Prediction of Histopathologic Grades of Myxofibrosarcoma with Radiomics based on Magnetic Resonance Imaging

Yubin Yao
Shantou Central Hospital

Yan Zhao
Shantou Central Hospital

Liejing Lu
Sun Yat-sen Memorial Hospital

Yongqiang Zhao
Shantou Central Hospital

Xiaokun Lin
The First People's Hospital of Jiexi

Jianfeng Xia
The First People's Hospital of Qinzhou

Xufeng Zheng
Shantou Central Hospital

Yi Shen
Shantou Central Hospital

Zonghuan Cai
Shantou Central Hospital

Yangkang Li
Cancer Hospital of Shantou University Medical College

Zehong Yang
Sun Yat-sen Memorial Hospital

Daiying Lin (lindaiying917@163.com)
Shantou Central Hospital

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Abstract

Purpose: To develop a radiomics-based model from preoperative magnetic resonance imaging (MRI) for predicting the histopathological grades of myxofibrosarcoma.

Methods: This retrospective study included 54 patients. The tumors were classified into high-grade and low-grade myxofibrosarcoma. The tumor size, signal intensity heterogeneity, margin, and surrounding tissue were evaluated on MRI. Using the least absolute shrinkage and selection operator (LASSO) algorithms, 1037 radiomics features were obtained from fat-suppressed T2-weighted images (T2WI), and a radiomics signature was established. Using multivariable logistic regression analysis, three models were built to predict the histopathologic grade of myxofibrosarcoma. A radiomics nomogram represents the integrative model. The three models' performance was evaluated using the receiver operating characteristics (ROC) and calibration curves.

Results: The high-grade myxofibrosarcoma had greater depth ($P = 0.027$), more frequent heterogeneous signal intensity at T2WI ($P = 0.015$), and tail sign ($P = 0.014$) than the low-grade tumor. The area under curve (AUC) of these conventional MRI features models was 0.648, 0.656, and 0.668, respectively. Seven radiomic features were selected by LASSO to construct the radiomics signature model, with an AUC of 0.791. The AUC of the integrative model based on radiomics signature and conventional MRI features was 0.875. The integrative model's calibration curve and insignificant Hosmer-Lemeshow test statistic ($P = 0.606$) revealed good calibration.

Conclusion: An integrative model using radiomics signature and three conventional MRI features can preoperatively predict low- or high-grade myxofibrosarcoma.

Introduction

Fibroblastic/myofibroblastic malignant tumor often involves the deep soft tissues of the extremities, trunk, head, and neck. According to the 2020 World Health Organization (WHO) Classification of Soft Tissue Tumors, myxofibrosarcoma belongs to the family of fibroblastic/myofibroblastic malignant tumors and myxofibrosarcoma is the predominant type [1, 2]. Myxofibrosarcoma is one of the most common histologic types of soft tissue sarcoma in adults, most commonly arising in the extremities as a slow-growing, painless mass [3, 4]. The histopathological grade is one of the most crucial elements in determining treatment options and predicting patient outcomes [5, 6]. For example, surgery is the primary treatment of low-grade myxofibrosarcoma, while treatment options for high-grade tumors often include neoadjuvant chemotherapy [7, 8]. Patients with high-grade myxofibrosarcoma benefit from early optimal adjuvant therapy [9–11]. Clinically, the percutaneous biopsy is often used to determine the histologic grades and type of the tumors. However, the accuracy of tumor grading depends on the accurate sampling of the highest-grade part of tumors and thus is vulnerable to undersampling or sampling error [12, 13]. In addition, myxofibrosarcoma can occur in deep soft tissue, increasing the difficulty of needle biopsy. Non-diagnostic or misdiagnosed results may occur in a percutaneous biopsy, leading to less
appropriate treatment and a poor prognosis [5, 13, 14]. Thus, an accurate and noninvasive method is highly desired to identify patients with high-grade or low-grade myxofibrosarcoma.

