Whole-body FSE STIR MR imaging of lymphoma

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Received 8 September 2010; accepted 6 November 2010
Available online 12 March 2011

KEYWORDS
Whole-body MRI; FSE STIR; Lymphoma

Abstract Purpose: To evaluate the role of FSE STIR whole body MRI in diagnosis and initial staging of malignant lymphoma, and can FSE STIR whole body MRI replace conventional staging procedures including computed tomography and bone marrow biopsy in initial staging of lymphoma. Materials and methods: Twenty one newly diagnosed histologically proven lymphoma patients underwent whole body MR imaging and conventional staging procedures including computed tomography and bone marrow biopsy for initial staging of lymphoma using Modified Ann Arbor staging system. Both methods evaluated positive involvement by lymphoma to the nodal and extra-nodal sites including parenchymal organs, serosal cavities and bone marrow. The numbers of involved nodal and extra-nodal sites detected by both methods were compared, then agreement and disagreement between whole-body MRI and conventional procedures regarding lesions detection and staging according to the Ann Arbor staging system were calculated, along with binomial exact 95% confidence intervals (CIs). Results: Twenty one patients had a total of 145 abnormalities. One hundred and twenty four were correctly diagnosed by conventional staging procedures, however, FSE STIR whole body MRI correctly diagnosed all the 144 abnormalities with 1 false negative and 3 false positive abnormalities with a total of detected abnormalities of 147 lesions. FSE STIR whole body MRI was significantly more accurate than conventional staging procedures in the diagnosis of positive lymphoma lesions (99.3%; 95% CI: 95.6–100.0%) versus (85.5%; 95% CI: 78.5–90.6%). FSE STIR whole body MRI correctly staged 20 out of 21 patients, Kappa test 0.93 (P < 0.001) while conventional staging procedures correctly staged 17 and incorrectly staged 4 cases, Kappa test 0.74 (P < 0.001).

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1. Introduction

Cancer is the second cause of death among children after accidents [1]. Lymphoma is the third childhood malignancy and accounts for 10% of child cancers, two thirds are NHL and one third is HD [2].

In hematological malignancies the patients’ prognosis and therapeutic options depend strongly on initial accurate diagnosis as well as tumor staging [3]. Clinical staging usually entails different radiological examinations so it can be time consuming and costly [4].

CT has historically been considered the standard imaging technique for staging, however, benign nodal enlargement is common among pediatric population [5,6]. Although MRI examination is a safer alternative technique, it has been limited by long examination time [7]. The advances in imaging technology and the introduction of moving patient platforms with integrated surface coil technology have greatly reduced the imaging time, especially for whole-body MR imaging [8–12].

Whole-body MRI has been widely adopted as a valuable imaging tool in oncology and particularly in assessing diseases that infiltrate through the body such as carcinoma and lymphoma [13]. A high-spatial-resolution whole body MRI examination with a reasonable time has been enabled by the rapidly evolving technique with the multi-channel phased array surface coils and parallel imaging acquisition [14,15]. Whole-body MR imaging with fast spin-echo (SE) short inversion time inversion recovery (STIR) sequences has been shown to be valuable for the evaluation of metastatic bone disease, staging and assessment of multifocal disease in adults [16–19], and for staging newly diagnosed small cell tumors in children [20]. MR has a complementary role to blind bone marrow biopsy in evaluating marrow involvement in both NHL and HD [21]. Neoplastic tissues as lymphomatous tissue have increased water that has high signal on STIR imaging enabling the detection of diseases [22,23].

The goal of this study is to evaluate the role of whole-body MRI in diagnosis and staging of lymphoma.

2. Material and methods

2.1. Patients

Our study included 21 newly diagnosed histologically proven lymphoma patients (12 males and 9 females) with age range of 12–70 years (mean 42 years). All patients were included after they had been properly informed and provided written informed consent. Exclusion criteria were contraindication to CT and MR imaging (e.g., pregnancy, and pacemaker, metallic implant, severe claustrophobia). All patients were subjected to physical examination, complete blood count, renal and hepatic function tests, conventional staging procedures (bone marrow biopsy and CT scans) and whole body MRI, radiological examinations were performed within one week of each other, before the start of treatment, and after 3 months of follow up.

2.2. Conventional staging procedures

2.2.1. CT scanning

CT imaging was performed using helical scanner (HiSpeed, GE Medical Systems). It included contrast enhanced imaging of the head, neck, chest, abdomen and pelvis. Examination of the head and neck was done with the acquisition of contiguous sections of 5-mm thickness while examination of the chest, abdomen and pelvis was done using 10 mm collimation. All patients received oral (Telebrix Gastro) and intravenous non-ionic contrast medium before scanning. The administered amount of CT contrast agents was adjusted according to age and weight (2 ml/kg).

