, when appropriate. The protocol is often modified or tailored to take advantage of the multiplanar capabilities of MR imaging or to acquire a multiplanar gradient susceptibility sequence. Additional sequences are obtained at the discretion of the monitoring physician.

Data Collection

For each patient, referring clinicians were asked to complete a brief pre-MR written questionnaire, and to participate in post-MR telephone interviews. MR imaging findings were obtained from a review of radiologic reports. Collected data included the number and type of previous brain imaging studies, the indications for the present examination, and any suspected or established medical diagnoses.

During the pre-MR interview, referring physicians were asked to list their presumptive clinical diagnosis and to grade its probability on a scale of 1 to 10, with 10 signifying absolute certainty. We refer to this quantity as the pre-MR probability of the presumptive clinical diagnosis.

In the post-MR questionnaire, referring clinicians were again asked to estimate their subjective probability of the presumptive clinical diagnosis (using the same scale). We express these probabilities as percentages by multiplying the reported probability rating by 10. Thus, these questions were designed to assess the change in subjective probability of the presumptive diagnosis resulting from the use of brain MR imaging.

A second set of post-MR questions was designed to assess the reported role that MR imaging played in influencing four domains of patient care: diagnosis, diagnostic workup, therapy, and prognostic assessment of the patients. The initial question in each category assessed whether MR imaging affected the variable being considered. For example, with regard to diagnostic workup, the initial question was whether the MR affected the diagnostic workup. (*Diagnostic workup* signified the extent to which the MR study influenced the need for additional diagnostic tests.) Each initial question was followed by a series of questions designed to elicit the specific means by which the process may have been affected by the results of MR imaging. This process was repeated for each of the four clinical domains studied (see the Appendix).

Data Analysis

Univariate comparisons of categorical variables were conducted by using the χ^2 statistic. Continuous measures were compared by using Student's t test. Nonparametric techniques were used when appropriate. The Yates correction for continuity was used when applicable.

The overall change in reported probability in the presumptive clinical diagnosis was analyzed by using the likelihood ratio (λ), according to the following equations:

> $\lambda(D)$ = posttest odds of D/pretest odds of D, where D = the presumptive clinical diagnosis and odds of D = probability that D is correct divided by the probability that D is incorrect.

The likelihood ratio (λ), as defined above, is a measure of the strength and direction of a change in probability that would result from new information, such as the results of a diagnostic test. The likelihood ratio is multiplied by the prior odds of the disease to result in a posttest odds of the disease. This measure has been used widely in the radiologic literature (13). This equation can be transformed to reflect an analogous measure, the log-likelihood ratio, which is defined as the log(λ). The log-likelihood ratio represents an additive measure of change in probability, as follows:

$$\log(\text{posttest odds of } D) = \log(\text{pretest odds of } D + \log[\lambda(D]).$$

Values of the log-likelihood ratio less than zero indicate that MR imaging provides evidence against the presumptive diagnosis. Likewise, log-likelihood ratios greater than zero show that MR imaging results increased the probability of the presumptive diagnosis. Because the log-likelihood ratio is a logarithmic scale, each unit represents a 10-fold change in the odds of the diagnosis.

To illustrate the calculation and the use of the log-likelihood ratio, consider the following example. A patient presents with signs of a CNS infection. The clinician's reported pre-MR probability of this presumptive diagnosis is 0.75. A brain MR study shows findings suggestive of viral encephalitis. The clinician's post-MR probability of CNS infection is 0.95. Thus, the pretest odds are 0.75/0.25, or

3 (sometimes called "three-to-one odds"). Posttest odds are 0.95/0.05, or 19. The likelihood ratio, λ, for brain MR imaging in this case is 19/3, or 6.3, indicating the degree to which the MR imaging results increased the probability of the diagnosis of CNS infection. The log-likelihood ratio is simply the log of λ, which in this case is log(6.3), or 0.8.

