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"Low Dose MR" Dixon Technique for Imaging FDG PET-MR Lymphoma

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Abstract

Introduction Hybrid PET-MR is a relatively new imaging modality with its major strength being the MR component offering superior soft tissue contrast. While PET/MRI offers the inherent advantage of reduced radiation dose, it has been shown to result in a markedly prolonged examination time becoming a challenge in children and sick patients. "Low dose MRI" is a term used in the nuclear medicine community to describe fast acquired PET-MR scan protocols that rely heavily on PET images for diagnosis. In this study, we sought to determine if the Dixon sequences obtained for attenuation correction could be used as a diagnostic sequence for interpreting PET-MRI lymphoma cases, potentially reducing scan time.

Materials and Methods Materials and Methods We retrospectively identified 40 patients who underwent ^{88}FDG PET-MR body imaging studies for staging or restaging lymphoma. A radiologist and nuclear medicine physician initially reviewed top of the head to mid thigh PET images, attenuation correction coronal Dixon MRI sequences, and PET-MR fusion with Dixon sequence. The same physicians reviewed the PET images, multi-sequence MR including the attenuation correction Dixon, and multi-sequence PET-MR fusion images The lesions were further characterized based on their imaging characteristics, size, SUVmax, and malignant potency. A consensus read followed.

Results All patients were adults with an average study age of 43.8 years. Our study consisted of 40 females and 48 males out of which 7 were for staging and 81 were for re-staging. All patients had systemic lymphoma. Thirty-seven of the studies had active lymph nodes on Dixon PET-MR that agreed with multi-sequence PET-MR which identified 33 positive cases (89.1%) having an average SUV 10.2 $\pm$ 7.74 SD. Four Dixon PET-MR cases did not detect lesions, with an average SUV 2.3 $\pm$ 0.55 SD, which was read as minimal residual activity. Multi-sequence MR identified 11 patients with enlarged lymph nodes without FDG uptake, which were not seen on Dixon MR. All 5

Keywords
- Dixon sequence
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studies with bones lesions were detected by Dixon PET-MR as well as 2 soft tissue organ lesions. Multi-sequence MR identified 1 patient with non-active, healed bone lesion. Fifty-five of these studies were true negatives. Compared to multi-sequence PET-MR, Dixon PET-MR demonstrated 89.2% sensitivity, 100% specificity with no false positive studies.

Conclusion The present study investigated the diagnostic potential of a fast protocol for integrated PET/MRI used for dedicated tumor staging of patients with lymphoma. In this retrospective study, Dixon PET-MR was shown to be sensitive and specific compared to multi-sequence PET-MR in the detection of lymphoma. The low number of these cases not detected had minimally active lymph nodes that resolved on subsequent imaging and probably were not clinically important.

Introduction

Combining positron emission tomography with magnetic resonance (PET/MR) is a relatively new imaging modality that has been showing an increase in demand within the United States. The superior soft tissue contrast, multiplanar acquisition, functional MR imaging, MR spectroscopy, and perfusion weighted imaging are some of the major strengths of the MR component when compared with computed tomography (CT) in PET/CT. The lack of ionization radiation in the MR acquisition appeals to pregnant patients and young or pediatric patients that require multiple PET scans during their treatment.[1]

Lymphoma is a malignancy of lymphocytes or lymphoblasts, resulting in unregulated growth of these cell lines that accounts for 4% of all cancers.[2] In children, lymphoma accounts for 10 to 15% of all cancers, being the third most common form of malignancy. Lymphoma is further divided into Hodgkin's and non-Hodgkin's lymphoma.[3] The American Cancer Society estimates for the calendar year of 2017, there were 80,500 people diagnosed with lymphoma in the United States with 8,260 of these cases from Hodgkin's disease.[4] Lymphoma cure rates range up to 90% in some studies, compared with other malignancies. More aggressive subtypes of lymphoma, such as Burkitt's lymphoma, have a rapid doubling time.[5] Prognosis depends both on histological subtype and staging, with imaging playing a pivotal role in treatment. Fluorodeoxyglucose (FDG) PET imaging, usually combined with CT, is an established modality for staging, restaging, and in the evaluation of treatment response.[6]

