European Journal of Nuclear Medicine and Molecular Imaging (2019) 46:1240–1247
https://doi.org/10.1007/s00259-018-4195-9

ORIGINAL ARTICLE

Use of ^{18}F-FDG PET/CT texture analysis to diagnose cardiac sarcoidosis

Osamu Manabe[1] · Hiroshi Ohira[2] · Kenji Hirata[1] · Souichiro Hayashi[1] · Masanao Naya[3] · Ichizo Tsujino[2] · Tadao Aikawa[3] · Kazuhiro Koyanagawa[3] · Noriko Oyama-Manabe[4] · Yuuki Tomiyama[1] · Keiichi Magota[1] · Keiichiro Yoshinaga[5] · Nagara Tamaki[6]

Received: 25 July 2018 / Accepted: 10 October 2018 / Published online: 16 October 2018

Abstract

Purpose ^{18}F-fluorodeoxyglocose positron emission tomography (FDG PET) plays a significant role in the diagnosis of cardiac sarcoidosis (CS). Texture analysis is a group of computational methods for evaluating the inhomogeneity among adjacent pixels or voxels. We investigated whether texture analysis applied to myocardial FDG uptake has diagnostic value in patients with CS.

Methods Thirty-seven CS patients (CS group), and 52 patients who underwent FDG PET/CT to detect malignant tumors with any FDG cardiac uptake (non-CS group) were studied. A total of 36 texture features from the histogram, gray-level co-occurrence matrix (GLCM), gray-level run length matrix (GLRLM), gray-level zone size matrix (GLZSM) and neighborhood gray-level difference matrix (NGLDM), were computed using polar map images. First, the inter-operator and inter-scan reproducibility of the texture features of the CS group were evaluated. Then, texture features of the patients with CS were compared to those without CS lesions.

Results Twenty-eight of the 36 texture features showed high inter-operator reproducibility with intraclass correlation coefficients (ICCs) over 0.80. In addition, 17 of the 36 showed high inter-scan reproducibility with ICCs over 0.80. The SUVmax showed no difference between the CS and non-CS group [7.36 ± 2.77 vs. 8.78 ± 4.65, $p = 0.45$, area under the curve (AUC) = 0.60]. By contrast, 16 of the 36 texture features could distinguish CS from non-CS grsoup with AUC > 0.80. Multivariate logistic regression analysis after hierarchical clustering concluded that long-run emphasis (LRE; $P = 0.0004$) and short-run low gray-level emphasis (SRLGE; $P = 0.016$) were significant independent factors that could distinguish between the CS and non-CS groups. Specifically, LRE was significantly higher in CS than in non-CS (30.1 ± 25.4 vs. 11.4 ± 4.6, $P < 0.0001$), with high diagnostic ability (AUC = 0.91), and had high inter-operator reproducibility (ICC = 0.98).

Conclusions The texture analysis had high inter-operator and high inter-scan reproducibility. Some of texture features showed higher diagnostic value than SUVmax for CS diagnosis. Therefore, texture analysis may have a role in semi-automated systems for diagnosing CS.

Keywords FDG · PET · Cardiac sarcoidosis · Texture analysis

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00259-018-4195-9) contains supplementary material, which is available to authorized users.

✉ Kenji Hirata
khirata@med.hokudai.ac.jp

1 Department of Nuclear Medicine, Hokkaido University Graduate School of Medicine, N15 W7, Kita-Ku, Sapporo, Hokkaido 0608638, Japan

2 First Department of Medicine, Hokkaido University Hospital, Sapporo, Japan

3 Department of Cardiovascular Medicine, Hokkaido University Hospital, Sapporo, Japan

4 Department of Diagnostic and Interventional Radiology, Hokkaido University Hospital, Sapporo, Japan

5 Diagnostic and Therapeutic Nuclear Medicine, National Institute of Radiological Science, Chiba, Japan

6 Department of Radiology, Kyoto Prefectural University of Medicine, Kyoto, Japan

Abbreviations

CMV	Cardiac metabolic volume
CMA	Cardiac metabolic activity
DA	Descending aorta
FDG	^{18}F-fluorodeoxyglucose
HRS	Heart Rhythm Society
JSSOG	Japanese Society of Sarcoidosis and Other Granulomatous disorders
PET	Positron emission tomography
SUVmax	Maximum standardized uptake value
SUVmean	Mean standardized uptake value
VOI	Volume-of-interest

Introduction

^{18}F-fluorodeoxyglucose (FDG) PET plays a significant role in the diagnosis and assessment of cardiac sarcoidosis (CS) [1–3]. Cardiac involvement remains an important prognostic factor for sarcoidosis patients, and a definitive and accurate diagnosis is desired. There are several methods for assessing the activity of CS including objective and quantitative assessments using FDG PET [1, 4, 5].