Results

Patient Characteristics

In our sample, the indications for brain MR imaging were quite varied. The single most frequent reason for obtaining an MR study was a change in neurologic examination (40%). The second most common indication listed was a change in cognitive ability (19%) (see Table 1).

As would be expected in inpatients who often have complex clinical histories and chronic neurologic conditions, a high percentage of patients had undergone previous neurologic imaging. Over half had previously undergone computed tomographic examination of the brain, and approximately one in five had undergone one or more previous MR examinations of the brain (see Table 2).

The presumptive clinical diagnoses were as varied as the sample studied (Table 3). Ischemic stroke and tumor, taken together, accounted for slightly more than 50% of the presumptive clinical diagnoses. Infection, hemorrhage, and vasculitis together accounted for an additional 20%.

Effect on the Presumptive Diagnosis

We were interested in the effect of MR imaging on the reported probability of the presumptive clinical diagnosis. As shown in Figure 1, MR imaging significantly improved clinicians' ability to discriminate between patients with and without disease by tending to move the probability of the presumptive diagnosis from uncertainty (ie, at probability between 25% and 75%) toward certainty (ie, at probability less than 25% or greater than 75%) ($P = .04$).

In 78 (76%) of cases, MR imaging resulted in a change in the probability of the presumptive diagnosis. Figure 2 shows the distribution of nonzero log-likelihood ratios for each MR examination. The examination resulted in a log-likelihood ratio of greater than 2.0 or less than −2.0 in 27 (26%) of 103 cases.

TABLE 1: Indications for MR imaging of the head for the 103 patients in our study sample

Indication	Percentage
Change in neurologic examination	40
Change in cognitive ability	19
Follow-up of a previous study	15
Headache	10
Seizure	7
Other	9

TABLE 2: Previous studies undergone by the 103 patients in our study sample

Previous Study	Percentage*
Computed tomography	54
Lumbar puncture	21
Magnetic resonance imaging	19
Electroencephalogram	10
Doppler examination of the carotid arteries	4
Carotid and/or cerebral angiography	4
Positron emission tomography	1

* Total exceeds 100% because some patients had more than one previous study.

TABLE 3: The most common presumptive clinical diagnoses among our study population

Presumptive Clinical Diagnosis	Percentage
Ischemic stroke	27
Tumor	26
Infection	10
Hemorrhage	6
Vasculitis	4
Other	28

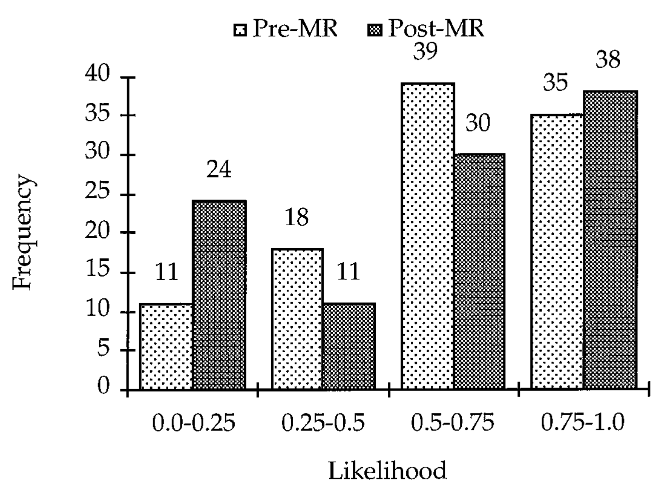

Fig 1. Pre- and post-MR reported probability of the presumptive diagnoses, grouped according to probability (n = 103).

