Contrast-enhanced FLAIR Versus Contrast-enhanced T1-Weighted Sequence of Magnetic Resonance Imaging for the Evaluation of Leptomeningeal Disease: Which one is Better?

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Abstract
Objectives: The purpose of this study was to compare the sensitivity of gadolinium-enhanced T1-weighted magnetic resonance imaging (MRI) and gadolinium-enhanced FLAIR (fluid attenuated inversion recovery) MRI in detecting leptomeningeal carcinomatosis.

Method: In all patients, all routine brain imaging sequences were performed, including T1- and T2-weighted axial and coronal unenhanced spin-echo sequences, FLAIR axial unenhanced sequence, as well as contrast-enhanced FLAIR, and T1-weighted sequences. These sequences were used in the study group consisted of 12 patients (5 male, 7 female, age range: 51-82; 4 breast carcinoma, 4 lung carcinoma, 2 melanoma, 2 lymphoma) with proven leptomeningeal carcinomatosis disease. Comparisons were made particularly between enhanced T1- and FLAIR-enhanced images.

Results: In all 12 patients with clinically proven leptomeningeal disease (10 metastatic carcinoma, 2 lymphoma), contrast-enhanced FLAIR sequence demonstrated better and more extensive and conspicuous enhancement when compared to contrast-enhanced T1 sequence.

Discussion: Gadolinium-enhanced FLAIR images were superior to gadolinium-enhanced T1 sequences for detecting pathologic leptomeninges.

Key words: Magnetic resonance, FLAIR, cerebrospinal fluid, leptomeninges

Conflict of interest: The authors reported no conflict of interest related to this article.

Introduction
In classical medicine, the most specific but relatively invasive method for the diagnosis of meningeal disease (either carcinomatosis or infection) is cytologic testing of cerebrospinal fluid (CSF) by lumbar puncture followed by laboratory microscopic evaluation. Even cytologic evaluation of CSF sometimes reveals false negative or inconclusive results.
gadolinium (1,2). However, several other researchers had better results with FLAIR sequence with gadolinium rather than T1 (3,4).

The FLAIR sequence is essentially an inversion recovery technique that uses inversion time to null signals from CSF. It has proven to be useful for diagnosing subarachnoid hemorrhage, as well as infectious and neoplastic subarachnoid space diseases (5).

Hyperintense signal compared to normal brain tissue and normal CSF highlights the finding because of T1 shortening and T2 elongation caused by blood degradation products. However, FLAIR sequence without contrast administration may not demonstrate the presence of leptomeningeal abnormality. Also anesthetic substances and inhaled oxygen may manifest increased signal intensity in the meninges with unenhanced FLAIR sequence.

Therefore, as suggested in the literature, non-contrast FLAIR images should be performed and compared with post-contrast FLAIR in all cases when investigation of leptomeningeal disease is the main purpose (1,2,3,4). Tsuchiya et al. suggested that when the sulci or cisterns show areas of hyperintensity on unenhanced FLAIR images in patients with cancer, meningeal carcinomatosis is strongly suspected and contrast-enhanced FLAIR images should
be obtained (4). Contrast administration may indicate the disease even if non-contrast images show no significant abnormality.

The aim of this study was to compare the sensitivity of gadolinium-enhanced T1-weighted MRI and gadolinium-enhanced FLAIR MR imaging in detecting leptomeningeal carcinomatosis.

**Method**

This study was approved by the Institutional Ethics Committee. Between April 2006 and April 2008, twelve patients (5 male, 7 female, age range: 51-82) with suspected leptomeningeal disease were evaluated with gadolinium-enhanced FLAIR and also by gadolinium-enhanced T1-weighted MRI images to compare these sequences for detecting leptomeningeal disease. The patients with leptomeningeal carcinomatosis had the following primary malignancies: breast carcinoma (4), melanoma (2), lung carcinoma (4), and lymphoma (2).

The diagnosis of meningeal carcinomatosis was based on the clinical symptoms and positive CSF cytology. Equivocal results were excluded from the study.

In our study, in one patient CSF analysis was negative or inconclusive, thus, meningeal biopsy was performed which was positive for leptomeningeal carcinomatosis.

**Figure 4a.** Lung carcinoma metastasis. T1 W enhanced image only shows parenchymal lesion on left temporal lobe. No leptomeningeal abnormality was seen

**Figure 4b.** FLAIR with contrast demonstrates diffuse leptomeningeal carcinomatosis. Abnormal leptomeningeal enhancement as well as parenchymal metastasis

**Figure 5a.** Patient with melanoma. T1 W enhanced image shows parenchymal round metastatic small lesions on left frontal lobe and right deep temporal lobe but not leptomeningeal disease

**Figure 5b.** FLAIR with contrast shows abnormal enhancement bilaterally in sylvian fissure regions and in leptomeningeal carcinomatosis as well

**Figure 6a.** Patient with lymphoma. T1 enhanced image is unremarkable

**Figure 6b.** Enhanced FLAIR image demonstrates abnormal leptomeningeal enhancement within the sulci overlying the left frontal lobe, only apparent on FLAIR with contrast image. Patient has lymphoma and leptomeningeal carcinomatosis
Neuroradiologists blindly evaluated each of the 12 cases. Each stated whether pathological leptomeningeal enhancement was present on a given case or not.