Several approaches for evaluating FDG uptake in the diagnosis and management of CS have been reported. The popular approaches include visual assessment [4], semi-quantitative analysis using standardized uptake value (SUV) [6] and volume-based analyses using cardiac metabolic volume (CMV) and cardiac metabolic activity (CMA) [7, 8].

Recent studies have described that the heterogeneity of FDG uptake provides diagnostic and prognostic advantages in CS patients [9, 10]. Texture analysis is a group of computational methods that extracts information about relationships among adjacent/surrounding pixels (2D) or voxels (3D) and evaluates inhomogeneity [11, 12]. For malignant diseases, texture analysis based on FDG PET data has been reported as showing the ability to differentiate primary and nodal tumors from normal tissue [13].

However, it is not clear whether FDG PET-based texture analysis has diagnostic value in patients with CS. Thus, the aim of this study was to evaluate whether myocardial FDG texture analysis could add diagnostic value beyond the standard FDG diagnostic indices in the diagnosis of CS. We also assessed the effect of the metabolic volume on texture features because previous reports have suggested that texture features are subject to uncertainty in small volumes [11, 14].

Methods

Subjects

We prospectively analyzed patients who were diagnosed as CS based on Japanese Society of Sarcoidosis and Other Granulomatous disorders (JSSOG) guidelines (CS group) [1]. Thirty-seven consecutive patients without oral steroid treatment prior to the FDG PET/CT scan were included between May 2010 and April 2017.

For the control group (non-CS group), 100 consecutive patients who underwent an FDG PET/CT scan for evaluating malignant tumors in 2013 were retrospectively analyzed. All non-CS patients suffered from a malignant disease or had been treated for a malignant disease. The fasting duration was obtained from the patient interview record before FDG administration. Patients who were < 20 years old, patients whose imaging protocol was different, and patients without any uptake in the myocardium were excluded from the control group. This study protocol was approved by the ethics committee of the Hokkaido University Graduate School of Medicine.

FDG PET/CT imaging acquisition

All CS patients fasted overnight (for at least 18 h) preceded by a low-carbohydrate diet, with less than 5 g of carbohydrate per meal (along with a boiled egg, tofu with bonito flakes, and grilled chicken breast with stir-fried vegetables) [15]. Non-CS patients were instructed not to consume any food other than plain water for at least 6 h prior to the time of injection of FDG, with no special dietary preparation such as a low-carbohydrate meal. Approximately 4.5 MBq/kg (body weight) of FDG was administered intravenously. CS patients were positioned supine in the PET/CT scanner at either 60 min (first scan; 3 min/bed for whole-body imaging) or 75 min (second scan; 5 min/bed for thoracic region) after tracer injection (Fig. 1). Non-CS patients were scanned at 60 min after the administration of FDG. All PET/CT imaging was performed using a Biograph 64 TruePoint TrueV scanner (Siemens Japan, Tokyo). The acquired datasets were corrected for attenuation by low-dose CT images, and were reconstructed using a point spread function-based iterative algorithm (TrueX, Siemens) with two iterations per 21 subsets, a matrix size of 168 × 168, a voxel size of 4.1 × 4.1 × 2.0 mm, and a Gaussian filter at 4.0 mm full-width at half-maximum. The transaxial and axial fields of view were 58.5 and 21.6 cm, respectively.

PET/CT imaging analysis

Standard measurement and generating a polar map

We investigated the glucose metabolic status of the cardiac lesions using SUVmax as standard measurement, CMV, CMA and features from texture analysis. Each physician thoroughly reviewed the PET images and selected the FDG-avid areas in the left ventricle (LV) region. In cases where myocardial FDG uptake and non-myocardial FDG uptake in adjacent structures (such as mediastinal lymph nodes) were connected, non-myocardial parts were carefully delineated and excluded. SUV was calculated as [tissue radioactivity (Bq/mL)] × [body weight (g)] / [injected radioactivity (Bq)] [1]. SUVmax was defined as the maximum SUV within the volume of interest. CMV and CMA were quantified in the same manner as previously described [16]. Each physician determined the location of the LV apex and the angle of the axis, reslicing the volume image to generate short-axis images. The ellipsoid model was used to approximate LV with CT morphologic information [1]. Short-axis slices were divided into 36 sectors (i.e., 10 degree each) [17], and a 256 × 256 polar map matrix was reconstructed from short-axis slices extending 16 layers from the apex to the basal portion with a linear interpolation method (Fig. 2).