When imaging children, MR is a preferred imaging modality over CT because of the reduced radiation exposure and high soft tissue contrast. When the pediatric patient or patient with disability is imaged, patient motion and respiratory artifact become a challenge especially with MR having shorter imaging time being preferred. Young patients and patients with disabilities are often unable to cooperate or perform breath holds.[7] These patients may require sedation or anesthesia to complete the study, which leads to longer wait times, increased financial cost, and potential short term, and long-term adverse effects.[8,9] This study aims to determine if the Dixon sequence obtained for attenuation correction could be used as a diagnostic sequence for interpreting PET-MR lymphoma cases, potentially reducing scan time, and subsequently reducing interpretation time for the nuclear radiologist.

Methods

Patients

In this institution review board approved study, we retrospectively identified 40 patients who underwent 88 FDG PET-MR body imaging studies for staging or restaging lymphoma from September 2013 until March 2018. Some of these patients underwent multiple studies. We excluded all patients that were younger than 18 years of age, pregnant women, and patients with a fasting blood glucose level greater than 150 mg/dL. We excluded all patients that did not have all the MR sequences from the top of the head to the mid-thigh, had technical issues such as excessive patient motion or artifact, or had non-FDG PET-MR scans.

Image Acquisition

Images were obtained using a 3 Tesla Siemens Biograph mMR integrated PET-MR scanner (Siemens Healthineers, Malvern, Pennsylvania, United States). The PET detector consists of a lutetium oxyorthosilicate scintillator attached to avalanche photodiodes. This scanner consists of 64 detector element rings that are arranged along the Z-axis. Each detector element ring contains 56 detector blocks, and each detector block contains 64 crystal elements. Individual crystal elements measure $4 \times 4 \times 20$ mm.

MR and PET images were obtained simultaneously while using a body radiofrequency coil. Images were obtained from the vertex of the skull to the mid-thigh. PET imaging was obtained using five bed positions at 5 minutes each. A dual echo T1-weighted gradient-recalled echo sequence was obtained to generate an MR attenuation correction map based on a Dixon segmentation. PET data was reconstructed utilizing an iterative reconstruction based on 3D ordinary Poisson ordered subsets expectation-maximization algorithm at 4 iterations and 21 subsets with a 4 mm Gaussian post-reconstruction image filter. The transaxial matrix size was $172 \times 172 \times 515$, with a transaxial field of view of 25.8×25.8 cm, and a voxel size of $4.17 \times 4.17 \times 2.03$ mm.

Table 1 Imaging protocol

	Sequences	Approximate scan time/s
Per bed position (total of 5 bed positions per patient)	GRE localizer 4-point Dixon T2 axial Haste free breathing, and 3D T1 axial radial Vibe	30 19 240
Bed adjustment per position		30
Total time per bed position		330
Total time for 5 bed positions		1,650
Head to mid-thigh	TSE Dixon spine	480
Head to mid-thigh	T2 blade fat-saturated, respiratory triggered	300
Total average scan time per patient		2,700–3,000

Abbreviations: GRE, gradient echo; TSE, turbo spine echo.

It was required for all patients to fast for a minimum of 4 hours prior to receiving 10 mCi (370 MBq) of FDG intravenously, with dose modification based on the patient's weight. Blood glucose levels were measured to be less than 150 mg/dL. After injection of the radiotracer, the patient was placed in a warm, quiet room and was instructed not talk or move excessively. PET-MR images were obtained 60 minutes after FDG administration.

Our imaging protocol for the diagnostic MR body sequences consisted first of an axial T1-weighted radial volumetric interpolated breath-hold examination with fat suppression. This was followed with an axial T2-weighted half-fourier acquisition single-shot turbo spin echo (HASTE) with breath holds. Afterward, a respiratory-triggered axial T2-weighted blade sequence with fat suppression and sagittal T1-weighted turbo spine echo with fat suppression Dixon sequence of the spine. Our average scan time was 35 minutes (►**Table 1**).