Because of its noninvasiveness and superior soft tissue contrast resolution, magnetic resonance imaging (MRI) is frequently used for diagnosing, preoperative evaluation, and postoperative follow-up of soft tissue sarcoma [9, 15, 16]. Soft-tissue sarcoma tumor grades can be predicted by tumor size, tumor margin, heterogeneous signal intensity on T2WI, peritumoral edema, and peritumoral contrast enhancement [5, 16–18]. However, these morphologic features are based on MRI, and their performance in predicting tumor grades remains to be improved.

Radiomics can extract from MRI high-dimensional radiomic features that cannot be examined visually [19]. It can fully determine in-depth information about tumors and provide a comprehensive view of the entire tumor, not just local samples [20]. Previously, radiomics has been reported helpful in predicting the histologic grade, local recurrence, distant metastasis, overall survival, and response to neoadjuvant therapy in patients with soft tissue sarcoma [9, 21, 22]. However, most of these studies included a large family of soft tissue sarcoma [9, 21, 23–26]. Whether radiomics based on MRI can predict the histopathologic grades remains inadequately determined. Our study hypothesized that the radiomics features could outperform the morphologic features in predicting the grade of myxofibrosarcoma. Therefore, based on preoperative MRI, our study aimed to establish a radiomics-based model to predict high- and low-grade myxofibrosarcoma.

Materials and Methods

Patients

A two-center, retrospective investigation was conducted. The Institutional Review Boards authorized the study. The study was exempt from written informed consent. From September 2009 to December 2021, a total of 98 patients with myxofibrosarcoma were detected in the hospital database. Inclusion criteria were (a) patients with a definitive pathologic diagnosis after surgical resection; (b) patients who had undergone MRI before surgery or neoadjuvant therapy. The patient enrollment pathway and exclusion criteria were shown in Fig. 1. In the end, 54 individuals were included in this study.

Histologic Analysis

According to the French Federation of Cancer Centers Sarcoma Group (FNCLCC) grading standard, tumor grade was determined (grade 1–3). The tumor grade is determined by adding the scores for the mitotic index, differentiation, and amount of necrosis assigned by the FNCLCC system [27]. In our study, all tumors were grouped into high-grade (grades 2 and 3) or low-grade (grade 1) myxofibrosarcoma.

MRI examination
MRI has performed on an Avanto or Aera 1.5T scanner (Siemens, Erlangen, Germany) or a 3.0 T MRI machine (Siemens Magnetom Verio 3.0 T) with a dedicated phased-array body coil. All patients underwent T1-weighted imaging (T1WI), T2-weighted imaging (T2WI), fat-suppressed T2WI, and contrast-enhanced T1WI.

**MRI morphologic Feature analysis**

The morphologic features on MRI were reviewed by two radiologists in a consensus and a blinded manner. They recorded the following features: (1) size (maximum dimension of tumor); (2) depth relative to the superficial fascia; (3) signal intensity heterogeneity on T1WI, T2WI, and contrast-enhanced T1WI (less than 50% heterogeneous or at least 50% heterogeneous); (4) margin on T1WI and T2WI (well defined, > 90% of margin clear; poorly defined, > 75% of margin not clear; or mixed margin, 10% – 25% of margin not clear); (5) hemorrhagic signal (high signal intensity on T1WI not compatible with the fatty signal on other MRI sequences); (6) necrotic signal (high signal on T2WI and fat-suppressed T2WI with no enhancement on contrast-enhanced T1WI); (7) peritumoral edema (high signal strength on fat-suppressed T2WI with infiltrative and feathery borders discernible from the apparent tumor borders and devoid of mass effects); (8) tail sign (a tapered tail-like high signal intensity alteration adjacent to the main mass on contrast-enhanced T1WI); (9) bone involvement. All these MRI features were assessed according to the previously reported guidelines [24, 28, 29].