Texture analysis

The polar map was then processed to calculate the texture features. The SUV was resampled using 64 discrete values from the lowest to the highest SUV. We calculated all 36 texture features described by Orlhac et al. [11]. Briefly, 5 features were computed from a histogram. Four matrices, consisting of a gray-level co-occurrence matrix (GLCM), gray-level run length matrix (GLRLM), gray-level zone size matrix (GLZSM), and neighborhood gray-level difference matrix (NGLDM), were generated. Thirty-one features were computed from the 4 matrices. Finally, a total of 36 texture features were calculated. We developed PTexture package using Python to compute texture features. The entire source codes of PTexture are available at www.github.com/metavol/ptexture. Further detail regarding the texture analysis is provided in the supplementary documentation (supplemental data 1).

Study design

For the assessment of inter-operator variability, two different operators (O.M. and S.H.) independently obtained each feature from the whole-body scan (first scan). An additional thoracic region scan (second scan) was acquired by one operator (S.H.) in the 33 patients who had been originally assessed by that operator, to evaluate the inter-scan viability. Non-CS patients were assessed by one operator (O.M.) for the comparison between CS and non-CS groups. The two operators were blinded to the clinical information and outcomes after FDG PET/CT studies to avoid any possible bias.

Statistical analyses

Data are expressed as means ± standard deviations (SDs). A p value of <0.05 was considered significant except for texture features. A p value of 0.0014 (=0.05/36), as adjusted by Bonferroni correction, was used for the texture features. Inter-operator and inter-scan reproducibility were assessed using intra-class correlation coefficients (ICCs). The area under the curve from receiver operating characteristic (ROC) analysis, sensitivity and specificity were calculated for the ability of the parameters to discriminate between CS and non-CS groups. The Wilcoxon signed-rank test was used for inter-group comparisons. Fisher's exact test was used to compare discrete data. Heat map analysis with ascendant hierarchical clustering was performed to assess the association of each texture feature. After summarizing the clustering, the typical features that had the highest rate of cluster variation to explain the same group, were used for the multivariate logistic regression analysis to determine the independent factors among all the variables to distinguish between CS and non-CS. Statistical calculations were carried out using SAS (JMP ver. 13, SAS, Cary, NC, USA).

Results

Characteristics of CS and non-CS patients

Characteristics of CS and non-CS patients included in this study are shown in Table 1. For the non-CS group, patients <20 years old ($n = 3$), different imaging time ($n = 1$), and without any cardiac uptake ($n = 44$) were excluded from the study. Therefore, a total of 52 patients (62.5 ± 13.0 years old, 33 males) were included in the non-CS group. Non-CS patients included 9 patients suffering from malignant lymphoma, 2 from squamous cell carcinoma of unknown primary lesion, and 41 from malignant tumors of the following primary foci: lung, 9; thyroid, 6; colon, 5; skin, 3; pharynx, 3; uterus, 3; bone, 2; esophagus, 2; liver, 2; pancreas, 1; renal, 1; bile duct, 1; ear canal, 1; gastric, 1 and breast, 1. Eight patients had diabetes mellitus. Gender and age showed no significant differences between the CS and non-CS group. However, the fasting period was longer and the fasting blood glucose (FBG) was lower for the CS group compared to the non-CS group.

Inter-operator reproducibility

The SUVmax was completely identical between the operators (7.3 ± 2.9 vs 7.3 ± 2.9, $R^2 = 1.00$, ICC = 1.00, $p < 0.0001$), while CMV (43.1 ± 59.1 ml vs 41.2 ± 59.1 ml, $R^2 = 0.98$, ICC = 0.99, $p < 0.0001$) and CMA (155.7 ± 205.6 ml vs 150.4 ± 205.6 ml, $R^2 = 0.99$, ICC = 0.99, $p < 0.0001$) also

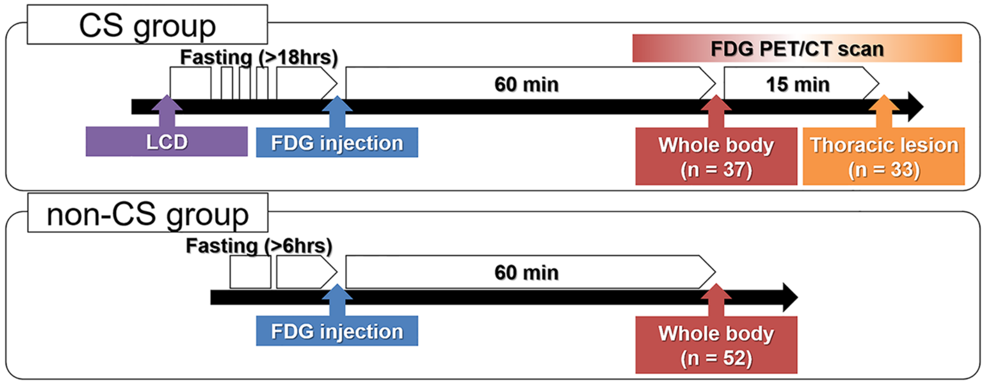

Fig. 1 FDG PET/CT imaging acquisition of cardiac sarcoidosis patients. The cardiac sarcoidosis (CS) group fasted for more than 18 h following a low-carbohydrate diet (LCD) preparation. The non-CS group fasted for over 6 h. Thirty-three of 37 CS patients were scanned twice for inter-scan reproducibility

showed high reproducibility (supplemental data 2). Regarding the texture features, 28 of 36 showed significantly high inter-operator reproducibility with ICC values over 0.80 (Fig. 3, supplemental data 2).