Image Analysis

A radiologist and nuclear medicine physician initially reviewed top of the head to mid-thigh PET images, attenuation correction coronal Dixon MRI sequences, and PET-MR fusion with Dixon sequence (Dixon PET-MR). MIM fusion software was used for viewing the images (version 6.5, MIM Software, Cleveland, Ohio, United States) Images of the brain were not reviewed. An interval of 6 weeks between the readings was chosen to avoid recognition bias. Afterward, the same physicians reviewed the PET images, multisequence MR including the attenuation correction Dixon, and multisequence PET-MR fusion images (multisequence PET-MR). Both readers were blinded to the patients' identification data. For each rating, the readers were instructed to identify manifestations of lymphoma on a site-specific analysis: nodal groups included Waldeyer ring, right and left cervical, right and left axillary, right and left internal mammary, diaphragmatic, anterior mediastinal or paratracheal, right and left hilar, subcarinal or posterior mediastinal, celiac or superior mesenteric, hepatic and splenic hilar, retroperitoneal, inferior mesenteric, right and left iliac, and right and left inguinal regions. In addition, several extra nodal regions were analyzed, including lungs, liver, spleen, kidneys, thyroid, adrenal glands, bones, stomach, intestines, as well as other different organs and tissues. The lesions were further characterized based on their imaging MRI signal characteristics, size, maximum standardized uptake value (SUVmax), and malignant potency. The accuracy for the identification of active lymphoma disease was calculated and the tumor stage for each examination was determined. Finally, the nuclear medicine physician and radiologist performed a consensus read. The medical records of these patients including pathology results, treatment history, and radiology reports were reviewed.

Results

Of the 88 total studies included in this study, of which 40 were female studies (45%) and 48 male studies (55%). The age range of the study patients was 21 to 75 years with an average patient age of 43.8 ± 15.7 years. All 88 PET-MR studies were performed to evaluate systemic lymphoma, out of which 29 were diagnosed with diffuse large B cell lymphoma, 22 with Hodgkin's lymphoma, and 13 patients with Burkitt's lymphoma (►**Table 2**).

Out of the 88 studies, a total of 37 of the studies (42%) had metabolically active lymph nodes on multisequence PET-MR (►**Fig. 1**). The average SUVmax of the identified lesions was

Table 2 Lymphoma types and number

Burkitt's lymphoma	13
Follicular	5
Hodgkin's lymphoma	22
Mantle cell	1
Small cell	3
Large B cell lymphoma	39
Marginal zone	1
Anaplastic	1
Natural killer T cell	1
PTLD	2