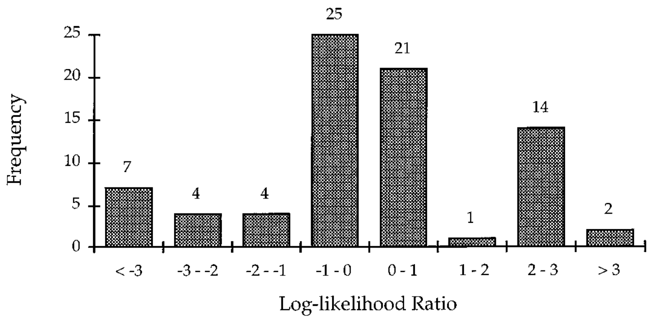

Fig 2. Frequency plot of the nonzero log-likelihood ratios (n = 78). Each unit of log-likelihood ratio represents a 10-fold change in the odds of the presumptive diagnosis. Negative values indicate cases in which reported posttest probability was less than pretest probability; positive values indicate the opposite. Thus, a likelihood ratio of −2 corresponds to a 100-fold decrease in the odds of the presumptive diagnosis.

TABLE 4: Most common reasons that the brain MR examination was thought to add diagnostic information

Additional Diagnostic Information	Percentage*
Ruled out a possible diagnosis	56
Confirmed the presumptive diagnosis	27
Determined the anatomic extent of disease	11
Uncovered an unsuspected problem	7
Resolved previously conflicting diagnostic results	0

* Total exceeds 100% because respondents could select more than one reason.

TABLE 5: Reported effect of brain MR imaging on subsequent diagnostic workup

Effect on Diagnostic Workup	Percentage
Prevented the need for additional diagnostic tests	17
Indicated the need for additional examinations of the brain	12
Suggested the need for additional consultation	1
Suggested the need for examination of another organ system	0

Note.—Respondents could select more than one effect.

Reported Effect on Subsequent Patient Care

Responses to our specific questions to referring physicians regarding the effect of MR findings on various domains of patient care, including diagnosis, workup, treatment, and prognosis, are as follows.

Physicians reported that MR imaging added diagnostic information in 89% of cases. No differences were detected in the ability of MR imaging to add additional information among various levels of pre-MR probability of the presumptive diagnosis. Table 4 shows the primary reasons for the additional diagnostic information.

TABLE 6: Reported effect of brain MR imaging on subsequent diagnostic workup, according to pre-MR probability of presumptive diagnosis (an effect was more likely at intermediate levels of probability)

Effect on Diagnostic Workup?	Pre-MR Probability of Presumptive Diagnosis, n (%)				
	0–25%	26–50%	51–75%	76–100%	Total
No	10 (13)	10 (13)	27 (34)	32 (41)	**79 (100)**
Yes	1 (4)	8 (33)	12 (50)	3 (13)	**24 (100)**
Total	**11 (11)**	**18 (17)**	**39 (38)**	**35 (34)**	**103 (100)**

TABLE 7: Reported effect of brain MR imaging on subsequent therapy

Effect on Therapy	Percentage, %
Changed the current therapeutic plan	13
Confirmed the current therapeutic plan	12
Resulted in withdrawal of therapy	5
Altered medications or doses	4
Other change in therapy	3

Note.—Respondents could select more than one effect.

Twenty-four percent of clinicians reported that MR imaging results would play a role in the subsequent diagnostic workup of the patient. Table 5 shows the specific reported effects on diagnostic workup. In most cases, the MR examination had an effect by completing the diagnostic workup or by suggesting an additional examination of the brain.

Table 6 shows the percentage of cases in which the MR examination had an effect on diagnostic workup, categorized according to the pre-MR probability of the presumptive diagnosis. Those patients whose presumptive diagnoses were thought to be at the extremes of probability (<25% or >75%) were less likely to have their workup affected by the results of MR imaging than were those whose presumptive diagnosis was thought to be in the uncertain range (between 25% and 75%) (16% versus 54%, $P < .01$).

About one third (34%) of referring physicians believed the MR imaging results caused a significant change in the patient's therapy. This percentage did not vary significantly according to pre-MR probability. Table 7 shows the results of follow-up questions designed to pinpoint the exact nature of the change.

Finally, we found that 47% of clinicians reported a significant change in their patients' prognoses on the basis of the brain MR imaging results. This effect was reported with significantly greater frequency when the pretest probability of disease was greater than 50% (28% versus 55%, $P = .02$).