2.2.2. Bone marrow assessment (bone marrow biopsy)

Marrow aspirates were taken from both iliac crests stained with Giemsa stain. Trephine biopsy samples were decalcified and stained with hematoxylin and eosin.

2.3. Whole-body MR imaging

Each patient included for study underwent imaging on a 1.5-T MR (Achieva, Philips Medical Systems, Netherland B.V.) scanner using a moving tabletop and tabletop extender, generating a longitudinal field of view of 200 cm and transverse field of view of 53 cm. In each case, images were acquired with a body coil with a moving tabletop technique in coronal and axial planes. The patients were supine with the arms placed by their sides and placed feet-first in the imager. The rolling table platform was positioned so that a transverse section in the isocenter of the imager aligned the basal thorax directly cranial to the liver. After obtaining localizing sequences, the entire body was covered from the vertex to the heels by coronal FSE STIR whole body sequences. Coronal scans were acquired in seven contiguous stations with 25 consecutive slices at each station. Scanning was done with a slice thickness of 7 mm and an interslice of 1 mm. Images were acquired under free breathing, except for the stations covering the chest, abdomen, and pelvis, which were acquired using breathholding. Images acquired in matching positions were automatically aligned to generate a seamless whole-body coronal image using software implemented in the standard operating console. Tissue excitation used FSE STIR with a TR of 6600 ms, a TE of 70 ms scan time of 39.4 s per station, seven stations in total. Axial images were acquired using a similar moving tabletop technique and STIR tissue excitation. After FSE STIR whole body MR image acquisition in the coronal and axial planes T1-weighted tissue excitation (TR/TE, 214/5) in coronal and axial planes were acquired using the same techniques.
Both conventional staging procedures (including computed tomography and bone marrow biopsy) and FSE STIR whole body MR imaging data findings were used in the staging of lymphoma patients using Modified Ann Arbor staging system (Table 1). To facilitate staging by either method the patient was concerned for nodal and extra-nodal involvement. Concerning nodal analysis the body was divided into lymph node or disease stations (intraparotid, Waldeyer ring, retropharyngeal, submandibular, cervical, supraclavicular, axillary, internal mammary, cardiophrenic, anterior mediastinum, right and left paratracheal including aortopulmonary nodes, subcardinal, hilar, posterior mediastinum, retrocural, porta hepatis, upper retroperitoneal (celiac and peripancreatic nodes), lower retroperitoneal, mesenteric, iliac and inguinal). Lymph nodes greater than 10 mm in the short-axis diameter were considered positive at CT and MR sequences. Extranodal involvement was divided into parenchymal, serosal and bone marrow involvement where pathology was evaluated by both methods (conventional staging procedures and coronal FSE STIR whole body MRI) as follows: area of abnormal attenuation/signal intensity (relative to the surrounding tissue) or mass lesion in the liver, spleen, kidney, stomach, bowel, pancreas, nodule or infiltration in the lung. Serosal involvement was evaluated as effusions in serosal cavities. Bone marrow involvement was diagnosed as foci of abnormal high signal in bone marrow on MR imaging, sclerotic or lytic bone lesions in CT and positive bone marrow biopsy for the presence of lymphoma.

The number of involved sites in lymph node stations, parenchymal organs serosal cavities and bone marrow, detected on coronal FSE STIR whole body MR imaging and on conventional staging procedures were compared. The proof of diagnosis or a final diagnosis was based on all imaging performed and on the outcome at follow up. Differences in staging between coronal FSE STIR whole-body MRI and conventional staging procedures were resolved using follow up studies (including CT & MRI) as the standard of reference. At follow-up, enlarged nodes, parenchymal organs, serosal and bone marrow abnormalities that decreased in size at follow-up imaging were considered positive for the presence of malignant lymphoma.

Agreement and disagreement between whole-body MRI and conventional procedures regarding lesions detection and staging according to the Ann Arbor staging system were calculated, along with binomial exact 95% confidence intervals (CIs), using SPSS version 10 software. An unweighted $k$ analysis (Kappa test) was used to test agreement between whole body MR imaging, conventional procedures and final diagnosis for lesion detection and staging. A $k$ less than 0.2 was considered to indicate poor agreement; 0.21–0.40, fair agreement; 0.41–0.60, moderate agreement; 0.61–0.80, good agreement; and 0.81–1, very good agreement. $P$ value < 0.05 was considered significant.