Inter-scan reproducibility

The SUVmean value of the blood pool measured in the descending aorta from the first scan was significantly higher than that from the second scan (1.7 ± 0.3 vs 1.6 ± 0.3, $p = 0.04$). The SUVmax, CMV and CMA from the first scan were 7.4 ± 3.1, 42.6 ± 63.2 ml and 153.4 ± 217.8 ml, respectively, and showed no significant differences from those of the second scan (7.2 ± 3.3, 47.0 ± 73.5 ml and 164.0 ± 244.6 ml, respectively). Seventeen of the 36 texture features showed significantly high inter-scan reproducibility with ICC values over 0.80 (supplemental data 3).

Distinction between CS and non-CS group

The SUVmax could not differentiate CS from non-CS patients (7.3 ± 2.9 vs 9.3 ± 4.9, $p = 0.10$). However, the CMV (43.1 ± 59.1 vs 136.3 ± 107.8 ml, $p = 0.0002$) and CMA (155.7 ± 205.6 vs 710.5 ± 666.6 ml, $p = 0.0001$) of the CS group were significantly smaller than those of the non-CS group. Almost all the texture parameters could distinguish CS from non-CS. AUC values from 16 of the 36 texture features showed high accuracy (AUC > 0.80) (supplemental data 4).

Hierarchical clustering brought similar PET features close to each other in the heat map chart, and 8 typical features were selected from 36 features (Fig. 3). Multivariate logistic regression analysis among these 8 features concluded that long-run emphasis (LRE; $P = 0.0004$) and short-run low gray-level emphasis (SRLGE; $P = 0.016$) were significant independent factors that could distinguish between CS and non-CS

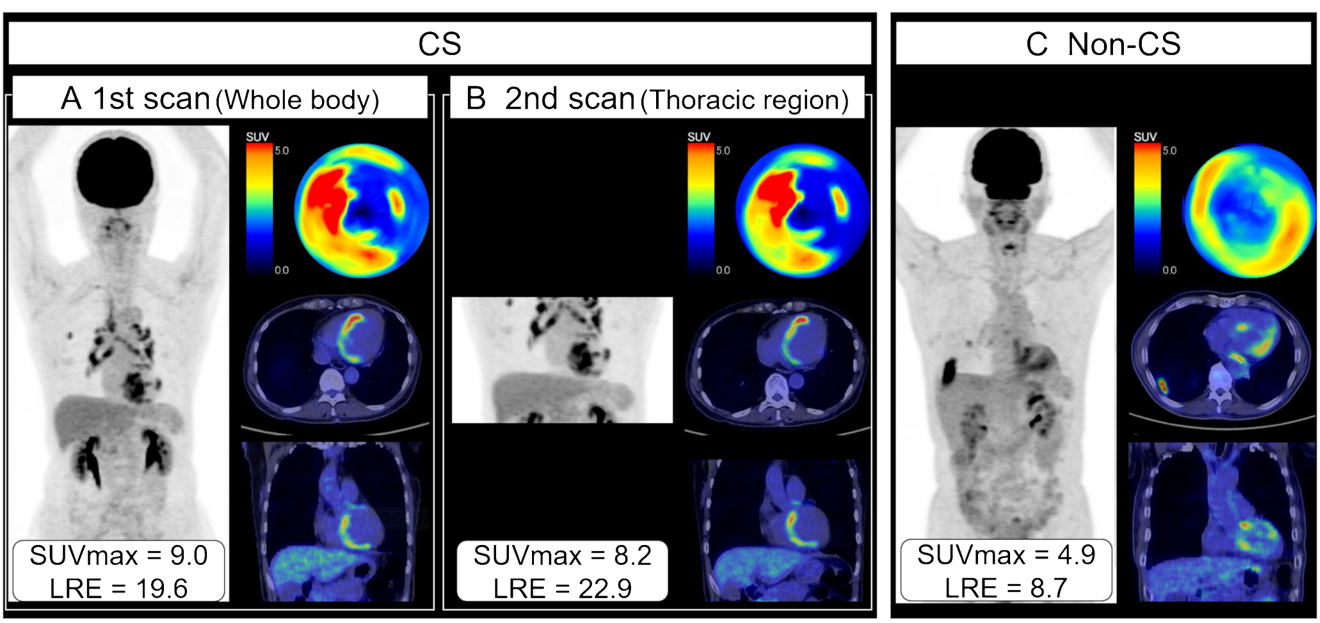

Fig. 2 Representative cases. Maximum intensity projection, polar map, PET/CT of axial and sagittal images of a cardiac sarcoidosis (CS) case at first (**a**) and second scans (**b**) and a non-CS case (**c**) are displayed, respectively. SUVmax values were 9.0, 8.2 and 4.9 for CS first scan, CS second scan and non-CS, respectively. Estimated long-run emphasis (LRE) values were 19.6, 22.9 and 8.7, respectively. Lung involvement and multiple uptakes at the mediastinal, hilar and right supraclavicular lymph nodes were also detected in the CS patient

