

# Texture analysis of conventional magnetic resonance imaging and diffusion-weighted imaging for distinguishing sinonasal non-Hodgkin's lymphoma from squamous cell carcinoma

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## Research Article

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# Abstract

**Background:** To evaluate the value of texture analysis (TA) of conventional magnetic resonance imaging (MRI) and diffusion-weighted imaging (DWI) in the differential diagnosis between sinonasal non-Hodgkin's lymphoma (NHL) and squamous cell carcinoma (SCC).

**Methods:** Twenty-one patients with sinonasal SCC and 15 patients with NHL were retrospectively enrolled. TAs were performed on T2-weighted image (T2WI), apparent diffusion coefficient (ADC) and contrast-enhanced T1-weighted image (T1WI). Texture parameters, including mean value, skewness, kurtosis, entropy and uniformity were obtained and compared between sinonasal SCC and NHL groups. Receiver operating characteristic (ROC) curves and logistic regression analyses were used to evaluate the diagnostic value and identify the independent TA parameters.

**Results:** The mean value and entropy of ADC, and mean value of contrast-enhanced T1WI were significantly lower in the sinonasal NHL group than those in the SCC group (all  $P < 0.05$ ). ROC analysis indicated that the entropy of ADC had the best diagnostic performance (AUC, 0.832; Sensitivity, 0.95; Specificity, 0.67; Cut-off value, 6.522). Logistic regression analysis showed that the entropy of ADC ( $P = 0.002$ , OR = 26.990) was the independent parameter for differentiating sinonasal NHL from SCC.

**Conclusion:** TA parameters of conventional MRI and DWI, particularly the entropy value of ADC, might be useful in the differentiating diagnosis between sinonasal NHL and SCC.

## Background

Sinonasal non-Hodgkin's lymphoma (NHL) and squamous cell carcinoma (SCC) are the two most common sinonasal malignancies [1, 2]. Surgery is the first-line treatment strategy for patients with sinonasal SCC, while combination of radiotherapy and chemotherapy is usually suggested for patients with sinonasal NHL [3]. Therefore, accurate differential diagnosis between NHL and SCC is crucial for establishing individual treatment regimens. Differential diagnosis based on the clinical symptoms is quite difficult, because of that these two kinds of tumors can have mimicking symptoms, such as localized pain, nasal obstruction, epistaxis, unilateral facial or nasal swelling, nasal discharge, and headache [4]. Thus, to find a simple and effective method for establishing a accurate differential diagnosis is urgently needed in clinical practise.

Preoperative computed tomography (CT) and magnetic resonance imaging (MRI) are commonly used for the non-invasive assessment of sinonasal tumors [5–7]. Sinonasal NHL and SCC often share similar imaging characteristics, thus result in the poor diagnostic accuracy of conventional structural images features [5]. Recently, several studies have demonstrated that the mean apparent diffusion coefficient (ADC), which allows the characterization of water molecules diffusion in tumor tissues, might be helpful in distinguishing sinonasal NHL from SCC [6–9]. However, the mean ADC value is the average value of whole regions of interest (ROIs) in tumor tissues, which does not reveal the heterogeneity of tumor tissues.

Texture analysis (TA) which characterizes an image by analyzing the distribution and relationship of pixel gray levels, has attracted more and more attention [10]. It provides more objective and quantitative information regarding tumor heterogeneity beyond visual inspection [10]. TA has demonstrated its superiority in differentiating and grading tumors, or predicting treatment response in various diseases [10–12]. However, to the best of our knowledge, no study has applied TA of MRI to differentiate sinonasal NHL from SCC until now.

Therefore, the purpose of our study is to evaluate the value of TA of conventional MRI and DWI in the differential diagnosis between sinonasal NHL and SCC.

## Methods

### Patients

This study was approved by our institutional review board, and informed consents were obtained from all patients before MRI examinations. We included the patients who: (1) had no previous history of biopsy, surgery or any other treatment; (2) underwent conventional MRI and DWI for pre-treatment evaluation of sinonasal tumors; (3) had an adequate MRI quality without motion and susceptibility artifacts; (4) had a final pathological diagnosis of sinonasal SCC or NHL. Finally, a total of 21 patients (male: female = 11:10; mean age,  $61.4 \pm 12.7$  years) with sinonasal SCC and 15 patients (male: female = 8:7; mean age,  $59.9 \pm 17.9$  years) with sinonasal NHL (9 with NK/T lymphoma, 6 with diffuse large B cell lymphoma) were included.