**Radiomics analysis**

Fat-suppressed T2WI images were used for radiomics analysis. A flow chart of the radiomics model building is shown in Fig. 2. The tumor was segmented, and the 3D volume of interest (VOI) was created using 3D-Slicer software (3D Slicer, Version 4.10.2) by one radiologist. The VOIs included the whole tumor mass and eliminated any surrounding edema that was evident. After tumor segmentation, N4ITK MRI bias field correction was implemented using Slicer3D (3D Slicer, Version 4.10.2) to adjust for intensity heterogeneity caused by field heterogeneity. Combat Harmonization was proposed to correct batch effects in radiomics multicenter cohorts. The maximum likelihood method estimates additive and multiplicative batch effects based on the given feature distribution. The R Combat script (https://github.com/Jfortin1/ComBatHarmonization) was applied to correct MRI scanner models. Using Pyradiomics (https://github.com/Radiomics/pyradiomics), 1037 radiomic features of the tumor were retrieved, including first-order statistics, shape-based histogram, GLCM, GLRLM, GLSZM, GLDM, NGTDM with or without imaging filters (Laplacian of Gaussian, Logarithm, and Wavelet). To assess intraobserver and interobserver reliability, the same radiologist repeated VOI segmentation and feature extraction two weeks later, and another radiologist with 15 years of experience also did VOI segmentation and feature extraction. Features with intraobserver and interobserver correlation coefficients (ICCs) > 0.75 were included in the feature selection using LASSO to construct the radiomics-based prediction model.
Radiomics-based prediction model development and performance

To establish prediction models, multivariable logistic regression analysis was used to discover the independent factors that best predict myxobrosarcoma grade using conventional MRI features and radiomics signatures determined by LASSO. A collinearity diagnosis was performed on the logistic regression model to test predictor independence. The integrative model was represented as an integrative nomogram. The calibration curve of the nomogram was obtained, and the Hosmer-Lemeshow test was employed to assess the nomogram's goodness of fit.

Statistical Analyses

Statistical analyses were performed using the SPSS statistical package (version 26.0; IBM, Chicago, IL) and R version 3.3.3 (R Development Core Team, Vienna, Austria). All tests were 2-tailed, and a $P$ value $<0.05$ was considered to indicate statistical significance. Differences in age and sex were analyzed using the Wilcoxon rank-sum test. The $\chi^2$ test was used to determine whether there was a significant difference between the morphologic MRI features of high-grade and low-grade myxofibrosarcoma. The radiomics features were chosen using a 5-fold cross-validation method to develop the radiomics model. Multivariate logistic regression modeling was used to determine the best morphologic MRI features and radiomics features that can best predict the grade of the tumor. An integrative model based on radiomics signature and significant MRI features was built. A nomogram was developed using the nomogram function from the RMS library in the software package R. To assess the calibration of the integrative model and integrative nomogram, calibration curves were plotted alongside the Hosmer–Lemeshow test. Using the receiver operating characteristic curve (ROC) analysis, the performance of three prediction models for predicting the grade of myxofibrosarcoma was determined. An area under the curve (AUC) and its confidence intervals (CIs) were calculated. The models' sensitivity, specificity, and accuracy were also determined. The AUCs of these models were compared with the DeLong test.

Result

Clinicopathologic Characteristics of patients

A total of 54 patients with myxofibrosarcoma ($59 \pm 12$ years) were included. Table 1 lists the clinicopathological characteristics of the patients. 32 patients had low-grade tumors, while 22 patients had high-grade tumors.
Table 1
The clinicopathologic characteristics and morphologic MRI features of myxofibrosarcoma patients with different grades