Abbreviation: PTLD, post-transplant lymphoproliferative disorder

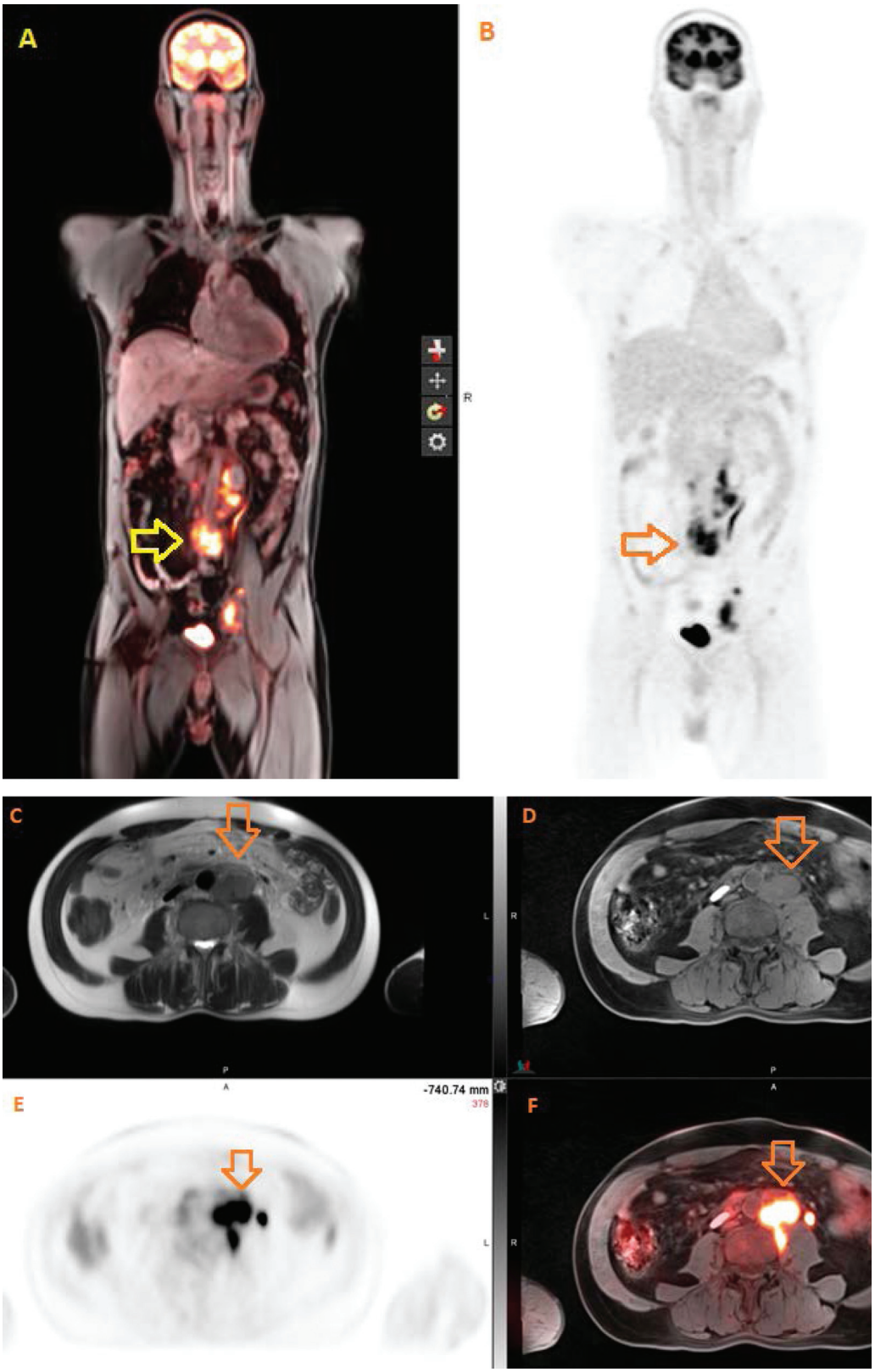

Fig. 1 A 47-year-old male with biopsy-proven diffuse large B cell lymphoma. (**A**) Water sequence of Dixon, coronal with positron emission tomography (PET) fusion demonstrating multiple, enlarged hypermetabolic retroperitoneal lymph node (*yellow arrow*). (**B**) Attenuation correction coronal, demonstrating the same hypermetabolic retroperitoneal lymph node (*orange arrows*). (**C**) T1 axial, enlarged retroperitoneal lymph nodes (*orange arrow*). (**D**) T2 fat-saturated axial, enlarged retroperitoneal lymph nodes (*orange arrow*). (**E**) PET axial, with hypermetabolic retroperitoneal lymph nodes. (**F**) T2 fat-saturated axial with PET fusion, demonstrating hypermetabolism associated with the enlarged retroperitoneal lymph nodes.