The parameters of the FLAIR sequence were arranged for maximizing the T1 signal and detecting leptomeningeal enhancement.

**Scanning Parameters**

All MR imaging examinations were performed on a 1.5 T superconducting system (General Electric Medical Systems, Milwaukee, WI).

For each patient, axial plane, unenhanced and enhanced T2-weighted FLAIR with flip angle 90, TR/TE range 9000/130-150 were obtained respectively. Slice thickness was 5 mm, slice interval 1 mm. Inversion time was 2000, number of excitations was 1, matrix was 256x160, and field of view was 22 cm. Parameters of the FLAIR sequence were arranged for maximizing the T1 signal and detecting leptomeningeal enhancement.

T1-weighted spin echo: Axial plane, flip angle 90, TR/TE 450/10-20. Slice thickness 5 mm, slice interval 1 mm. Number of excitations 2, matrix 256x224, field of view 22 cm.

T1 FLAIR: Flip angle 90, TR/TE 2180/8-20. Slice thickness 5 mm, slice interval 1 mm. Inversion time 750, number of excitations 2, matrix 256x224, field of view 22 cm.


gadopentate dimeglumine (Magnevist; Berlex Laboratories, Wayne, NJ) was administered at 0.1mmol/kg body weight, a total of approximately 15 to 30 ml.

FLAIR sequence is well accepted as a sensitive technique for the detection of subarachnoid hemorrhage (6).

In our 12-patient series, we performed both T1 first or FLAIR first studies and evaluated most of the patients with MRI more than once. Superiority of FLAIR did not differ depending upon which sequence was performed first. Since the meninges do not have a blood-brain barrier, the order of timing of the MR images after the gadolinium enhancement is likely not an important factor.

Mathews et al. suggested that it made no difference which enhanced sequence was done first (7). Griffiths et al. obtained FLAIR sequence prior to T1 and demonstrated equal or better enhancement with FLAIR (3).

**Results**

In all patients, all routine brain imaging sequences were performed, including T1- and T2-weighted axial and coronal unenhanced spin-echo sequences, FLAIR axial unenhanced sequence, as well as contrast-enhanced FLAIR, and T1-weighted sequences.

All cases demonstrated (and neuroradiologist agreed) more conspicuous enhancement with the FLAIR T2-weighted sequence compared to T1-weighted MR sequence (spin echo T1 or FLAIR T1).

Contrast-enhanced T1 and FLAIR sequences were assessed independently. There were no significant discrepancies between reviewers’ final decisions, and they agreed with full consensus regarding the presence or absence of leptomeningeal enhancement or superiority of FLAIR or T1 with gadolinium enhancement to detect leptomeningeal disease.

Abnormal meningeal enhancement appeared either equivalent or was better seen with FLAIR or was only detected with FLAIR imaging.

Enhanced FLAIR T2-weighted imaging generally demonstrated better sulcal contrast enhancement compared to enhanced FLAIR T1 and enhanced spin echo T1 sequences.

The patients with leptomeningeal carcinomatosis and imaging findings are summarized in Table 1. In all cases, FLAIR T2 sequences without and with gadolinum and FLAIR T1 sequence with gadolinium were used. In most cases spin-echo T1-weighted sequence with gadolinium was also used. Results of T1 spin-echo and enhanced T1 FLAIR sequence images were similar. 11 of 12 patients had more than one follow-up MRI examination.

Figure 1a, b: A 50-year-old female had known diagnosis of breast carcinoma. Slight enhancement of cerebellar sulci is only seen with MRI FLAIR sequence contrast-enhanced axial image, but not with T1-weighted contrast-enhanced sequence. CSF was positive for adenocarcinoma metastasis. The diagnosis was leptomeningeal metastasis of breast carcinoma.

Figure 2a, b: A 51-year-old male patient presented with melanoma. Extensive ependymal and ventricular abnormal enhancement on FLAIR images with contrast is consistent with leptomeningeal metastasis. T1-weighted enhanced images demonstrated ependymal enhancement but did not show leptomeningeal metastasis. CSF was negative for malignancy. Meningeal biopsies from the enhancing regions were negative. Due to imaging findings and a high clinical suspicion, ventricular biopsy was performed, which revealed melanoma metastasis.