<table>
<thead>
<tr>
<th>Feature</th>
<th>Low Grade (n = 22)</th>
<th>High Grade (n = 32)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>51.23 ± 16.87</td>
<td>51.16 ± 21.59</td>
<td>0.990</td>
</tr>
<tr>
<td>Sex</td>
<td>0.752</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>8 (36.36%)</td>
<td>13 (40.62%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>14 (63.64%)</td>
<td>19 (59.38%)</td>
<td></td>
</tr>
<tr>
<td>Size(cm)</td>
<td>8.12 ± 5.09</td>
<td>7.81 ± 4.27</td>
<td>0.811</td>
</tr>
<tr>
<td>Depth</td>
<td>0.027*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superficial</td>
<td>12 (54.55%)</td>
<td>8 (25%)</td>
<td></td>
</tr>
<tr>
<td>Deep</td>
<td>10 (45.45%)</td>
<td>24 (75%)</td>
<td></td>
</tr>
<tr>
<td>Margin definitions at T1WI</td>
<td>0.906</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well defined</td>
<td>11 (50%)</td>
<td>15 (46.88%)</td>
<td></td>
</tr>
<tr>
<td>Mixed definition</td>
<td>7 (31.82%)</td>
<td>12 (37.5%)</td>
<td></td>
</tr>
<tr>
<td>Poorly defined</td>
<td>4 (18.18%)</td>
<td>5 (15.63%)</td>
<td></td>
</tr>
<tr>
<td>Margin definitions at T2WI</td>
<td>0.978</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Well defined</td>
<td>13 (59.09%)</td>
<td>18 (56.52%)</td>
<td></td>
</tr>
<tr>
<td>Mixed definition</td>
<td>7 (31.82%)</td>
<td>11 (34.38%)</td>
<td></td>
</tr>
<tr>
<td>Poorly defined</td>
<td>2 (9.09%)</td>
<td>3 (9.38%)</td>
<td></td>
</tr>
<tr>
<td>Heterogeneous signal intensity on T1WI</td>
<td>0.851</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50%</td>
<td>16 (72.73%)</td>
<td>24 (75%)</td>
<td></td>
</tr>
<tr>
<td>≥ 50%</td>
<td>6 (27.27%)</td>
<td>8 (25%)</td>
<td></td>
</tr>
<tr>
<td>Heterogeneous signal intensity on T2WI</td>
<td>0.015*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50%</td>
<td>11 (50%)</td>
<td>6 (18.75%)</td>
<td></td>
</tr>
<tr>
<td>≥ 50%</td>
<td>11 (50%)</td>
<td>26 (81.25%)</td>
<td></td>
</tr>
<tr>
<td>Heterogeneous signal intensity on contrast-enhanced T1WI</td>
<td>0.184</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Feature</td>
<td>Low Grade (n = 22)</td>
<td>High Grade (n = 32)</td>
<td>(P) Value</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-------------------</td>
<td>---------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>(\geq 50%)</td>
<td>7 (31.82%)</td>
<td>16 (50%)</td>
<td></td>
</tr>
<tr>
<td>Hemorrhagic signal</td>
<td></td>
<td></td>
<td>0.459</td>
</tr>
<tr>
<td>No</td>
<td>16 (72.73%)</td>
<td>26 (81.25%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>6 (27.27%)</td>
<td>6 (18.75%)</td>
<td></td>
</tr>
<tr>
<td>Necrotic signal</td>
<td></td>
<td></td>
<td>0.801</td>
</tr>
<tr>
<td>No</td>
<td>13 (59.09%)</td>
<td>20 (62.5%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>9 (40.91%)</td>
<td>12 (37.5%)</td>
<td></td>
</tr>
<tr>
<td>Peritumoral edema</td>
<td></td>
<td></td>
<td>0.413</td>
</tr>
<tr>
<td>No</td>
<td>7 (31.82%)</td>
<td>7 (21.88%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>15 (68.18%)</td>
<td>25 (78.13%)</td>
<td></td>
</tr>
<tr>
<td>Tail sign</td>
<td></td>
<td></td>
<td>(0.014^*)</td>
</tr>
<tr>
<td>No</td>
<td>17 (77.27%)</td>
<td>14 (43.75%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5 (22.73%)</td>
<td>18 (56.25%)</td>
<td></td>
</tr>
<tr>
<td>Bone invasion</td>
<td></td>
<td></td>
<td>0.958</td>
</tr>
<tr>
<td>No</td>
<td>18 (81.82%)</td>
<td>26 (81.25%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4 (18.18%)</td>
<td>6 (18.75%)</td>
<td></td>
</tr>
</tbody>
</table>

