Background:
Lymphoma is the commonest hematological malignancy in the world. The evaluation of bone marrow (BM) status is a key process in the initial workup of patients diagnosed with lymphoma. The BM is the most common site of extranodal involvement in lymphoid malignancies and the frequency of BM involvement varies according to the lymphoma subtype. Currently, noninvasive clinical staging by computed tomography (CT), or positron emission tomography (PET)-CT cannot fully assess BM involvement, which is possible only by pathological staging (aspiration and trephine biopsy). However, the invasive procedure is not indicated for fragile, critical illness patients and poor performance status patients. 18F-FDG PET / CT is used clinically for the determination of disease status in patients with lymphoma. However, the visual analysis of 18F-FDG diffuse bone marrow uptake in detecting bone marrow involvement (BMI) in routine clinical practice is still challenging.

Aims:
To create a machine learning algorithm of 18F-FDG PET/CT for identifying bone marrow involvement in lymphoma patients.

Methods:
Lymphoma patients underwent both bone marrow biopsy (BMB) and 18F-FDG PET/CT within one week were eligible. We took BMB results as the gold standard for bone marrow involvement. The bone marrow 18F-FDG uptake was visually diagnosed as positive and negative by two senior nuclear medicine experts. Totally, 1118 PET radiomic features were extracted to provide a more thoroughly understanding of the embedded pattern automatically. To select the most valuable and predictive features, an unsupervised consensus clustering method was first performed to analyze the feature correlations and then used to guide a random forest supervised machine learning model for feature importance analysis. We set 80% of PET images as training dataset and the rest as independent validation dataset. Cross-validation and independent validation were conducted to justify the performance of our model.

Results:
Totally, 529 consecutive lymphoma patients with 1,118 PET images were performed in this model. The representative example of deep learning detection showed at figure. In terms of bone marrow involvement images, 227 images were for training, 44 images and 51 images were for validation and test, respectively. As non-bone marrow involvement, 555 images were as training set, 84 images and 157 images were took as validation and test.

The sensitivity, specificity, and accuracy of visual analysis for BMI diagnosis were 63.6%, 68.7%, and 71.2%, respectively. With the cross-validation on the training group, the machine learning model correctly predicted 93/112 patients in BMI. The sensitivity, specificity, and accuracy of the machine learning model in BMI detection were 91.3%, 80.8%, and 83.3%, respectively, significantly higher than the ones in visual analysis (P < 0.05). The evaluation on the independent test group showed that the machine learning model could achieve 85.1% accuracy.
Summary/Conclusion:

18F-FDG PET/CT radiomic analysis with machine learning model provided a quantitative, objective and efficient mechanism for identifying BMI in the patients with suspected lymphoma. It is suggested in particular for the diagnosis of BMI in the patients with 18F-FDG diffuse uptake patterns. Our algorithm could provide a potential simply, non-inferior and rapid detection ability of lymphoma with bone marrow involvement to replace invasive bone marrow biopsy for patients who are ineligible for invasive procedure.