Table 1 Patient characteristics

	CS group ($n = 37$)	non-CS group ($n = 52$)	p value
Gender (male/female)	16/21	30/22	0.18
Age	59.7 ± 14.9	62.5 ± 13.0	0.57
Fasting time (hour)	20.5 ± 1.5	14.0 ± 3.4	< 0.0001
FBG (mg/dl)	89.8 ± 13.8	113.0 ± 20.3	< 0.0001
Meets JSSOG criteria	37 (100%)	0 (0%)	
Injection dose (MBq)	251.3 ± 38.9	243.7 ± 58.1	0.42

CS cardiac sarcoidosis, *FBG* fasting blood glucose, *JSSOG* Japanese Society of Sarcoidosis and Other Granulomatous disorders

Table 2 Multivariate logistic regression analysis

	Likelihood ratio	p value
RLNU	1.8	0.19
LRE	12.7	0.0004
SRLGE	5.8	0.016
HGRE	3.0	0.081
Correlation	0.17	0.68
SZHGE	0.9	0.34
LZHGE	0.2	0.69
SZE	0.4	0.54

RLNU run-length non-uniformity, *LRE* long-run emphasis, *SRLGE* short-run low gray-level emphasis, *HGRE* high gray-level run emphasis, *SZHGE* short-zone high gray-level emphasis, *LZHGE* long-zone high gray-level emphasis, *SZE* short-zone emphasis

(Table 2). In specific, LRE was significantly higher in the CS than in the non-CS group (30.1 ± 25.4 vs. 11.4 ± 4.6, $P < 0.0001$), with high diagnostic ability (AUC = 0.91), and had high inter-operator reproducibility (ICC = 0.98) (Fig. 4).

There was no significant difference in the frequency of patients with CMV over 10 ml in the CS (27/37) and non-CS groups (44/52) ($P = 0.19$). When patients were divided into CMV > 10 ml and CMV ≤ 10 ml groups, LRE was still significantly different in the CS ($n = 27$) and the non-CS ($n = 44$) patients (27.3 ± 15.9 vs. 10.8 ± 4.0, $p < 0.0001$) with CMV > 10 ml. Likewise, in patients with CMV ≤ 10 ml, LRE was still significantly different in the CS ($n = 10$) and non-CS ($n = 8$) groups (37.8 ± 42.0 vs 14.6 ± 6.6, $p = 0.013$).

Discussion

We investigated whether texture analysis applied to myocardial FDG uptake has diagnostic value for CS. The estimated textural features on FDG PET showed high reproducibility and diagnostic value. Texture parameters may be useful for characterizing the heterogeneity of myocardial FDG uptake in CS compared to the less heterogeneous, physiological FDG uptake in the non-CS group. The current results suggest the potential application of this method to fully automated diagnosis in the future.

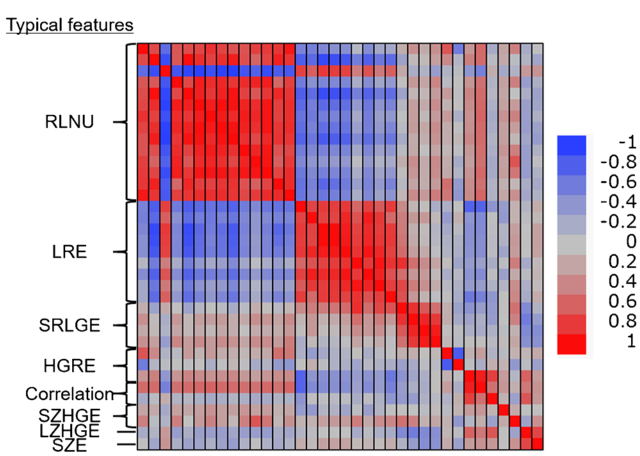

Fig. 3 Heat map chart with texture feature diagram. The heat map chart was generated in the colour scale of blue to red through gray. Thirty-six texture features were divided into 8 groups. The representative features are selected as RLNU, LRE, SRLGE, HGRE, LZHGE, SZE and SZHGE. Abbreviations are the same as in Table 2