### Morphologic MRI Features

Three MRI features, depth, heterogeneous signal intensity on T2WI, and tail sign, were more frequently found in high-grade myxofibrosarcoma than in low-grade tumors (Table 1). High-grade tumors were more likely to occur in deep-seated locations \((P = 0.027)\), showed heterogeneous signal intensity on T2WI \((P = 0.015)\), and had a tail sign \((P = 0.014)\). The remaining nine MRI characteristics did not differ significantly between high-grade and low-grade myxofibrosarcoma. \((P > 0.05)\). Figure 3 illustrates how the conventional MRI features can help predict the patient's final grade.

### Radiomics Features

Among 1037 features extracted from fat-suppressed T2WI, the seven radiomic features were chosen by Lasso Regression to construct the radiomic model. The parameter \(\lambda = 0.0778409\) was used as the optimal value in Fig. 4A and 4B. The selected radiomics features are shown in Fig. 4C.
Development of an integrative prediction model

Among the three individual MRI features, including the depth, heterogeneous signal intensity at T2WI and tail sign, and the radiomics signature, multivariable logistic regression analysis showed that only the radiomics signature was an independent risk factor for the high grade of myxofibrosarcoma \((P = 0.003)\) (Table 2). Three MRI features were incorporated with the radiomics signature to develop the integrative model and presented as a nomogram (Fig. 5A). The AUCs of the prediction models are shown in Table 3, and the ROCs are shown in Fig. 5C. The integrative model had an AUC of 0.875 (95% CI: 0.785, 0.965), which was higher than that of the tail sign model [AUC, 0.668 (95%CI: 0.521, 0.814), \(P= 0.001\)] and radiomics model [AUC, 0.791 (95%CI: 0.672, 0.911), \(P = 0.125\)]. The calibration curve and an insignificant Hosmer-Lemeshow test result \((P = 0.606)\) indicated that the nomogram of the integrative model was calibrated correctly (Fig. 5B).

Table 2
Risk factors of MRI features and radiomics signature for myxofibrosarcoma prediction

<table>
<thead>
<tr>
<th>Variable</th>
<th>(\beta)</th>
<th>Odds ratio</th>
<th>(P)value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depth</td>
<td>1.341</td>
<td>3.824 (0.699, 20.924)</td>
<td>0.122</td>
</tr>
<tr>
<td>Heterogeneous signal intensity on T2WI</td>
<td>1.704</td>
<td>5.496 (0.899, 33.585)</td>
<td>0.065</td>
</tr>
<tr>
<td>Tail sign</td>
<td>1.689</td>
<td>5.416 (0.893, 32.840)</td>
<td>0.066</td>
</tr>
<tr>
<td>Radiomics signature</td>
<td>3.566</td>
<td>35.363 (3.280, 381.269)</td>
<td>0.003*</td>
</tr>
</tbody>
</table>

Abbreviation: MRI = magnetic resonance imaging, T2WI = T2-weighted imaging
Table 3
Diagnostic performance of prediction models for myxofibrosarcoma

<table>
<thead>
<tr>
<th>Feature and radiomics model</th>
<th>AUC</th>
<th>Threshold</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depth</td>
<td>0.648</td>
<td>0.5</td>
<td>75.00</td>
<td>54.55</td>
<td>66.67</td>
<td>0.067</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(56.60, 88.54)</td>
<td>(32.21, 75.61)</td>
<td>(52.53, 78.91)</td>
<td></td>
</tr>
<tr>
<td>Heterogeneous signal intensity on T2WI</td>
<td>0.656</td>
<td>0.5</td>
<td>81.25</td>
<td>50.00</td>
<td>68.52</td>
<td>0.053</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(63.56, 92.79)</td>
<td>(28.22, 71.78)</td>
<td>(54.45, 80.48)</td>
<td></td>
</tr>
<tr>
<td>Tail sign</td>
<td>0.668</td>
<td>0.5</td>
<td>56.25</td>
<td>77.27</td>
<td>64.81</td>
<td>0.038*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(37.66, 73.64)</td>
<td>(54.63, 92.18)</td>
<td>(50.62, 77.32)</td>
<td></td>
</tr>
<tr>
<td>Radiomics signature</td>
<td>0.791</td>
<td>0.120</td>
<td>87.50</td>
<td>59.09</td>
<td>75.93</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(71.01, 96.49)</td>
<td>(36.35, 79.29)</td>
<td>(62.36, 86.51)</td>
<td></td>
</tr>
<tr>
<td>Integrative model</td>
<td>0.875</td>
<td>0.372</td>
<td>81.25</td>
<td>81.82</td>
<td>81.48</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(63.56, 92.79)</td>
<td>(59.72, 94.81)</td>
<td>(68.57, 90.75)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: T2WI = T2-weighted imaging