Discussion

This study provides an example of the types of evaluations that can be made to assess the role of MR imaging in the clinical treatment of patients. We elicited presumptive diagnoses before the MR examination under study. These diagnoses were often made, in part, on the basis of the responding physicians' assessment of the results of prior diagnostic imaging.

Diagnostic tests are thought to be most useful when clinical uncertainty is highest (ie, at intermediate probabilities) (14). Our study supported this theoretical benefit of diagnostic tests, both through a shift toward diagnostic certainty and through the effect of MR imaging results on diagnostic management and confirmation of the prognosis. MR results in this study significantly improved physicians' ability to discriminate between patients with and without disease. Posttest probabilities of disease were more likely to approach certainty (above 75% or below 25%) than were pretest estimates. Furthermore, diagnostic workup was more likely to be affected by the MR examination in patients with uncertain diagnoses (probability of 25% to 75%) than in patients with certain diagnoses (above 75% or below 25%).

The likelihood ratio is a helpful method to characterize the usefulness of diagnostic clinical information. Thus, our analysis of likelihood ratios provides a benchmark for the diagnostic information obtained from brain MR imaging. Our estimates of likelihood ratios were conservative, since the likelihood ratio may underestimate the value of testing when there are more than two diseases under consideration (such as when the brain MR study resulted in the diagnosis of an unsuspected problem). However, we found that our responding clinicians typically were entertaining only one or two likely hypotheses, and we believe this bias was small. While approximation methods are available to compute a lower boundary on the likelihood ratio in this situation (15), we believed that tabulating the responses to questions that characterized the nature of the diagnostic information was more clinically relevant (see Table 4).

MR imaging of the brain affected diagnosis more than it did workup, therapy, or prognosis. This pattern is not surprising, since few of the neurologic diseases that afflict an inpatient population have adequate therapies.

Prognosis was affected most significantly at higher levels of pre-MR confidence. Thus, it appears that patients in whom there is a high probability that the presumptive diagnosis is accurate (ie, who have a known or preexisting disease) are more likely to have their prognosis affected by the results of an MR examination.

Our study is the latest in a series of investigations that have assessed the effect of MR imaging on the diagnosis and subsequent treatment of patients. Our study showed that MR imaging ruled out a diagnosis or suggested a new one in 63% of cases. The MR examination confirmed the existence of or determined the extent of known disease in an additional 38%. Changes in diagnostic workup and therapy planning occurred 24% and 34% of the time, respectively. Physicians reported that MR imaging had an effect on prognosis 47% of the time. Szczepura et al (16) performed a similar study with 782 inpatients in 1989, with subsequent follow-up of 158 cases. They found that MR imaging changed the principal diagnosis in 20% of cases and increased confidence in the diagnosis in an additional 30%. Referring physicians made management changes in 27% of cases, and reported increased confidence in planned management in an additional 29% of cases. Their experimental design did not address changes in prognosis, but they found no improvement in patients' quality of life at 6 months. Dixon et al (17) performed a similar study with 200 patients referred for imaging of the brain (100 patients) and spine (100 patients). They found that MR imaging altered the leading diagnosis in 21% of cases. Referring physicians reported increased confidence in the diagnosis in 54% of cases. In an analogous study conducted a decade ago, Franken et al (18) showed that MR imaging refined or changed the suspected diagnosis in 16% of 189 patients, increased confidence in the existing diagnosis in an additional 34%, and resulted in altered therapy in over half the cases.