### MRI scan

MRI was performed using a 3T scanner (Verio, Siemens Healthcare Sector, Erlangen, Germany) with a 12-channel head and neck coil. MRI protocol included the following sequences: unenhanced axial T1-weighted imaging (TR/TE = 811/7.1 ms, section thickness = 4 mm, field of view [FOV] = 220×220 mm, matrix = 384×384); axial T2-weighted imaging with fat saturation (TR/TE = 4000/87 ms, section thickness = 4 mm, FOV = 220×220 mm, matrix = 384×384); coronal T2-weighted imaging (TR/TE = 3800/88 ms, section thickness = 4 mm, FOV = 220×220 mm, matrix = 384×384), and contrast-enhanced axial T1-weighted imaging (CE-T1WI) (TR/TE = 811/7.1ms, section thickness = 4mm, FOV = 220×220mm, matrix = 384×384). For CE-T1WI, a standard dose of 0.1 mmol/kg of gadolinium-diethylene triamine pentaacetic acid (Omniscan, GE Healthcare, Dublin, Ireland) was administrated at a rate of 4 mL/s, followed by a 20 mL normal saline

Readout-segmented echo planar imaging sequence (RESOLVE) was used for DWI scan. Detailed imaging parameters were showed as follows: diffusion schema, Stejskal–Tanner; fat suppression, frequency selective; b values, 0 and 1000 s/mm<sup>2</sup>; orthogonal directions, 3; TR/TE, 5060/76 ms; slice number, 20; number of excitations, 1; FOV, 220×220mm; slice thickness, 4 mm without gap; matrix, 224×224; phase-encoding direction, anteroposterior; echo spacing, 0.4 ms; number of readout segments, 5. Total acquisition time of DWI based on RESOLVE technique was 2 min 45 s.

## Image Analyses

MR images were analyzed by two radiologists (with 7 and 3 years of experience in head and neck radiology, respectively) who were blinded to the study design and pathological information. T2WI and ADC map were registered to the CE-T1WI. ROIs were manually drawn in dedicated image processing software (FireVoxel; CAI2R; New York University, NY) with a filtration-histogram approach [13]. Tumor ROIs were manually delineated around all the slices on T2WI, ADC and CE-T1WI (**Figure 1**). Three-dimensional (3D) volumes of interest (VOIs) were constructed by summing ROIs drawn in each section. Large necrotic, cystic or hemorrhagic areas were carefully avoided with reference to T2WI and CE-T1WI. Lastly, volumetric regions were isotropically resampled to the in-plane resolution (voxel size = 1×1×1 mm) using cubic interpolation to ensure the conservation of scales and directions when deriving the 3D features [14]. After the VOIs were placed, following quantitative texture parameters were automatically obtained: mean value, skewness, kurtosis, uniformity, energy and entropy, which are based on histogram analysis and the gray-level co-occurrence matrix (GLCM) method [15].

## Statistical analyses

Numeric data were averaged over all patients, and reported as mean ± standard deviation. Data normality was tested by using the Kolmogorov–Smirnov test. Fisher’s exact test was applied to assess the difference of binary variables between two groups. Texture parameters were compared between two groups using unpaired Student’s t-test or Manne-Whitney U-test as appropriate. Receiver operating characteristic (ROC) curves were performed to assess the performance of each significant texture parameter in the differential diagnosis between sinonasal NHL and SCC. Area under the ROC curve (AUC), sensitivity, and specificity were calculated. All of the significant TA parameters were stepped into a multivariate logistic regression analysis to identify the independent parameter for differentiating sinonasal NHL from SCC. Inter-reader agreement was evaluated using intra-class correlation coefficient (ICC) with 95% confidence intervals, and classified as excellent (ICC ≥ 0.81), good (ICC = 0.61-0.80), moderate (ICC = 0.41-0.60), and poor (ICC < 0.40). All statistical analyses were performed by using MedCalc (version 13.0; Mariakerke, Belgium) and SPSS (version 24.0; IBM Corp., Armonk, NY, USA). A two-sided P value less than 0.05 was considered to be statistically significant.