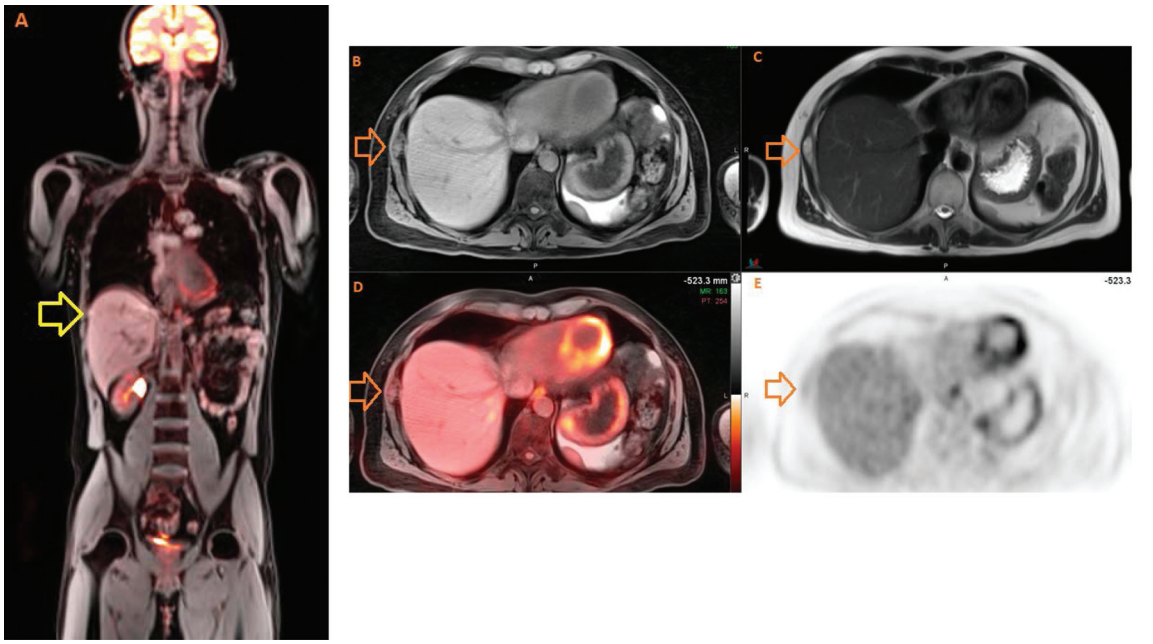

Fig. 2 A 37-year-old male with biopsy-proven Hodgkin's lymphoma. (**A**) Water sequence of Dixon, coronal with positron emission tomography (PET) fusion, demonstrating a subtle, enlarged perihepatic soft tissue lesion, initially missed on interpretation (*yellow arrow*). (**B**) T2 fat-saturated axial, perihepatic soft tissue lesion (**C**) T1 axial enlarged perihepatic soft tissue lesion. (**D**) T2 fat saturation with PET fusion, mild hypermetabolism associated with this lesion. (**E**) Axial PET images.

10.2 ± 7.74 SD (standard deviation). Dixon PET-MR identified 33 positive cases (89.2%) in patients, and did not identify 4 patients (10.8%) with metabolically active lymph nodes seen on multisequential PET-MR (►**Fig. 2**). These four cases all occurred in restaging studies showing low-level residual lymph node activity, described as "minimal residual activity" with an average SUVmax 2.3 ± 0.55 SD. Multisequence PET-MR identified 11 patients with enlarged lymph nodes greater than 1 cm in short axis diameter without FDG uptake, which were not seen on Dixon PET-MR. These enlarged lymph nodes were thought to reflect treated lesions.

When reviewing extranodal disease, there were five studies that demonstrated FDG active bones lesions that were identified by both the Dixon PET-MR and multisequence PET-MR with all lesions showing corresponding MR changes in both groups. The multisequence PET-MR identified 1 patient with a nonactive, healed bone lesion that was not seen on the Dixon PET-MR. There were additionally two other lesions of extranodal disease identified on both the Dixon and multisequence PET-MR. One metastatic lesion was in the lung parenchyma and another was in the thoracic paraspinal soft tissues.

Dixon PET-MR fusion demonstrated a sensitivity of 89.2% and specificity of 100% when compared with multisequence PET-MR. There were 55 true negative studies. There were no false positive cases in Dixon PET-MR fusion.