These studies represent important benchmarks for brain MR imaging, despite the fact that they were conducted well before the advent of many of the recent innovations in MR technique, such as fast imaging, MR angiography,

TABLE 8: Comparison of the results of the current study with three prior studies done with similar methods

Study	No. of Patients	Setting	Percentage of Reported Effect on:				
			Change in Diagnosis	Diagnostic Confidence	Workup	Therapy	Prognosis
Present	103	Brain/inpatients	63	38	24	34	47
Szczepura, 1991 (16)	782	Neurosciences	20	30	. . .	27	. . .
Dixon, 1991 (17)	200	Brain/spine	21	54	. . .	62	. . .
Franken, 1986 (18)	145	Brain	16	34	. . .	55	37

and magnetization transfer imaging. The passage of time, the evolution of technology, and the confidence with which radiologists interpret MR findings may, in part, explain the stronger effect on diagnosis and treatment seen in our study than that observed by these other investigators (see Table 8 for comparison).

Our study is unique among this group of studies because it (*a*) quantified the magnitude of change in probability using the likelihood ratio, (*b*) assessed the impact of MR imaging according to the prior probability of disease, and (*c*) measured the specific reported impact of MR imaging on all four domains of patient care: diagnosis, diagnostic workup, therapy, and prognosis.

We had insufficient data with which to draw meaningful conclusions about potential differences among referring neurologists and referring internists. Internists, because they see a "primary care" population, may refer patients with a lower prevalence of disease overall. Since these patients are likely to have normal studies that make only minor contributions to patient workup, treatment, and prognosis, brain MR imaging may ultimately show a smaller effect in this group. On the other hand, neurologists, because of their specialty skills, may similarly report that brain MR imaging makes only a minor contribution relative to their overall clinical assessments. A larger study sample would be required to answer these questions with confidence.

Our results were also affected by our choice of study population: we restricted our sample exclusively to medical and neurologic inpatients, who are more likely to have visible pathologic conditions and to be in the acute phase of their illness. This sampling strategy limited the generalizability of our results to other clinical settings and maximized the observable effect on diagnosis.

Fryback and Thornbury divided the technology assessment process for diagnostic imaging into several stages (19): 1) technical efficacy (is image resolution adequate to demonstrate findings?) 2) diagnostic accuracy efficacy (do technical measures, such as areas under the receiver operating characteristic curve, demonstrate incremental accuracy from the technology?) 3) diagnostic thinking efficacy (how much diagnostic information is provided by the imaging technology and to which groups of patients?) 4) therapeutic efficacy (is patient treatment influenced by imaging results?) 5) patient outcome efficacy (how does the technology compare with others in terms of patient outcome?) and 6) societal efficacy (would widespread guidelines for implementation of the technology benefit society?). Most studies to date have shown the capabilities of MR imaging in regard to stages 1 and 2. Our results, like those of others, show effects at stages 3 and 4. However, these findings need to be explored further, and stages 5 and 6 remain largely untested at present. Data of the kind presented here can be helpful in designing cost-effectiveness studies of brain MR imaging in specific clinical settings.

In conclusion, we have shown that in a diverse tertiary-care inpatient population, MR imaging had a significant impact on the four domains of patient care tested: diagnosis, diagnostic workup, therapy, and prognosis. The vast majority of referring physicians (89%) thought that brain MR imaging added significant diagnostic information, even though over half the patients studied had undergone previous cross-sectional imaging of the brain. Referring clinicians reported a significant effect on prognosis in almost half the cases (47%), particularly when the pretest probability of disease was high. MR imaging played a smaller role in directing further diagnostic testing (24%) and therapy (34%), primarily for patients in whom the pretest probability of disease was intermediate. Thus, our study provides indirect evidence for the societal efficacy of brain MR imaging in inpatients, and shows that such efficacy is most likely among patients with intermediate to high pretest probability of disease.