## Results

There were no significant differences in patients gender (P = 0.995) and age (P = 0.778) between sinonasal NHL and SCC groups. Excellent inter-reader agreements were achieved in the measurement of TA parameters (ICC, 0.819–0.855). Detailed TA parameters of T2WI, ADC, and CE-T1WI are summarized in Table 1. There was no significant difference in all TA parameters derived from T2WI between two groups (all P > 0.05). As to the TA parameters from ADC, the mean value and entropy of ADC were lower in the sinonasal NHL group than those in the SCC group (P = 0.024, P = 0.001, respectively). As to the TA parameters from CE-T1WI, the mean value of CE-T1WI were higher in the SCC group (P = 0.008) than that in the NHL group (Fig. 2).

Table 1  
Comparison of texture parameters between sinonasal SCC and NHL

Parameters		SCC	NHL	P
T2WI	mean value	993.253 ± 163.565	640.480 ± 85.526	0.066
	skewness	0.048 ± 0.098	-0.176 ± 0.125	0.163
	kurtosis	1.069 ± 0.215	1.467 ± 0.339	0.303
	uniformity	0.825 ± 0.011	0.823 ± 0.022	0.931
	energy	0.011 ± 0.001	0.012 ± 0.001	0.210
	entropy	6.827 ± 0.053	6.710 ± 0.101	0.314
	ADC	mean value	0.846 ± 0.035	0.708 ± 0.049
skewness		0.466 ± 0.144	0.619 ± 0.193	0.521
kurtosis		2.029 ± 0.385	2.961 ± 0.897	0.351
uniformity		0.781 ± 0.014	0.7601 ± 0.017	0.352
energy		0.011 ± 0.001	0.013 ± 0.001	0.321
entropy		6.850 ± 0.056	6.121 ± 0.174	0.001
CE-T1WI		mean value	1589.549 ± 181.250	1009.407 ± 90.155
	skewness	-0.086 ± 0.082	-0.007 ± 0.091	0.527
	kurtosis	0.465 ± 0.184	-0.004 ± 0.179	0.086
	uniformity	0.853 ± 0.008	0.819 ± 0.016	0.050
	energy	0.009 ± 0.000	0.008 ± 0.000	0.173
	entropy	7.046 ± 0.067	7.167 ± 0.055	0.203
	Note: SCC indicates squamous cell carcinoma; NHL, non-Hodgkin's lymphoma; T2WI, T2-weighted image; ADC, apparent diffusion coefficient; CE-T1WI, contrast-enhanced T1-weighted image.			

The results of ROC analysis are shown in Table 2. The optimal TA parameter alone was the ADC-entropy, which yielded an AUC, sensitivity and specificity of 0.832, 95.2% and 66.7%, respectively (Fig. 3). Logistic regression analysis showed that ADC-entropy (P = 0.002, OR = 26.990) was the independent parameter for differentiating sinonasal NHL from SCC. Representative cases of sinonasal NHL and SCC are shown in Fig. 4.

Table 2

Performance of significant texture analysis parameters in the differential diagnosis between sinonasal SCC and NHL.

Parameters	Area under curve (95% CI)	P	Sensitivity (%)	Specificity (%)	cut-off
ADC-mean value	0.711 (0.524–0.898)	0.033	90.5	60	0.662
ADC-entropy	0.832 (0.695–0.969)	0.001	95.2	66.7	6.522
CE-T1WI-mean value	0.740 (0.576–0.903)	0.015	85.7	60	887.436

Note: SCC indicates squamous cell carcinoma; NHL, non-Hodgkin's lymphoma; ADC, apparent diffusion coefficient; CE-T1WI, contrast-enhanced T1-weighted image.