Discussion

FDG PET has been demonstrated to be useful in multiple studies in the staging and restaging of lymphoma. The principal advantage of PET over CT is the ability of PET to detect abnormal lymph nodes and extranodal disease before structure changes are seen.[10] PET imaging can upstage lymphoma, detect occult lesions within the spleen, bone, and gastrointestinal tracts that may be missed by CT or MR. PET has a high negative predictive value in the evaluation of bone marrow involvement compared with other imaging.[11] Another important feature of PET is the ability to quantify uptake using standardized uptake value, which can differentiate indolent from aggressive lymphomas and detect transformation of a low-grade tumor into an aggressive type.[12]

Osseous involvement of lymphoma is uncommon, but with advanced stage disease bone involvement can occur. The increased FDG activity is usually seen on PET imaging, but is considered nonspecific if no changes are seen on corresponding MRI or CT images, especially for marrow involvement. Multisequence MRI is more sensitive in identifying marrow infiltrative processes when compared with CT or PET imaging alone; however, many whole body PET-MR protocols have MR limited protocols.[13] Marrow infiltration on MRI is demonstrated by loss of normal fatty marrow signal on T1 imaging. Osseous involvement can be diffuse or focal, and when there is concern, biopsy is required for pathological confirmation. Despite the ability of MRI to evaluate osseous marrow, CT is still considered superior than MRI in the evaluation of cortical destruction.[14] In our study both the Dixon PET-MR and multi-sequence PET-MR detected the same number of bone lesions when all lesions showing MR changes on both the Dixon and multisequence images.

MRI is also superior to CT in evaluating abdominal and pelvic organs. Splenic lymphoma has a higher detection rate by MRI than CT. Splenic lesions demonstrate mild T2 hyperintensity, and mild T1 hypointense to mild T1 hyperintensity. Typically, these lesions do not enhance after intravenous

contrast administration, but they demonstrate increased FDG activity. For our study we did not detect any FDG avid lesion in the spleen. Although a nonspecific sign, the spleen is usually enlarged in size with involvement that can be detected on both the Dixon and multi-sequence PET-MR. Microscopically infiltrative lymphomatous involvement of the spleen would still be challenging to detect with both PET-MR and PET-CT.[15]

Primary lung lymphoma is rare, but secondary pulmonary involvement is not as infrequent. CT is still superior to MRI in evaluating the lung parenchyma, specifically in the detection of lung nodules, metastasis, and lymphomatous involvement. Pulmonary lymphoma when present can be detected by both PET/MR and PET/CT,[16] although more subtle cases depicted by interlobular septal thickening and ground glass densities can go undetected on MRI.[16] In the one patient we had with lung involvement in this study, both Dixon PET-MR and multisequence PET-MR detected the single lesion with PET playing the major role in delineating the lesion.

The diagnostic utility of PET/MRI for malignancy is considered higher than MRI alone.[17] The more dominant disadvantages that PET/MRI faces against PET/CT are of increased cost, increased scan time, limited availability, decreased familiarity, and limited evaluation of pulmonary parenchyma.[18–20]

Similar studies have been conducted in patients with known malignancies utilizing "fast PET/MRI protocols" compared with PET/CT.[21,22] The former article focused on pediatric patients, and the latter of the two articles demonstrated a very similar protocol to ours. Both of these studies specifically focused on patients with lymphoma. Other studies that also focused on lymphoma noted the Dixon sequences provided insufficient anatomical information due to the low spatial resolution.[23,24] This disparity in the literature intrigued us to conduct our own study.

Our study investigated the diagnostic potential of a fast protocol for integrated PET/MRI used for dedicated tumor staging of patients with lymphoma. Combining simultaneously obtained PET and MRI data for image interpretation enabled a significantly better diagnostic performance for the assessment of nodal manifestations of lymphoma. Studies comparing PET with PET/CT to date typically have shown a 4 to 15% improvement in overall accuracy of staging/restaging and a 30 to 50% improvement in the confidence of lesion localization.[10] The main contributing factor to this increase is the ability to anatomically locate the area of hypermetabolism. We suggest that specifically for lymphoma, a fast scan may be an acceptable alternative. In our study, the four lymph nodes that were not detected by the Dixon PET-MR had only minimal FDG uptake and unlikely would have any significant impact on the clinical decision.