### Table 1 Cotswold modification of Ann ArboR Staging of Hodgkin and non-Hodgkin lymphoma [24].

<table>
<thead>
<tr>
<th>Stage</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>In 1 lymph region only</td>
</tr>
<tr>
<td>II</td>
<td>In ≥ 2 lymph regions on the same side of the diaphragm</td>
</tr>
<tr>
<td>III</td>
<td>In the lymph nodes, spleen, or both and on both sides of the diaphragm</td>
</tr>
<tr>
<td>IV</td>
<td>Extranodal involvement (e.g., bone marrow, lung, liver)</td>
</tr>
</tbody>
</table>

* Subclassification E indicates extranodal involvement adjacent to an involved lymph node (e.g., disease of mediastinal nodes and hilar adenopathy with adjacent lung infiltration is classified as stage II E).

### Table 2 Detection of nodal and extra-nodal lymphoma lesions by FSE STIR whole body MRI and conventional staging procedures.

<table>
<thead>
<tr>
<th></th>
<th>FSE STIR whole body imaging</th>
<th>Conventional staging procedures</th>
<th>Final diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nodal lesions</td>
<td>96</td>
<td>89</td>
<td>94</td>
</tr>
<tr>
<td>Extra-nodal lesions</td>
<td>51</td>
<td>35</td>
<td>51</td>
</tr>
<tr>
<td>*Parenchymal</td>
<td>17</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td>Liver</td>
<td>5</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Spleen</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Kidneys</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Stomach</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Bowel</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Lung</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>*Serosal (pleural)</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>*Bone marrow Foci</td>
<td>32</td>
<td>18</td>
<td>32</td>
</tr>
<tr>
<td>Total</td>
<td>147</td>
<td>124</td>
<td>145</td>
</tr>
</tbody>
</table>

A total of 21 newly diagnosed histologically proven lymphoma patients (16 patients had NHL and 5 patients had HD) underwent initial staging by two separate procedures; conventional staging procedures (included computed tomography and bone marrow biopsy) and coronal FSE STIR whole body MRI. Twenty one patients had a total of 145 abnormalities according to the final diagnosis proved by all the imaging performed and on the outcome at follow up (Table 2). One hundred and twenty four were correctly diagnosed by conventional staging procedures. Whole body MRI correctly diagnosed 144 abnormalities with 1 false negative abnormality, and had 3 false positive abnormalities with a total of detected abnormalities by coronal FSE STIR whole body MRI 147 abnormality. A total of 94 lymph nodes for malignant lymphoma were present, 89 positive nodes were detected by conventional staging procedures, however, coronal FSE STIR whole body MRI detected 93 diseased nodes with 1 false negative and 3 false positive nodes with a total of 96 positive nodes as shown in Table 2. Fifty-one lesions were present as extranodal lymphomatous involvement (17 parenchymal, 2 serosal, 32 bone marrow); conventional staging procedures detected 35 out of the 51 lesions and whole body MRI correctly detected all the 51 lesions. Parenchymal lymphomatous involvement were present in 17 organs and were as follows: liver ($n = 5$), spleen ($n = 6$), the kidneys ($n = 1$), stomach (1), bowel (1) and lungs ($n = 3$). On conventional staging procedures, 15 of the 17 involved parenchymal organs were correctly diagnosed, and on whole-body MR imaging, all organ involvements were detected. Two pleural effusions were present and were correctly diagnosed by both procedures.
Twenty one patients had 32 bone marrow lesions according to the final diagnosis. Coronal FSE STIR whole-body MR imaging detected more bone marrow lesions \((n = 32)\) than did conventional staging procedures \((n = 18)\). Conventional staging procedures detected only 18 of 32 involved sites.

So, whole body MRI correctly diagnosed \((144)\) lesions out of \((145)\) lesions \((99.3\%; 95\% CI: 95.6–100.0\%)\). On the other hand conventional staging correctly diagnosed \((124)\) lesions out of \((145)\) lesions \((85.5\%; 95\% CI: 78.5–90.6\%)\). Both whole body MRI and conventional procedures were in agreement in \((125)\) lesions \((124\) positive and one negative lesions), while there was no agreement in \([23]\) lesions with overall agreement of Kappa test \(0.07\) \((P < 0.05)\).