## Discussion

Due to its close relationship with individual treatment strategy, the differential diagnosis between sinonasal NHL and SCC was always one important clinical and research topic. As to conventional CT and MRI features, previous studies reported that bony erosion, tumor necrosis and soft tissue invasion might be useful for differential diagnosis [6, 7]. However, semi-quantitative assessment of imaging features was a subjective process, and the underlying information beyond the imaging was not fully excavated. As a promising approach, TA can provide more objective and quantitative information regarding tumor heterogeneity beyond visual inspection [10]. Therefore, in present study, we aimed to evaluate the performance of TA of ADC map and conventional MRI in differentiating sinonasal NHL from SCC. As a result, we found significant differences in ADC-mean value, ADC-entropy and CE-T1WI-mean value between two groups. Meanwhile, ADC-entropy might be the most promising parameter in the diagnosis of sinonasal NHL from SCC.

In present study, we found that there was no significant difference in those texture parameters of T2WI, which was in line with previous studies [6, 7]. They also reported that there was no significant difference in the signal intensity on T2WI between two groups [6, 7]. Our study found that sinonasal SCC showed significantly higher mean value of CE-T1WI than NHL. This result was in good agreement with previous studies using dynamic-contrast enhanced MRI, in which NHL showed hypovascular perfusion [16, 17]. Xiao Z et al. also indicated that SCC had higher  $f \leftrightarrow D^*$  values than NHL by using intravoxel incoherent motion (IVIM) DWI, and  $f \leftrightarrow D^*$  could be regarded as a promising imaging biomarker for the characterization of tumor perfusion [18]. Wang et al. reported that intratumoral heterogeneity and architecture of sinonasal tumors, such as tumor angiogenesis, might be revealed on CE-T1WI [19]. These results indicate that texture parameters may improve the diagnostic utility of CE-T1WI in the differentiation between NHL and SCC.

Currently, DWI was commonly used for preoperative diagnosis and grade of sinonasal tumors in clinical practice [6–10]. In our study, we found that the mean value of ADC was significantly lower in NHL than in

SCC, which was in line with previous studies [6–10]. However, mean ADC value ignored the tumor heterogeneity, which was an important characteristic of malignant tumors. Entropy was a crucial texture parameter associated with the intra-lesion heterogeneity [20]. It has been proved to be a useful index for differentiating and grading tumors, and predicting disease prognosis [20]. Our study showed that SCC showed higher entropy of ADC than NHL, which was consistent with previous study [7]. Kim et al indicated that SCC was more heterogenous than NHL, due to intratumoral necrosis and hemorrhage [7]. Moreover, RESOLVE technique was used for DWI scan in our study. Compared with the widely used single-shot echo-planar (SS-EPI) technique, RESOLVE showed superiority in reducing distortion and artifact, and improving the overall imaging quality [21]. High image quality might be an important cornerstone for subsequent image analysis.

This study has several limitations should be noted. First, we did not correlate the TA parameters of studied sinonasal NHL and SCC with the corresponding pathologic evaluation. Second, besides DWI scan, no other functional MRI techniques were combined used for pre-treatment assessment. Thirdly, further radiomics analyze were not performed in this study due to limited sample size. Future study integrating more study population, more functional MRI modalities, and also radiomics analysis would be more attractive.

## **Conclusion**

Our preliminary study found that TA parameter of conventional MRI and DWI, especially the entropy of ADC, might be useful for preoperative differential diagnosis between sinonasal NHL and SCC.

## **Abbreviations**

TA: texture analysis; SCC: squamous cell carcinoma; NHL: non-Hodgkin's lymphoma; DWI: diffusion-weighted imaging; ADC: apparent diffusion coefficient; T2WI: T2-weighted image; CE-T1WI: contrast-enhanced T1-weighted image; CT: computed tomography; MRI: magnetic resonance imaging; FOV: field of view [FOV]; RESOLVE: Readout-segmented echo planar imaging sequence; 3D: Three-dimensional; VOIs: volumes of interest; ICC: intra-class correlation coefficient.

## **Declarations**

### **Ethics approval and consent to participate**

This prospective study was approved by the Ethics Committee of The First

Affiliated Hospital of Nanjing Medical University, and written informed

consents were obtained from all patients.

### **Consent for publication**

Not applicable.

### **Availability of data and materials**

The data of this study are available from the corresponding author on reasonable request.

### **Competing interests**

Not applicable.

### **Funding**

No funding were received.