Accurate staging of lymphoma patients is mandatory to identify tumor localizations, as well as disease extent, which provides important prognostic information and helps to select an appropriate treatment strategy.[25] Low-dose MRI sequences using the Dixon technique for interpretation can play a role in PET-MR imaging when scan time becomes important. This may be necessary in patients who receive anesthesia for their scans, have serious comorbidity, or claustrophobia.[26] The shorter imaging time may also give us the ability to perform other more complex multiplanar, multisequence dedicated MR of a particular area such as the neck or liver that would potentially add value to patient care without potentially increasing the total scan time. Our reviewers felt the attenuation correction Dixon only PET-MR sequences were easy to read that reduced the total read time for each study. In addition, a less experienced general nuclear medicine physician can easily interpret the Dixon PET-MR without consulting a MR trained specialist while feeling comfortable in providing a stage and diagnosis.

There were a few limitations of this study. First, we evaluated the utility of MR sequences in PET-MR comparing the Dixon and multisequence MR acquisition. For both studies, we used a 5-minute bed position time for PET. If a shorter sequence is required in the clinical setting, the PET acquisition time would also be shorter that would potentially result in a loss of resolution and less detectability. Another study would have to be done to compare lesion detectability with various image acquisition times in specific PET-MR cameras. This study had a small number of patients included in the study. A larger sample size would increase the power of our study. In addition, because of the smaller number of patients there was a mix of lymphoma subtypes. Subgroup analyses would have been desirable, yet, would not have been reasonable due to the limited patient numbers. Not all lesions had histopathological confirmation and PET-MR multisequence was considered the gold standard in this study. A prospective study with a larger sample size addressing these limitations would be necessary for confirmation of our results.

Conclusion

Dixon technique is shown to be sensitive and specific compared with multisequence PET-MR in the detection of lymphoma. The low number of cases not detected had minimally active lymph nodes that resolved on subsequent imaging and probably were not clinically important.

Funding
None.

Conflict of Interest
None declared.

References

1 Brent RL. Saving lives and changing family histories: appropriate counseling of pregnant women and men and women of reproductive age, concerning the risk of diagnostic radiation exposures during and before pregnancy. Am J Obstet Gynecol 2009;200(01):4–24
2 Frampas E. Lymphomas: basic points that radiologists should know. Diagn Interv Imaging 2013;94(02):131–144
3 Johnson SA, Kumar A, Matasar MJ, Schöder H, Rademaker J. Imaging for staging and response assessment in lymphoma. Radiology 2015;276(02):323–338
4 Siegel RL, Miller KD, Jemal A. Cancer statistics, 2017. CA Cancer J Clin 2017;67(01):7–30