Discussion

Our study demonstrated that three conventional MRI features and seven radiomic features derived from fat-suppressed T2WI were associated with the histopathologic grade of myxofibrosarcoma. The model based on radiomics signature showed good performance in predicting the grade of myxofibrosarcoma. Additionally, in predicting histologic tumor grades, an integrative model incorporating depth, heterogeneous signal intensity on T2WI, tail sign, and radiomics signature outperformed the models based on morphologic MRI characteristics and radiomics signature alone.

Preoperative histologic grading plays a crucial role in treating patients with fibroblastic/myofibroblastic malignant tumors. Due to tumor heterogeneity, it is recognized that initial grading by biopsy samples may underestimate the final grade confirmed by the surgical specimen [14, 29]. In our study, three conventional MRI features, including depth, heterogeneous signal intensity at T2WI, and tail sign, were associated with the histologic grade of myxofibrosarcoma. The high-grade tumor more frequently had heterogeneous signal intensity at T2WI and tail sign. These results were consistent with previous studies [5, 29]. Crombé et al. found that heterogeneous signal intensity at T2WI >50% predicted the high-grade soft tissue tumor [29]. Zhao et al. reported that heterogeneous signal intensity at T2WI >50% could predict the high-grade
soft tissue tumor [5]. The tail sign was a characteristic MRI finding of myxofibrosarcoma caused by significant tumor cell infiltration along the subcutaneous tissue's deep fascia and fibrous septa. This sign was related to poorer local recurrence-free survival and is also a predictor of the high-grade tumor [30]. In our study, high-grade myxofibrosarcoma was more likely to occur in deep-seated locations. However, this result was inconsistent with previous studies [5, 29]. One probable reason may be that myxofibrosarcoma represents only a tiny proportion of soft tissue sarcoma enrolled in their studies. In our research, we include 54 patients with myxofibrosarcoma. In contrast, they had a large group of soft tissue sarcoma. Notably, the diagnostic performances of three conventional MRI features are not high, with an AUC of 0.648, 0.656, and 0.668, respectively. Wang et al. reported that the diagnostic performance of MRI features, such as margins in differentiating malignant and benign soft-tissue tumors, was also suboptimal, with an AUC of 0.68 [24]. Conventional morphologic MRI features help predict the histologic grade of myxofibrosarcoma, but their diagnostic performances are still necessary to improve.

Besides morphologic MRI features, radiomics signature based on MRI has been demonstrated to have excellent performance in predicting the histological grade in various soft tissue tumors [9, 21, 23–26]. In our study, we only analyzed patients with myxofibrosarcoma. The radiomic features were extracted from fat-suppressed T2WI, which showed a good prediction performance with an AUC of 0.791. Compared with conventional MRI features, the radiomics signature model predicted the grade of the tumor more accurately. The performance of the radiomics signature in our study is comparable with that reported by Yan et al., with an AUC of 0.829 based on unenhanced T1WI and fat-suppressed T2WI in their study [9]. Peeken et al. also developed a radiomics model based on contrast-enhanced fat-saturated T1WI and fat-suppressed T2WI, with a reported AUC of 0.76 [21]. Moreover, the diagnostic efficacy achievable with these MRI sequences was comparable. The fat-suppressed T2WI was more reproducible and practicable in clinical practice.