### **Authors' contributions**

All the authors made substantial contributions to this manuscript, for study design (WFY), MRI protocol setting (SGY, LJ, XXQ), acquisition of data (SGY, LMP, YM), draft of manuscript (SGY) and manuscript revision (WFY). This authors have given final approval of this manuscript to be published. All authors have read and approved the manuscript.

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## Figures

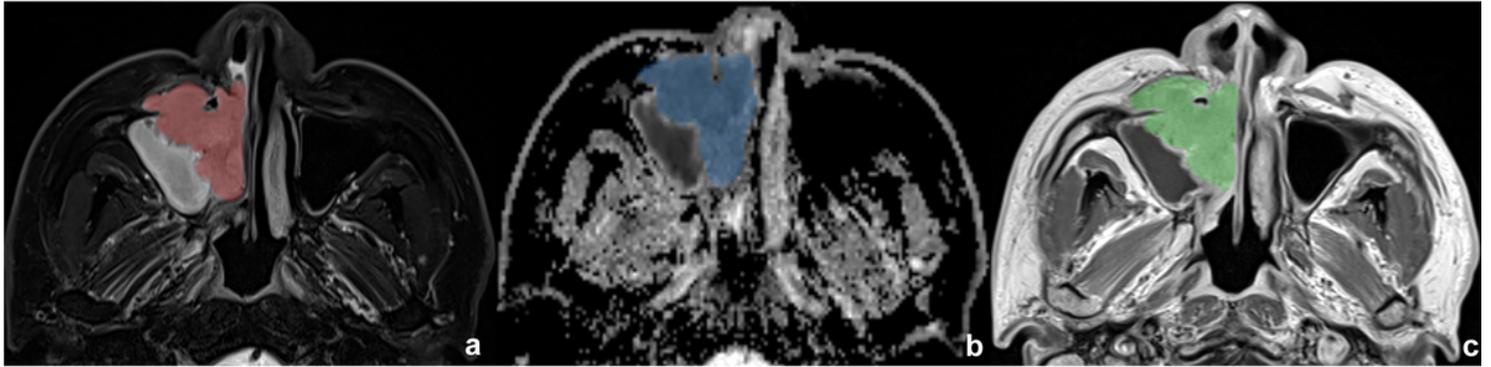


Figure 1

Schematic images of region of interest placement on T2WI (a), ADC (b) and contrast-enhanced T1WI (c).