FDG PET plays an important role in CS patients' diagnosis, management, and treatment monitoring [5]. The use of the SUVmax is a common semi-quantitative method in clinical practice for establishing diagnosis, evaluating disease activity and monitoring response to therapy [6, 18]. However, the SUVmax reflects the value of a single voxel and thus does not account for the entire distribution of a target lesion's metabolism [1]. Volume-based analyses of parameters measured by FDG PET such as CMV and CMA have been used as assessment tools to guide the titration of immunosuppressive therapy and predict cardiac events [7, 8]. In our study, CMV and CMA were significantly different between the CS and non-CS group. However, there was a certain overlap in the distribution. Physiological FDG uptake in the LV wall is not restricted to diffuse uptake; therefore, distinguishing between physiological and inflammatory lesions is sometimes difficult [4, 16, 19]. Quantitative evaluation of heterogeneity of FDG uptake has shown diagnostic and prognostic advantages in CS patients [9, 10]. CS tissue in the myocardium shows heterogeneity, both macroscopically and microscopically [20]. FDG PET/CT is a favorable tool for noninvasive exploration of intra-disease heterogeneity based on spatial distribution of uptake. Sperry et al. reported that the heterogeneity of myocardial FDG uptake, represented using coefficient of variance (CoV), provided a prognostic marker of adverse cardiac events [10].

Texture analysis is a group of computational methods that can quantify the inhomogeneity between adjacent pixels or voxels [11]. The application of texture analysis in morphological imaging such as magnetic resonance and CT has expanded since the early 1990s [21, 22]. The measurement of texture

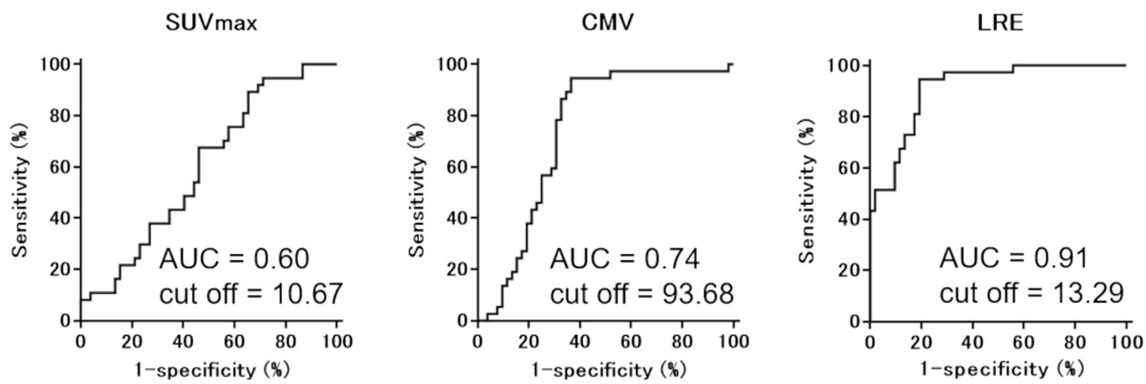

Fig. 4 ROC curves. The area under the curve (AUC) value of long-run emphasis (LRE) from texture analysis was significantly higher than those from SUVmax and cardiac metabolic volume (CMV)

indices from FDG PET images to assess intra-tumor heterogeneity has been proposed as a measure that might distinguish between malignant and benign tumors and predict tumor response to therapy and prognosis [23].

When it comes to cardiac lesions, texture analysis has already been applied to magnetic resonance imaging (MRI) [24, 25]. Larroza et al. attempted to apply texture analysis to late gadolinium enhancement MRI and cine MRI of the heart. They concluded that texture analysis could be used to distinguish between acute myocardial infarction and chronic myocardial infarction [25]. To the best of our knowledge, this is the first report to extend the concept of the FDG PET texture analysis to cardiac disease evaluation. Although FDG PET/CT images suffer from modest spatial resolution, it has been hypothesized that a polar map distribution could bring more insight into lesion heterogeneity than SUVmax or metabolic volume. In our results, some of the texture features showed high inter-operator and inter-scan reproducibility and were capable of distinguishing CS from non-CS patients. In our result, LRE was a significant indicator that could distinguish CS from non-CS patients with high inter-operator and diagnostic abilities. LRE measures the distribution of long homogeneous runs; a higher value indicates coarse textures. Therefore, this result indicated that the CS group and non-CS group had significantly different homogeneous uptake patterns.