In our study, an integrative model based on morphologic MRI features and radiomics signature had the highest AUC (AUC = 0.875) than the conventional tail sign (AUC = 0.668) and the radiomics signature model (AUC = 0.791). To our knowledge, it is the first study that combines morphologic MRI features and radiomics signature to establish an integrative tumor-grade prediction model for myxofibrosarcoma. This integrative model also demonstrated good calibration (Hosmer-Lemeshow test statistic, \( P = 0.606 \)) and a greater net benefit across a broad range of threshold probabilities between 0.12 and 0.5. Yan et al. showed a higher AUC of an integrative radiomics nomogram (incorporating the radiomics signature based on fat-suppressed T2WI and risk factors of the clinical and MRI morphological variables) based on unenhanced T1WI and fat-suppressed T2WI in predicting soft tissue sarcomas with low-grade and high-grade differentiation [9]. Wang et al. developed an integrative radiomics nomogram. They found that the model (AUC = 0.94) performed well for screening malignancy in soft tissue sarcoma, which was better than the clinical model (AUC = 0.68) and the radiomics signature model (AUC = 0.86) [24]. Collectively, the integrative model based on morphologic MRI features and radiomics signature is likely better than the radiomics signature model in predicting the histopathological classification of myxofibrosarcoma. When a tumor cannot be accessed anatomically during biopsy or when the biopsy result is unclear, a radiomics-based integrative model from preoperative MRI with good predictive performance would provide
additional information to identify patients with high-grade tumors who might need adjuvant systemic therapy [9]. In clinical practice, the integrative model might be more helpful for decision-making for patients with myxofibrosarcoma.

Our study has some limitations. First, although this is a two-center study, we did not create a validation dataset because this is a retrospective study with a relatively small sample size. Although myxofibrosarcoma is the predominant type of fibroblastic/myofibroblastic malignant tumors, they are still relatively rare, and the number of patients obtained from the two centers is limited. The prediction model developed in our study requires further validation with a larger sample size from the multicenter. Finally, we only used fat-suppressed T2WI-based radiomics features to build our radiomics nomogram. Other routine sequences, such as T1WI, T2WI, and contrast-enhanced T1WI, were not included in the radiomics study. Future studies should explore a new model based on whole MRI sequences.

In conclusion, an integrative model from preoperative MRI outperformed models of conventional MRI features and radiomics signatures in distinguishing low-grade and high-grade myxofibrosarcoma. This integrative model incorporating the radiomics signature established from fat-suppressed T2-weighted images and three conventional MRI features can be helpful for preoperatively predicting low-grade or high-grade myxofibrosarcoma, which might be beneficial for clinical decision-making for patients with myxofibrosarcoma.

**Abbreviations**

MRI = magnetic resonance imaging

T1WI = T1-weighted imaging

T2WI = T2-weighted imaging

LASSO = least absolute shrinkage and selection operator

ROC = receiver operating characteristic

AUC = area under the curve

CI = confidence interval

**Declarations**

**Ethics approval and consent to participate**

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Ethics Committee. Informed consent was obtained from all participants before their inclusion
in the study. Institutional Review Board approval was obtained from Sun Yat-Sen Memorial Hospital of Sun Yat-Sen University (Guangzhou, China) and Shantou Central Hospital (Shantou, China).

**Consent for publication**

Written consent for publication was obtained from all participants or their legal guardians. Any identifiable information has been removed or anonymized to protect the participants’ privacy.

**Availability of data and material**

The data and materials supporting the conclusions of this study are available upon request from the corresponding author.

**Competing interests**

The authors declare that they have no competing interests. The authors have no relevant financial or non-financial interests to disclose.