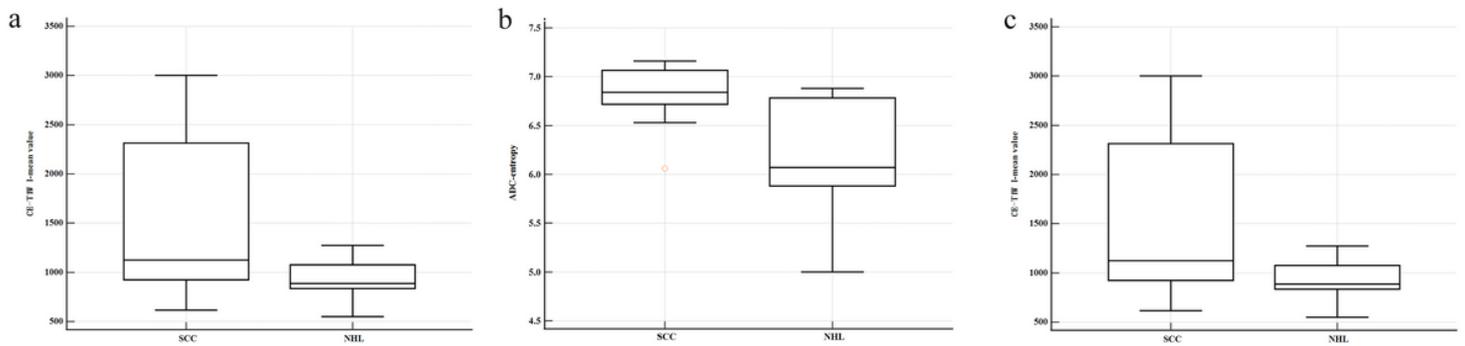
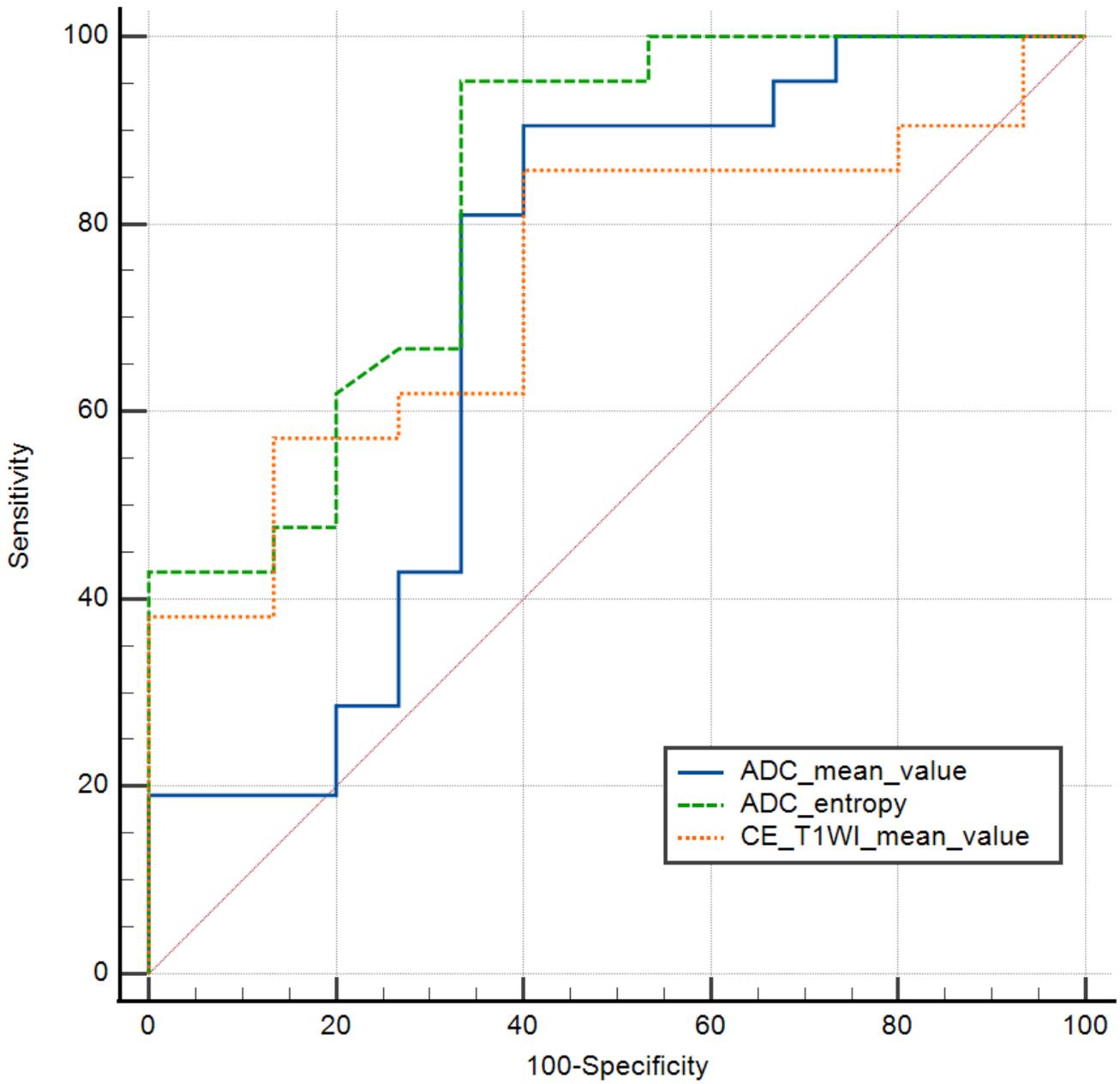