The final clinical staging of the 21 patients as shown in illustrative cases (Figs. 1–4) was as follows; stage I \((n = 3)\), stage II \((n = 4)\), stage III \((n = 6)\) and stage IV \((n = 8)\). Coronal FSE STIR whole body MRI correctly staged 20 out of 21 patients referring to the final staging Kappa test \(0.93\) \((P < 0.001)\) as shown in Tables 3 and 4, however, 1 patient only in stage II was overstaged as in stage III. This patient had multiple enlarged abdominal lymph node stations with additional 2 false positive mediastinal lymph node stations. Concerning clinical staging by conventional procedures 17 patients were correctly staged, Kappa test \(0.74\) \((P < 0.001)\). All patients with stage I were correctly staged \((3\) of \(3)\). In stage II: 3 out of 4 patients were correctly staged and 1 patient was understaged as stage I due to an additional right cervical lymph node that was not detected by CT and detected by MRI. In stage III: all the 6 patients were correctly staged. In stage IV: 5 out of 8 patients were correctly staged and 3 patients were understaged \((2\) cases as stage III and one case as stage II) as in these 3 patients coronal FSE STIR whole body MRI revealed multifocal bone

![Figure 1](image-url)
4. Discussion

Assessment of pathological classification and disease extent in malignant lymphoma is crucial for the prognosis and therapy. Accurate staging is important in treatment planning and selection and monitoring the appropriate therapy. Contrast enhanced computed tomography is the imaging technique commonly used due to its widespread availability and relatively low cost, however, the major disadvantages of it is exposure of the patient to ionizing radiation which may induce secondary cancers and the administration of iodinated contrast agents which may cause adverse reactions as nephrotoxicity and anaphylactic shock. Whole body MRI offers a whole body overview of disease that infiltrates throughout the body, such as carcinoma and lymphoma. It does not involve any radiation exposure or administration of oral or intravenous contrast media. FSE STIR whole body MR imaging of lymphoma.

Figure 2  Female patient, 45 years old, clinically staged as stage III lymphoma. Selected images of coronal FSE STIR whole body MRI (a–c) show multiple enlarged variable sized amalgamated lymph node stations on both sides of the diaphragm at the mediastinal (a) and abdominal (b and c) regions displaying high signal intensity. Axial STIR (d–f) show the different abdominal lymph node stations which is of high signal intensity. Axial CT cuts (g–i) show the enlarged mediastinal (g) and abdominal (h and i) lymph node stations.

marrow involvement outside the iliac bones not evident on CT and blind iliac bone marrow biopsy.
MRI offers fat suppression over the whole body without the need of accurate shimming and so is useful for whole body MRI. Lymphomatous tissue, like all neoplastic tissues, has increased water content that returns high signal on STIR.

Figure 3  Female patient, 44 years old initially staged as stage V lymphoma. Selected images of coronal FSE STIR whole body MRI (a–e) show heterogeneous high bone marrow signal intensity lesions involving both femoral (a and b) and tibial shafts (c and d) which were not detected by computed tomography or bone marrow biopsy.
imaging, enabling the detection of lymphometous involvement of bone marrow, lymph nodes and parenchymal organs [33–36,13,22,23].

FSE STIR whole body MRI was significantly more accurate than conventional staging procedures including CT and bone marrow biopsy in detecting nodal and extra-nodal lymphomatous lesions [(99.3%; 95% CI: 95.6–100.0%) versus (85.5%; 95% CI: 78.5–90.6%)]. This is consistent with other study [37] who reported that whole-body MR imaging was significantly more sensitive in detecting sites of lymphomatous involvement than was the conventional imaging (sensitivity was 99% vs. 84%, $P < 0.001$).

This study included 21 patients had 94 positive nodal stations for lymphoma. CT detected 89 nodal stations of them, however, FSE STIR whole body MRI detected 93 one plus another 3 false positive nodal stations. The explanation of higher accuracy of FSE STIR whole body MRI in detecting nodal lesions is its high spatial resolution and superior soft tissue contrast. This is consistent with the previous study [4] which proved high sensitivity for the detection of lymph nodes larger than 12 mm and the only missed nodes were calcified. In this study we had 3 false positive nodal station detected by FSE STIR whole body MRI when compared with T1WI at which lymph nodes appear of low signal intensity against the high

**Figure 4** Female patient, 19 years old initially staged as stage V lymphoma due to diffuse bone marrow involvement. Selected images of coronal FSE STIR whole body MRI (a–c) show high bone marrow signal intensity lesion involving the left humeral head and upper shaft, another focal high signal intensity lesions are seen at right femoral mid-shaft (b) and left femoral upper shaft (c). These lesions were not detected by computed tomography or bone marrow biopsy.

