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# Comparison of PET-CT and magnetic resonance diffusion weighted imaging with body suppression (DWIBS) for initial staging of malignant lymphomas

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ABSTRACT

*Objective:* To evaluate the clinical impact of diffusion-weighted whole-body imaging with background body signal suppression (DWIBS) in staging of malignant lymphoma.
*Methods:* Twenty-three patients with proven malignant lymphomas were prospectively enrolled. DWIBS ($b=0$, $1000\,s/mm^2$) examinations and PET-CT were performed respectively on an Intera 1.5 T unit and a Gyroscan PET-CT scan (Philips Medical system, Best, the Netherland). The criteria for positive node involvement were a size over 10 mm or an apparent diffusion coefficient (ADC) value under $0.75\,10^{-3}\,mm^2/s$ for nodes under 10 mm. For extranodal analysis, a high or heterogeneous signal on DWIBS was considered as positive. In cases of discordance, the reference standard for each region or organ was established at 6 months after the diagnosis according to all available clinical, biological information, as well as histological evidence or follow-up to prove or disprove the presence of disease.
*Results:* DWIBS and PET-CT results were congruent in 333 node regions on the 345 areas analyzed, with excellent agreement ($\kappa=0.97$, $P<0.0001$). From 433 organs analyzed (one patient had splenectomy) extranodal disease was detected in 22 organs on DWIBS. The two imaging techniques agreed on 430 organs ($\kappa=0.99$, $P<0.0001$). Finally, Ann Arbor stages based on DWIBS and those of PET/CT were in agreement for 23 patients.
*Conclusions:* For malignant lymphoma in a pre-therapeutic context, agreement between diffusion-weighted whole-body imaging and PET/CT is high for Ann Arbor staging.


## 1. Introduction

Hodgkin and non-Hodgkin lymphoma are the most common primary hematopoietic malignancies. Contrast-enhanced multi-detector computed tomography (MDCT is the imaging technique most commonly used for staging patients in a prognostic group and for evaluating the follow-up. Positron emission tomography (PET) with 2-[fluorine-18] fluoro-2-deoxy-D-glucose (FDG) (FDG) is highly sensitive and specific, and integrated PET/CT is now widely used in staging and evaluating treatment response [1]. However, there exist some limitations to the technique: (1) Cerebral lymphoma and some false hot intestinal spots are sometimes difficult to characterize due to physiologic accumulation of FDG; (2) PET/CT shows not only tumor-specific uptake, but also increased accumulation through various benign conditions such as inflammation or red cell regeneration; (3) The method is irradiant even if it is widely accepted that the benefits of proper staging using PET/CT outweigh its disadvantages [2].

Diffusion-weighted magnetic resonance imaging noninvasively probes random microscopic motion of water molecules in the body. Because of their high cellularity and elevated nuclear-to-cytoplasm ratio, lymphomas have relatively high signal intensity on DWI compared to normal tissues [3]. Lymphomas also have lower apparent diffusion coefficients (ADC) than other tumor types in different body regions [4]. Associated with background body signal suppression, diffusion-weighted whole-body imaging with

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background body signal suppression (DWIBS) provides homogeneous fat suppression and thereby helps to visualize the spread of the disease at first glance [5]. In addition, the high signal-to-noise ratio obtained allows high b value, which enhances specificity in detection of high cellularity. However, to date there are very few reports on the possible interest of DWIBS in cases of lymphoma [6–8].

In this prospective study, we wish to compare the performance of DWIBS and PET/CT for evaluation of lymphomas in pre-therapeutic staging.

## 2. Materials and methods

### 2.1. Patients

All patients with aggressive lymphoma newly diagnosed between June 2008 and October 2009 were eligible for this prospective study provided that they were adults with histological proven malignant lymphoma requiring pre-treatment staging. Exclusion criteria were applied to patients with other malignancies or hematological disorders and contraindications to MRI, such as claustrophobia and implanted pacemakers or neurostimulators.

The study was approved by the Ethics Committee of our hospital and written consent forms were obtained from all participants.

In all patients, histological diagnosis was established by excision or biopsy of a node. Histological samples were classified in accordance with the WHO recommendations [9].

Pre-treatment evaluation included physical examination, performance status evaluation, complete blood count, renal and hepatic function tests and serum lactate dehydrogenase (LDH) levels.

During the inclusion period, 23 patients who met the inclusion criteria underwent both whole-body DWIBS and integrated FDG PET/CT within an average of 3.5 days (range, 1–9 days) of each other. No treatment was given before the end of staging, which was based on the Ann Arbor system, with physical examination, CE-CT scanner, integrated FDG PET/CT and bone marrow biopsy. Characteristics of the studied population are shown in Table 1.