Figure 3a, b: An 81-year-old male patient had lung carcinoma. Abnormal leptomeningeal enhancement within the right central sulcus and several adjacent sulci are seen on FLAIR images with contrast. T1 with contrast does not show any abnormal enhancement.

Differential diagnosis is inflammatory, infectious or neoplastic meningeal process. CSF was positive for malignancy and diagnosis of leptomeningeal carcinomatosis was made.

Figure 4a, b: A 58-year-old female patient was diagnosed with lung carcinoma. Marked pial enhancement in both cerebral hemispheres is seen on FLAIR with contrast. However, abnormal enhancement is not appreciated with T1 contrast. CSF was positive for malignancy. The diagnosis was leptomeningeal carcinomatosis from lung carcinoma metastasis. Left parenchymal temporal lobe enhancing mass lesion is also seen with both sequences.

Figure 5a, b: A 56-year-old female had a known history of melanoma. Extensive abnormal subarachnoid space enhancement is seen on FLAIR but not with T1 contrast image. Parenchymal small round metastatic enhancing lesions on left frontal lobe and right deep temporal lobe are better seen on T1WI contrast image rather than FLAIR. CSF was positive for malignancy, evidence of leptomeningeal carcinomatosis.

Figure 6a, b: A 75-year-old female had lymphoma. Abnormal leptomeningeal enhancement within the sulci overlying the left frontal lobe is only apparent on FLAIR with contrast. T1 images with contrast are unremarkable.

Table 1 lists the patients with leptomeningeal carcinomatosis, their primary tumor and imaging findings.

**Discussion**

FLAIR sequence without contrast did not illustrate the leptomeningeal pathology in most cases in our patients. FLAIR sequence is well accepted as a sensitive technique for the
detection of subarachnoid hemorrhage (6). Hyperintense signal compared to brain and normal CSF highlights this finding because of T1 shortening and T2 elongation caused by blood degradation products (6). Tsuchiya et al. speculated that tumor cells in meningeal carcinomatosis induce an increase in CSF proteins, which is a typical laboratory finding (4). Therefore, increase in CSF proteins produces a change that is similar to that of seen in subarachnoid hemorrhage on FLAIR sequence images (4). Tsuchiya et al. suggested that when the sulci or cisterns show areas of hyperintensity on unenhanced FLAIR images in patients with cancer, meningeal carcinomatosis is strongly suspected and contrast-enhanced FLAIR images should be obtained. They also claimed that since they performed FLAIR enhanced images after T1 contrast-enhanced sequence, effect of delayed enhancement may have been a factor. However, Mathews et al. suggested that it made no difference which enhanced sequence was done first (7). Griffiths et al. obtained the FLAIR sequence prior to T1 and demonstrated equal or better enhancement with FLAIR (3).

In our 12-patient series, we did both T1 first and FLAIR first and we evaluated most of the patients more than once with MR imaging. Superiority of FLAIR did not differ depending on which sequence was performed first. Since the meninges do not have a blood-brain barrier, the order of timing of the MR images after the gadolinium is likely not an important factor.

Griffiths et al. demonstrated that better results can be obtained with FLAIR compared to T1 in demonstrating meningeal disease in children with Sturge-Weber syndrome (benign leptomeningeal angiomatosis) and medulloblastoma (3).}

Gadolinium shortens both T1 and T2 of tissues in which it has accumulated. T1 shortening is the predominant effect which provides enhancement of a lesion. Gadolinium accumulates in the extracellular space and influences the MR relaxation of nearby tissue protons. Intraxial lesions enhance when blood-brain barrier breaks down, and extraaxial lesions usually enhance due to high vascularity (8).

In our study, the superiority of gadolinium enhanced FLAIR to T1 in demonstrating pathologic meningeal processes may be due to following effects:

1) Well-known nulling of normal CSF signal by FLAIR unmasks and delineates the pathologic signal in sulci. Additive effect of T2 hyperintensity displays the abnormality more obviously.

2) Slow flowing blood is not usually hyperintense on postcontrast FLAIR but frequently is hyperintense on postcontrast T1-weighted images. Enhancing cortical vessels are typical with routine T1 postcontrast images, and can be confused with meningeal enhancement (1). FLAIR images do not demonstrate contrast enhancement in vessels with slow flow; this allows clearer discrimination of enhancing abnormal meninges and enhancing cortical veins. A sequence eliminating signal intensity from normal vasculature makes a significant contribution to detecting leptomeningeal disease.