Appendix

Case Report Form: Pre-Study Questionnaire

HUP #: ________________________________ Date of MRI:__/__/__
Location: ________________________________ __ Medicine __ Neurology
Physician: ________________________________ Beeper #: ______________

Studies and pertinent findings done this admission before MRI for this problem:

________ previous MRI; if more than one, this is the _______ (e.g. 2nd, 3rd, etc.) MRI
________ CT scan, in E.R. __ or on floor __ __________ Doppler
________ EEG __________ angiogram
________ lumbar puncture __________ PET/SPECT scan
________ other ________________________________

Indication for study (check one that best applies):

________ change in cognitive ability __________ headache
________ cranial nerve palsy/dizziness/vertigo __________ seizure disorder
________ abnormal neuro exam __________ F/U lesion seen on CT
________ other ________________________________

Please rank the most likely diagnoses at the time test was ordered:

________ tumor __________ stroke
________ vasculitis __________ hemorrhage
________ vascular malformation __________ TIA/RIND
________ primary neurologic disease __________ infection
________ other

Certainty of presumptive diagnosis (house staff opinion):

Unlikely Likely
0----1----2----3----4----5----6----7----8----9----10

Is there a diagnosis other than the presumptive diagnosis you are trying to rule out or exclude with this study? ______ yes ______ no

If yes, what diagnosis? ________________________________ and the certainty:

Unlikely Likely
0----1----2----3----4----5----6----7----8----9----10

Does this patient have AIDS? _______ yes _______ no

Which of the following is most responsible for ordering the test? (check one only)

________ resident __________ intern
________ attending __________ fellow
________ requested by consult service
________ required by protocol for investigational research

What do you expect the primary result of this study to be?
(check as many as apply, leave blank if inappropriate)

________ MRI will confirm the presumptive diagnosis
________ MRI will rule out a diagnosis
________ MRI will indicate if further diagnostic work-up is required
________ MRI will delineate the anatomy involved by the disease
________ MRI will confirm the current therapeutic plan
________ MRI will result in a change in the current therapeutic plan
________ MRI will clarify the prognosis of the patient

If this MRI study were not available, how would you proceed?

________ obtain CT
________ obtain other diagnostic study
________ diagnose, treat, and make prognosis presumptively (for highest ranked diagnosis above)
________ make no changes in current diagnosis, treatment, or prognosis

Case Report Form: Post-Study Interview

Date of interview: __/__/__ Interviewer: ________________________________
HUP #: ____ Date of MRI:__/__/__
Physician: ____ Beeper #: ______________
Rank: _______ Attending _______ Fellow _______ Resident
_______ Intern _______ Extern

Post-study diagnosis
____

Pre-study diagnosis (from MRI request form)
____

Did the MRI result in a change in the diagnosis? _______ yes _______ no
Certainty of presumptive diagnosis
Unlikely Likely
0−−−−1−−−−2−−−−3−−−−4−−−−5−−−−6−−−−7−−−−8−−−−9−−−−10
Certainty of post-study diagnosis
Unlikely Likely
0−−−−1−−−−2−−−−3−−−−4−−−−5−−−−6−−−−7−−−−8−−−−9−−−−10

Did this study add other diagnostic information?
________ confirm suspected diagnosis
________ result in the diagnosis of unsuspected problem
________ resolve conflicting diagnostic results
________ determine extent of anatomy affected by disease
________ ruled out a diagnosis, if so, what dx:
________ other ____

Was there a significant change in diagnostic management? _______ yes _______ no
If so, check those that apply:
________ was another diagnostic evaluation of the head required as a result of the MRI?
if so, what: _____________________________________
________ was diagnostic evaluation of another organ system required as a result of the MRI?
if so, what: _____________________________________
________ was another consultation required as a result of the MRI?
________ did the MRI prevent the need for pursuing other diagnostic tests?
________ other ____

Was there a significant change in therapeutic management? _______ yes _______ no
If so, check those that apply:
________ did the MRI confirm current therapeutic management?
________ were medications altered as a result of the MRI?
________ were other procedures recommended as a result of the MRI?
________ were treatments withdrawn as a result of the MRI?
________ other ____

Was there a significant change in prognosis? _______ yes _______ no
If so, check those that apply:
________ confirm prognosis
________ change prognosis
________ confirm normal prognosis based on absence of significant findings
________ other ____

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Please see the Commentary on page 1255 in this issue.