The determination of which texture features are most useful for diagnosis may depend on the target disease. There are several proposals to differentiate disease using texture analysis [26]. For malignant tumors, Orlhac et al. indicated that homogeneity, entropy, short-run emphasis (SRE), LRE, low gray-level zone emphasis (LGZE), and high gray-level zone emphasis (HGZE) were the most robust with respect to the segmentation method in each texture correlation group [11]. Our results showed that LRE was a significant independent factor that could distinguish between CS and non-CS with high inter-operator reproducibility (ICC = 0.98) and high diagnostic ability (AUC = 0.91), making it especially useful in a clinical setting. In the current study, LRE showed a significant difference between CS and non-CS for both the large and small CMV (CMV > 10 ml vs. ≤ 10 ml) patient groups. Previous studies have suggested that texture features are difficult to use when the active volume is small, especially less than 10 ml [11, 14]. In our study, the texture features were assessed using the same matrix size with a polar map. Therefore, the metabolic volume might not be associated with the ability of LRE to differentiate between CS and non-CS under these conditions.

Limitations

This study has some methodological limitations. In this study, all the patients were scanned without respiratory or electrocardiogram gating. The effects of respiratory or cardiac motion were not investigated. However, PET studies of lung cancer have reported that texture parameters might be affected by respiratory motion [27, 28]. There has been no report comparing texture parameters with and without electrocardiogram gating. Our study did not determine the effect of gating; therefore, further clinical investigations into this issue are warranted. Also, at our institution, fasting for more than 18 h preceded by a low-carbohydrate meal has become the standard pre-scan protocol for assessing cardiac sarcoidosis by FDG PET, to reduce physiological LV uptake [15]. Therefore, the fasting conditions were not the same between the CS and non-CS groups and are reflected in the different FBG values for the two groups. Multivariate logistic regression analysis showed that LRE and SRLGE were significant predictors even including FBG (supplemental data 5). However, further prospective studies with the same imaging protocol will be needed to investigate this issue.

Conclusions

We conducted a texture analysis for cardiac FDG uptake that showed high inter-operator and high inter-scan reproducibility.

Some texture features showed higher diagnostic value than SUVmax in discriminating CS from non-CS. Therefore, texture analysis may have a role in future semi-automated systems for diagnosing CS.

Acknowledgements We thank Eriko Suzuki, MT for her support of this study.

Compliance with ethical standards

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the principles of the 1964 Declaration Helsinki and its later amendments or comparable ethical standards.

Conflict of interest All authors have no conflicts of interest to disclose.

Informed consent Written informed consent was obtained prior to the study for the CS patients and with a waiver of the need for written informed consent for the control group.