### 2.2. PET-CT

Positron emission tomography (PET) was carried out using a hybrid PET/CT imager (Gemini Scan, Philips Medical Solutions, Nederland's) after injection of 18-fluorodesoxyglucose (FDG). The injected activity was 5 MegaBecquerel (MBq) per kilo corresponding to an activity ranging from 367 to 866 MBq (median 439 MBq); the patients had fasted for 8–16 h before injection (median 13 h) and presented a glucose blood level ranging from 4 to 7.9 mmol/L (median 5.55 mmol/L). A rest period of 60 min was observed before injection. The delay between FDG injection and PET images acquisition ranged from 46 to 63 min (median 54 min). The PET examination consisted in 7–9 bed-steps of 2–3 min each, from the top of the skull to the mild femoral region and in additional 2 min bed-steps for the lower limbs. CT images were recorded for attenuation correction and image fusion using a low-dose CT protocol (helical acquisition, 160 kV, 80 mAs). PET images reconstruction was performed using a RAMLA-3D algorithm (eight subsets, four iterations, Gaussian post-filtering). Fused images were visually interpreted together.

**Table 1**
Characteristics of the 23 patients included in the study.

| Characteristics | values |
|---|---|
| Median age (range) | 51 years (18-84 years) |
| Gender (M/F) | 11/12 |
| Pathology (WHO) | Hodgkin disease (HD) 5 |
| | Diffuse large B-cell (DLBCL) 16 |
| | Burkitt lymphoma 2 |
| Serum LDH level | N 13 |
| | >N 10 |
| Clinical stage | I 8 |
| (Ann Arbor Stage) | II 3 |
| | III 5 |
| | IV 7 |

Ranges are in parentheses; N = normal values.The Ann Arbor stage is based on physical examination, contrast-enhanced CT, integrated FDG PET/CT and bone marrow biopsy.

### 2.3. Whole-body MRI

MR imaging examination was performed in the supine position on a 1.5 T unit (Intera; Philips Medical Systems, The Netherland) with a 6 multichannel body coil. To cover the axial and appendicular skeleton, three 3D contiguous axial acquisitions were used: DWIBS was performed by using a short TI inversion recovery echo-planar imaging (STIR-EPI) sequence with free breathing. Total scan time for 3 stations was approximately 15 min with coverage from head to thigh (960 mm coverage). Each station was composed of 80 axial slices with a thickness of 4 mm without slice gap. Imaging parameters were as follows: repetition time (TR) = 5834 ms, echo time (TE) = 72 ms, inversion time (TI) = 180 ms and a field of view of 48 cm. The matrix was $384 \times 384$ and a parallel imaging factor of 2 was used. No respiratory gating was performed during the acquisition. No intravenous contrast agent was administered. The entire total body MR imaging with 3 sequences was performed within 40 min, including T1 and STIR imaging, and patient positioning. The diffusion gradients were applied in three orthogonal directions with $b = 0$ and 1000 s/mm$^2$. High-resolution maximum intensity projection (MIP) images were reconstructed and black–white inverse gray scale was used in all cases.

### 2.4. Image analysis

DWIBS examinations were interpreted by two radiologists in consensus, one with 5 years' and the other with 12 years' experience in MR imaging. They were unaware of any clinical and PET/CT findings, except for the patient's diagnosis. Inverted black-and-white gray scale was used and the window was adapted to obtain white background. Axial images were studied and coronal MIP (maximal intensity projection) reconstructions used to present the findings. Lesion detection was performed on $b = 1000$ and size measurement on $b = 0$. The two readers analyzed in consensus on whether a lymph node region or an organ was involved (i.e. positive or negative). Lymph node involvement was considered as positive according to two criteria: (1) size: according to IWG (international working group) criteria [10], a lymph node larger than 10 mm in its longest transverse diameter was considered positive for lymphoma involvement, except for those with a clearly identified fatty hilum and thin cortex; (2) DWIBS analysis: for 16 regions (cervical, supraclavicular, internal mammary and diaphragmatic, anterior mediastinal, paratracheal, hilar, subcarinal and posterior mediastinal, celiac and superior mesenteric, hepatic and splenic hilar, retroperitoneal and periaortic, inferior mesenteric lymph nodes), signal intensity was visually assessed. For 2 regions, axillary and femoral, the cut-off size was 15 mm. In addition, because it is very common to observe lymph nodes with restricted diffusion in these area, apparent diffusion coefficient (ADC) value was calculated on a region of interest (ROI) manually drawn to include the entire cross-section of the lesion excluding any necrotic areas (i.e. areas of high signal intensity close to that of CSF on b0 images). An ADC valued inferior to 0.75 $10^{-3}$ mm$^2$/s was considered as positive with regard to involvement. This threshold was determined from a review of the literature showing a mean ADC value for normal lymph nodes of