**Table 3** Initial lymphoma staging by FSE STIR whole body MRI and conventional staging procedures.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Correct FSE STIR whole body MRI staging No.</th>
<th>Incorrect FSE STIR whole body MRI staging No.</th>
<th>Correct conventional staging No.</th>
<th>Incorrect conventional staging</th>
<th>Final staging No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>3</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>II</td>
<td>3</td>
<td>1 (Overstaged as stage III)</td>
<td>3</td>
<td>1 (Understaged as stage I)</td>
<td>4</td>
</tr>
<tr>
<td>III</td>
<td>6</td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>IV</td>
<td>8</td>
<td>0</td>
<td>5</td>
<td>3 (2 Understaged as stage III and 1 understaged as stage II)</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>1</td>
<td>17</td>
<td>4</td>
<td>21</td>
</tr>
</tbody>
</table>
signal intensity of the surrounding fat. This is also found in other study [4] in which whole body MRI detected only 1 false positive nodal station concerning lymph nodes above 12 mm and the study [37] in which FSE STIR whole body MRI detected all the positive 51 nodal stations plus additional 6 false positive nodal stations which revealed either diffuse edematous changes or ascites as the cause of the increased signal. The 1 false negative or missed lymph node station by FSE STIR whole body MRI in our study was mediastinal but did not affect the staging as there were other several detected positive mediastinal stations in the same patient.

Both CT and FSE STIR whole body MRI were equal and diagnosed all parenchymal and seosal lesions, however, in the other study [37] there were 14 parenchymal lesions, 13 lesions detected by conventional methods and 15 lesions detected by whole body MRI (1 false positive lung lesion) but both procedures detected 4 out of 5 serosal lesions.

FSE STIR whole body MRI was more accurate in detecting bone marrow involvement by lymphoma than combined CT and bone marrow biopsy. FSE STIR whole body MRI detected all bone marrow lesions (n = 32), however, conventional methods detected only 18 lesions. This is consistent with other previous studies [38,37] in which conventional methods detected 7 out of 18 bone marrow lesions, however, FSE STIR whole body MRI detected all the 18 bone marrow lesions plus 1 false positive lesion due to recent biopsy.

The limited sensitivity of the blind bone marrow biopsy in the detection of bone marrow lesions in malignant lymphoma can be explained by the sampling errors as MRI pattern of bone marrow infiltration is nodular in 65% of patients with Hodgkin’s lymphoma and in 85% of aggressive lymphomas. This is why iliac crest biopsy may be normal despite bone marrow infiltration in other areas. Whole-body MRI-guided bone marrow biopsy has the potential to reduce sampling errors. In addition, this approach may reduce the number of unnecessary bone marrow biopsies, which are invasive, painful, and have a small but non-negligible risk of complications [39-41].

Concerning clinical staging of our patients FSE STIR whole body MRI correctly staged 20 out of 21 patients but incorrectly staged 1 patient of stage II as stage III due to additional false positive lymph node detected by FSE STIR whole body MRI. Conventional staging procedures correctly staged 17 and incorrectly staged 4 cases. One of these 4 cases was stage II and understaged as stage I due to missed right cervical lymph node not detected by CT, however, the other 3 cases were stage IV and understaged due to missed bone marrow lesions by CT and bone marrow biopsy. This study is consistent with two previous studies that reported the feasibility of whole-body MRI using STIR. The first one [4] performed a study in 23 adults (both for initial staging and restaging) and found that whole-body MRI using STIR enables disease staging and that it compared favorably with CT for the detection of lymph nodes larger than 12 mm in short-axis diameter and for the detection of bone marrow involvement. The other one [37] performed a study in 8 children (both for initial staging and restaging) and reported that whole-body MRI using STIR is a sensitive technique for staging malignant lymphoma and that it is superior to blind bone marrow biopsy and conventional imaging in the detection of bone marrow involvement, at initial diagnosis. When bone marrow involvement is detected by FSE STIR whole body MRI and missed by other conventional modalities it overstages the patient to stage IV whatever its stage by conventional methods so if the MR study was performed as first imaging study and showed bone marrow involvement consistent with a stage IV, further imaging might not be necessary.

FSE STIR whole body MRI is a highly sensitive method in initial staging of lymphoma as it offers a whole view of the body including positive lymph node stations, parenchymal, serosal and bone marrow lesions. FSE STIR whole body MRI is more accurate than conventional staging procedures in staging of lymphoma especially in the detection of bone marrow involvement.

References

Whole-body FSE STIR MR imaging of lymphoma