References

1. Manabe O, Ohira H, Yoshinaga K, Naya M, Oyama-Manabe N, Tamaki N. Qualitative and quantitative assessments of cardiac sarcoidosis using 18F-FDG PET. Ann Nucl Cardiol. 2017;3:117–20.
2. Chareonthaitawee P, Beanlands RS, Chen W, et al. Joint SNMMI-ASNC expert consensus document on the role of (18)F-FDG PET/CT in cardiac sarcoid detection and therapy monitoring. J Nucl Cardiol. 2017;24:1741–58.
3. Terasaki F, Yoshinaga K. New guidelines for diagnosis of cardiac sarcoidosis in Japan. Annals of Nuclear Cardiology. 2017;3:42–5.
4. Ohira H, Mc Ardle B, deKemp R, et al. Inter- and intra- observer agreement of FDG-PET/CT image interpretation in patients referred for assessment of cardiac sarcoidosis. J Nucl Med. 2017;58:1324–9.
5. Yoshinaga K, Manabe O, Ohira H, Tamaki N. Focus issue on cardiac sarcoidosis from international congress of nuclear cardiology and cardiac CT(ICNC 12) symposium: improving the detectability of cardiac sarcoidosis—practical aspects of 18F- fluorodeoxyglucose positron emission tomography imaging for diagnosis of cardiac sarcoidosis—. Ann Nucl Cardiol. 2015;1:87–94.
6. Yokoyama R, Miyagawa M, Okayama H, et al. Quantitative analysis of myocardial 18F-fluorodeoxyglucose uptake by PET/CT for detection of cardiac sarcoidosis. Int J Cardiol. 2015;195:180–7.
7. Osborne MT, Hulten EA, Singh A, et al. Reduction in (1)(8)F-fluorodeoxyglucose uptake on serial cardiac positron emission tomography is associated with improved left ventricular ejection fraction in patients with cardiac sarcoidosis. J Nucl Cardiol. 2014;21:166–74.
8. Ahmadian A, Brogan A, Berman J, et al. Quantitative interpretation of FDG PET/CT with myocardial perfusion imaging increases diagnostic information in the evaluation of cardiac sarcoidosis. J Nucl Cardiol. 2014;21:925–39.
9. Schildt JV, Loimaala AJ, Hippelainen ET, Ahonen AA. Heterogeneity of myocardial 2-[18F]fluoro-2-deoxy-D-glucose uptake is a typical feature in cardiac sarcoidosis: a study of 231 patients. Eur Heart J Cardiovasc Imaging. 2018;19:293–8.
10. Sperry BW, Tamarappoo BK, Oldan JD, et al. Prognostic impact of extent, severity, and heterogeneity of abnormalities on 18F-FDG PET scans for suspected cardiac sarcoidosis. JACC Cardiovasc Imaging. 2018;11:336–45.
11. Orlhac F, Soussan M, Maisonobe JA, Garcia CA, Vanderlinden B, Buvat I. Tumor texture analysis in 18F-FDG PET: relationships between texture parameters, histogram indices, standardized uptake values, metabolic volumes, and total lesion glycolysis. J Nucl Med. 2014;55:414–22.
12. Orlhac F, Theze B, Soussan M, Boisgard R, Buvat I. Multiscale texture analysis: from 18F-FDG PET images to histologic images. J Nucl Med. 2016;57:1823–8.
13. Yu H, Caldwell C, Mah K, et al. Automated radiation targeting in head-and-neck cancer using region-based texture analysis of PET and CT images. Int J Radiat Oncol Biol Phys. 2009;75:618–25.
14. Hatt M, Majdoub M, Vallieres M, et al. 18F-FDG PET uptake characterization through texture analysis: investigating the complementary nature of heterogeneity and functional tumor volume in a multi-cancer site patient cohort. J Nucl Med. 2015;56:38–44.
15. Manabe O, Yoshinaga K, Ohira H, et al. The effects of 18-h fasting with low-carbohydrate diet preparation on suppressed physiological myocardial (18)F-fluorodeoxyglucose (FDG) uptake and possible minimal effects of unfractionated heparin use in patients with suspected cardiac involvement sarcoidosis. J Nucl Cardiol. 2016;23:244–52.
16. Manabe O, Kroenke M, Aikawa T, et al. Volume-based glucose metabolic analysis of FDG PET/CT: the optimum threshold and conditions to suppress physiological myocardial uptake. J Nucl Cardiol. 2017. https://doi.org/10.1007/s12350-017-1122-6.
17. Yamagishi H, Akioka K, Hirata K, et al. A reverse flow-metabolism mismatch pattern on PET is related to multivessel disease in patients with acute myocardial infarction. J Nucl Med. 1999;40:1492–8.
18. Mc Ardle BA, Birnie DH, Klein R, et al. Is there an association between clinical presentation and the location and extent of myocardial involvement of cardiac sarcoidosis as assessed by (1)(8)F-fluorodoexyglucose positron emission tomography? Circ Cardiovasc Imaging. 2013;6:617–26.
19. Ito K, Okazaki O, Morooka M, Kubota K, Minamimoto R, Hiroe M. Visual findings of (18)F-fluorodeoxyglucose positron emission tomography/computed tomography in patients with cardiac sarcoidosis. Intern Med. 2014;53:2041–9.
20. Tavora F, Cresswell N, Li L, Ripple M, Solomon C, Burke A. Comparison of necropsy findings in patients with sarcoidosis dying suddenly from cardiac sarcoidosis versus dying suddenly from other causes. Am J Cardiol. 2009;104:571–7.
21. Mir AH, Hanmandlu M, Tandon SN. Texture analysis of CT-images for early detection of liver malignancy. Biomed Sci Instrum. 1995;31:213–7.
22. Schad LR, Bluml S, Zuna I. MR tissue characterization of intracranial tumors by means of texture analysis. Magn Reson Imaging. 1993;11:889–96.
23. Hatt M, Tixier F, Pierce L, Kinahan PE, Le Rest CC, Visvikis D. Characterization of PET/CT images using texture analysis: the past, the present... Any future? Eur J Nucl Med Mol Imaging. 2017;44:151–65.
24. Baessler B, Mannil M, Oebel S, Maintz D, Alkadhi H, Manka R. Subacute and Chronic left ventricular myocardial scar: accuracy of texture analysis on nonenhanced cine MR images. Radiology. 2018;286:103–12.
25. Larroza A, Materka A, Lopez-Lereu MP, Monmeneu JV, Bodi V, Moratal D. Differentiation between acute and chronic myocardial infarction by means of texture analysis of late gadolinium enhancement and cine cardiac magnetic resonance imaging. Eur J Radiol. 2017;92:78–83.

26. Papp L, Poetsch N, Grahovac M, et al. Glioma survival prediction with the combined analysis of in vivo 11C-MET-PET, ex vivo and patient features by supervised machine learning. J Nucl Med. 2018;59:892–9.
27. Yip S, McCall K, Aristophanous M, Chen AB, Aerts HJ, Berbeco R. Comparison of texture features derived from static and respiratory-gated PET images in non-small cell lung cancer. PLoS One. 2014;9:e115510.
28. Oliver JA, Budzevich M, Zhang GG, Dilling TJ, Latifi K, Moros EG. Variability of image features computed from conventional and respiratory-gated PET/CT images of lung cancer. Transl Oncol. 2015;8:524–34.