5 Biko DM, Anupindi SA, Hernandez A, Kersun L, Bellah R. Childhood Burkitt lymphoma: abdominal and pelvic imaging findings. AJR Am J Roentgenol 2009;192(05):1304–1315
6 Toma P, Granata C, Rossi A, Garaventa A. Multimodality imaging of Hodgkin disease and non-Hodgkin lymphomas in children. Radiographics 2007;27(05):1335–1354
7 Jaimes C, Kirsch JE, Gee MS. Fast, free-breathing and motion-minimized techniques for pediatric body magnetic resonance imaging. Pediatr Radiol 2018;48(09):1197–1208
8 Arlachov Y, Ganatra RH. Sedation/anaesthesia in paediatric radiology. Br J Radiol 2012;85(1019):e1018–e1031
9 Wilder RT, Flick RP, Sprung J, et al. Early exposure to anesthesia and learning disabilities in a population-based birth cohort. Anesthesiology 2009;110(04):796–804
10 Moog F, Bangerter M, Diederichs CG, et al. Lymphoma: role of whole-body 2-deoxy-2-[F-18]fluoro-D-glucose (FDG) PET in nodal staging. Radiology 1997;203(03):795–800
11 Ngeow JYY, Quek RHH, Ng DCE, et al. High SUV uptake on FDG-PET/CT predicts for an aggressive B-cell lymphoma in a prospective study of primary FDG-PET/CT staging in lymphoma. Ann Oncol 2009;20(09):1543–1547
12 Bruzzi JF, Macapinlac H, Tsimberidou AM, et al. Detection of Richter's transformation of chronic lymphocytic leukemia by PET/CT. J Nucl Med 2006;47(08):1267–1273
13 Zhou HY, Gao F, Bu B, et al. Primary bone lymphoma: a case report and review of the literature. Oncol Lett 2014;8(04):1551–1556
14 Afaq A, Fraioli F, Sidhu H, et al. Comparison of PET/MRI with PET/CT in the evaluation of disease status in lymphoma. Clin Nucl Med 2017;42(01):e1–e7
15 Ricci ZJ, Kaul B, Stein MW, et al. Improving diagnosis of atraumatic splenic lesions, Part III: malignant lesions. Clin Imaging 2016;40 (05):846–855
16 Kim JH, Lee SH, Park J, et al. Primary pulmonary non-Hodgkin's lymphoma. Jpn J Clin Oncol 2004;34(09):510–514
17 Ehman EC, Johnson GB, Villanueva-Meyer JE, et al. PET/MRI: where might it replace PET/CT? J Magn Reson Imaging 2017;46 (05):1247–1262
18 Martin O, Schaarschmidt BM, Kirchner J, et al. PET/MRI versus PET/CT for whole-body staging: results from a single-center observational study on 1,003 sequential examinations. J Nucl Med 2020;61(08):1131–1136
19 Mayerhoefer ME, Prosch H, Beer L, et al. PET/MRI versus PET/CT in oncology: a prospective single-center study of 330 examinations focusing on implications for patient management and cost considerations. Eur J Nucl Med Mol Imaging 2020;47(01):51–60
20 Kirchner J, Sawicki LM, Suntharalingam S, et al. Whole-body staging of female patients with recurrent pelvic malignancies: ultra-fast 18F-FDG PET/MRI compared to 18F-FDG PET/CT and CT. PLoS One 2017;12(02):e0172553
21 Sher AC, Seghers V, Paldino MJ, et al. Assessment of sequential PET/MRI in comparison with PET/CT of pediatric lymphoma: a prospective study. AJR Am J Roentgenol 2016;206(03):623–631
22 Grueneisen J, Sawicki LM, Schaarschmidt BM, et al. Evaluation of a fast protocol for staging lymphoma patients with integrated PET/MRI. PLoS One 2016;11(06):e0157880. Doi: 10.1371/journal.pone.0157880
23 Jeong JH, Cho IH, Kong EJ, Chun KA. Evaluation of Dixon sequence on hybrid PET/MR compared with contrast-enhanced PET/CT for PET-positive lesions. Nucl Med Mol Imaging 2014;48(01):26–32
24 Cheson BD, Fisher RI, Barrington SF, et al; Alliance, Australasian Leukaemia and Lymphoma Group Eastern Cooperative Oncology Group European Mantle Cell Lymphoma Consortium Italian Lymphoma Foundation European Organisation for Research Treatment of Cancer/Dutch Hemato-Oncology Group Grupo Español de Médula Ósea German High-Grade Lymphoma Study Group German Hodgkin's Study Group Japanese Lymphorra Study Group Lymphoma Study Association NCIC Clinical Trials Group Nordic Lymphoma Study Group Southwest Oncology Group United Kingdom National Cancer Research Institute. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. J Clin Oncol 2014;32(27):3059–3068
25 Kim YW, Mansfield LT. Fool me twice: delayed diagnoses in radiology with emphasis on perpetuated errors. AJR Am J Roentgenol 2014;202(03):465–470
26 Braunstein S, Nakamura JL. Radiotherapy-induced malignancies: review of clinical features, pathobiology, and evolving approaches for mitigating risk. Front Oncol 2013;3:73. Doi: 10.3389/fonc.2013.00073