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**Credit authorship contribution statement**

**Yubin Yao**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing the main manuscript text, Funding acquisition.

**Yan Zhao**: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing the main manuscript text.

**Liejing Lu**: Conceptualization, Data curation, Investigation, Methodology, Prepared figures 1-5 and table 1-3.

**Yongqiang Zhao**: Data curation, Formal analysis, Methodology.

**Xiaokun Lin**: Data curation, Formal analysis, Methodology.

**Jianfeng Xia**: Data curation, Formal analysis.
Xufeng Zheng: Data curation, Formal analysis.

Yi Shen: Data curation, Formal analysis.

Zonghuan Cai: Data curation, Formal analysis.

Yangkang Li: Conceptualization, Data curation, Investigation.

Zehong Yang: Conceptualization, Formal analysis, Investigation, Methodology, Writing - review & editing, Project administration, Supervision, Validation.

Daiying Lin: Conceptualization, Formal analysis, Investigation, Methodology, Writing - review & editing, Project administration, Supervision, Validation.

All authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

References


Figures
Data of patients with clinical pathologically confirmed myxofibrosarcoma (n = 98)

Excluded for the following reasons (n = 27):
- Patients did not receive MR examination (n = 10)
- Patients received biopsy or surgery prior to MR examination (n = 12)
- Patients with the non-diagnostic image quality of MRI images (n = 5)

Preoperative myxofibrosarcoma MRI available (n = 71)

Excluded for the following reasons (n = 17):
- Patients with inclusive histopathologic grade (n = 12)
- Patients with incomplete clinical data (n = 5)

Patients enrolled in this retrospective study (n = 54)

Figure 1

Flowchart of the study.
**Figure 2**

Radiomics signature workflow and study flowchart.

**Figure 3**
MR images of a 54-year-old man with low-grade myxofibrosarcoma (A-D) and a 73-year-old man with high-grade myxofibrosarcoma (E-H). (A) Coronal T2WI MR image showed a mass with relatively homogeneously hyperintense. The mass had low-signal-intensity internal septations. (B) Coronal fat-suppressed T2WI MR image showed the mass was relatively homogeneously hyperintense, with no perilesional edema and tail sign. (C) Coronal T1WI MR image shows the homogeneous mass was relatively isointense compared to skeletal muscle. (D) Microscopically (hematoxylin-eosin stain; ×40), the tumor cells were arranged in an irregular, loosely lobulated pattern and had a myxoid stroma. The nuclei were relatively uniform, ovoid, and small. (E) Coronal T2WI MR image shows a large mass with heterogeneous signal intensities in at least 50% of volume. (F) Coronal fat-suppressed T2WI MR image showed the mass was heterogeneous hyperintense, with perilesional edema (arrowheads and white arrow) (G) Coronal T1WI MR image showed the mass was in the deep soft tissue of the left upper arm. (H) In this microscopic image (hematoxylin-eosin stain; ×40), the cellular atypia was evident, and the nuclei of tumor cells were large, hyperchromatic, and showed prominent nucleoli.
Feature selection employing the least absolute shrinkage and selection operator (LASSO) regression technique and radiomics signature performance. (A) The LASSO model's tuning parameter ($\lambda$) was selected via five-fold cross-validation based on minimum criteria. The area under the curve (AUC) was plotted versus log ($\lambda$). At the optimal values, a vertical line with dots was constructed using the minimal criteria and one standard error of the minimum criteria. The $\lambda$ value was set as 0.0778409 according to a 5-fold cross-validation in this study. (B) The LASSO coefficient profiles of the 1037 features. The dotted vertical line was plotted at the selected $\lambda$ value, resulting in 7 non-zero-coefficient features. (C) The 7 radiomics features with accordingly coefficients of the radiomics model.
Radiomics nomogram, calibration curves, and receiver operating characteristic curves of the predictive models. (A) A nomogram based on radiomics for predicting the malignant status of myxofibrosarcoma. (B) Calibration curves of the radiomics nomogram (Hosmer-Lemeshow test statistic, $P = 0.606$). (C) The ROC curves for predicting myxofibrosarcoma histopathological grade of three individual MRI features model (Depth, Heterogeneous signal intensity on T2WI, and Tail sign), Radiomic signature model, and Integrative model.