On the other hand, sulcal hyperintensity on FLAIR images can occur without apparent CSF abnormality and may be the result of mass effect and vascular disease, an increase in blood pool or a small amount of protein leakage, and in-flow enhancement of

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**Table 1. Patients with leptomeningeal carcinomatosis and imaging findings**

<table>
<thead>
<tr>
<th>Patient Pathology</th>
<th>Meningeal Pathology</th>
<th>FLAIR (w/o) MRI Finding</th>
<th>FLAIR (w) MRI Finding</th>
<th>T1 (w)</th>
<th>CSF</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Breast Ca</td>
<td>N/A</td>
<td>No abn</td>
<td>Min. meningeal enhancement on cerebellar sulci</td>
<td>No abn +</td>
<td>whole brain external beam radiation</td>
<td></td>
</tr>
<tr>
<td>2. Lung Ca</td>
<td>N/A</td>
<td>No abn</td>
<td>R central sulci, scattered sulci enhancement on L</td>
<td>No abn +</td>
<td>RT and chemo for lung mass (nothing for brain)</td>
<td></td>
</tr>
<tr>
<td>3. Lung Ca</td>
<td>N/A</td>
<td>No abn</td>
<td>R Frontoparietal junction convexity enhancement</td>
<td>subtle +</td>
<td>whole brain external beam radiation</td>
<td></td>
</tr>
<tr>
<td>4. Lung Ca</td>
<td>N/A</td>
<td>subtle</td>
<td>Multiple parenchymal mets. + Bil sulcal diffuse enhancement</td>
<td>subtle +</td>
<td>chemo &amp; RT</td>
<td></td>
</tr>
<tr>
<td>5. Melanoma</td>
<td>Melanoma met, V bx</td>
<td>R atrial abn sig</td>
<td>Widespread leptomeningeal &amp; IV enhancement</td>
<td>less prom _</td>
<td>whole brain external beam radiation</td>
<td></td>
</tr>
<tr>
<td>6. Melanoma</td>
<td>N/A</td>
<td>No abn</td>
<td>Leptomeningeal 8 multiple punctate parenchymal enhancement</td>
<td>less prom radiation +</td>
<td>whole brain external beam</td>
<td></td>
</tr>
<tr>
<td>7. Lymphoma</td>
<td>N/A</td>
<td>No abn</td>
<td>L F lobe leptomeningeal enhancement</td>
<td>subtle +</td>
<td>chemo &amp; RT</td>
<td></td>
</tr>
<tr>
<td>8. Breast Ca</td>
<td>N/A</td>
<td>No abn</td>
<td>L F lobe leptomeningeal enhancement</td>
<td>No abn +</td>
<td>whole brain external beam radiation</td>
<td></td>
</tr>
<tr>
<td>9. Breast Ca</td>
<td>N/A</td>
<td>No abn</td>
<td>Widespread</td>
<td>prom +</td>
<td>whole brain external beam radiation</td>
<td></td>
</tr>
<tr>
<td>10. Breast Ca</td>
<td>N/A</td>
<td>No abn</td>
<td>Leptomeningeal enhancement on cerebellar sulci</td>
<td>No abn +</td>
<td>whole brain external beam radiation</td>
<td></td>
</tr>
<tr>
<td>11. Lymphoma</td>
<td>N/A</td>
<td>No abn</td>
<td>R F lobe leptomeningeal enhancement</td>
<td>No abn +</td>
<td>chemo &amp; RT</td>
<td></td>
</tr>
<tr>
<td>12. Lung Ca</td>
<td>N/A</td>
<td>No abn</td>
<td>R parietal convexity enhancement</td>
<td>subtle +</td>
<td>whole brain external beam radiation</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** Ca: carcinoma; N/A: not applicable; abn: abnormal; sig: signal; L: left; R: right; F: frontal; IV: intraventricular; Min: minimal; prom: prominent; RT: radiotherapy; chemo: chemotherapy; V bx: ventricular biopsy; w/o: without; w: with.
congested blood. All these may contribute to sulcal hyperintensity on FLAIR images. Contrast images are carefully compared with the precontrast FLAIR images. (1, 9)

Also, since anesthetic substances and inhaled oxygen showed increased signal intensity in the meninges with FLAIR unenhanced sequence, non contrast FLAIR images should be compared with postcontrast FLAIR in all cases.

**Conclusion**

Our limited study demonstrated that, there are distinct advantages of contrast-enhanced FLAIR sequences over enhanced T1 in demonstrating meningeal disease. However, parenchymal lesions appear better on T1 with contrast. Since using both T1 and FLAIR with contrast as well as noncontrast FLAIR will increase sensitivity and specificity of MR imaging, using all three sequence will enhance the quality and accuracy of leptomeningeal disease evaluation.

**Study Limitations**

This study is not a large-patient series. Most of the articles about the subject in the literature consist of 6 to 25 patients. However, our study showed a distinctive evidence of FLAIR superiority to postgadolinium T1 images for detection of leptomeningeal carcinomatosis.

Although we performed more than one MRI examination in one month apart in most of our patients, we did not have long-term follow-up. We did not use a control group that we performed all three sequences (pre-contrast FLAIR, post-contrast FLAIR and post-contrast T1).

**References**