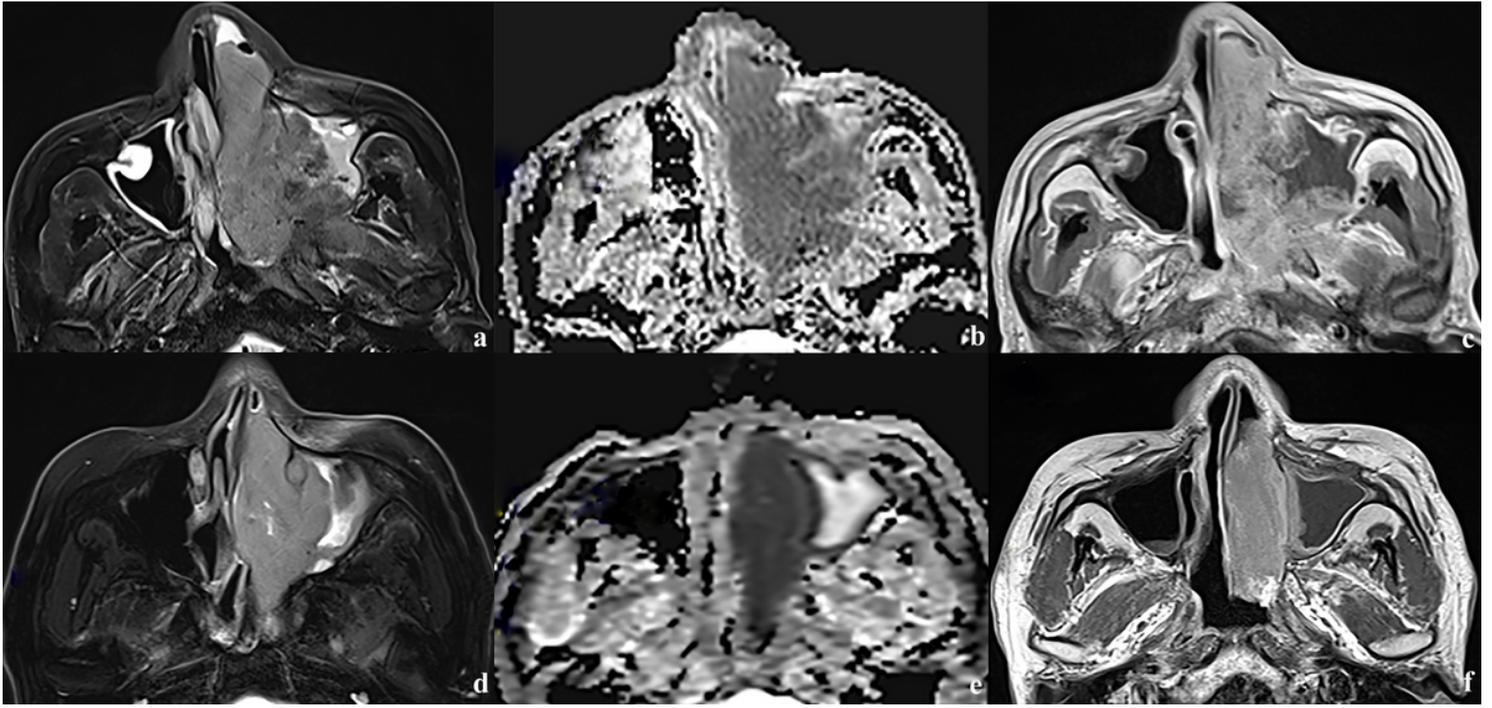
Figure 2

Box plots show the comparisons of significant texture analysis parameters between sinonasal SCC and NHL.



**Figure 3**

Performance of significant texture analysis parameters for differential diagnosing sinonasal SCC from NHL.



**Figure 4**

**a-c.** A 71-year-old man with left sinonasal SCC. Axial T2WI (a) showed a slightly hyperintensity mass. The mean values and entropy of ADC map (b) was  $0.840 (\times 10^{-3} \text{mm}^2/\text{s})$  and 7.080, respectively. Axial CE-T1WI (c) showed high degree of enhancement (mean value = 1180.830). **d-f.** A 64-year-old man with left sinonasal NHL. Axial T2WI (d) showed a moderately hyperintensity mass. The mean values and entropy of ADC map (e) was  $0.501 (\times 10^{-3} \text{mm}^2/\text{s})$  and 6.107, respectively. Axial CE-T1WI (f) showed intermediate degree of enhancement (mean value = 921.741).