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ORIGINAL RESEARCH

MRI Differential Diagnosis and Guidance for Puncture Biopsy of Musculoskeletal Dedifferentiated Liposarcoma and Well Differentiated Liposarcoma

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Objective: The study aimed to investigate the significantly different imaging characteristics of musculoskeletal dedifferentiated liposarcoma (DDLP) and well differentiated liposarcoma (WDLP) on MRI, which in turn could guide puncture biopsy.

Materials and Methods: This study included 14 patients with DDLP and 16 patients with WDLP, all of whom were confirmed by histopathological examination. The MRI manifestations of these two pathologies were retrospectively reviewed and compared. Furthermore, a step-by-step procedure regarding preoperative puncture biopsy of fatty masses that are suspicious for WD/DD was designed.

Results: Fatty signals can be found in almost all WDs, with a greater proportion of non-fatty areas in DD compared to WD, and it is reasonable to consider WD more likely when the non-fatty areas of the tumor are <25% ($p < 0.05$), while it is reasonable to consider DD more likely when the non-fatty areas of the tumor are >50% ($p < 0.05$), and the MRI signals in DD are more complex, inhomogeneous ($p < 0.01$), usually showed significant enhancement ($p < 0.01$), and the margins of the tumor were usually indistinct ($p < 0.01$); and imaging features such as tumor size, vascularity, necrosis, and peritumoral edema did not serve as distinguishing features between the two ($p > 0.05$).

Conclusion: DD has a greater proportion of non-fatty components, with more complex and inhomogeneous MRI signals, and typically shows significant enhancement, with usually indistinct margins of the tumor, in which the inhomogeneous manifestations are associated with the histological components. The possibility of DD should be considered in fatty tumors with non-fatty areas > 25%, for which puncture biopsy is necessary, while simultaneous puncture of low, moderate, high-signal areas within the non-fatty area could improve the accuracy of preoperative puncture pathology.

Keywords: liposarcoma, dedifferentiated liposarcoma, well-differentiated liposarcoma, magnetic resonance imaging, puncture biopsy

Introduction

Liposarcoma is the second most common type of soft tissue sarcoma, accounting for 10–35% of all soft tissue sarcomas.[1] Currently, the World Health Organization classifies liposarcoma into five subtypes,[2] with well-differentiated liposarcoma (WDLP) and dedifferentiated liposarcoma (DDLP) together forming the largest subgroup of liposarcoma. WDLP accounts for approximately 50%, while the DDLP accounts for about 20%.[1] These two types of liposarcoma have a higher incidence in adults aged 60 to 70, often occurring in the limbs or retroperitoneum, and occasionally in the paratesticular region, mediastinum, and head and neck. Most patients usually present with slowly enlarging, painless masses, although a few may experience symptoms such as pain and tenderness. In cases occurring in the retroperitoneum, patients may experience abdominal pain or distension, or there may be local compression of structures leading to conditions such as intestinal or urinary obstruction.

WDLP are typically composed of mature adipocytes with variable cell sizes and minimal nuclear atypia. These tumors generally exhibit low malignant potential and are unlikely to metastasize, though they may recur locally.[3] Post-surgical long-term control is high, with 5-year overall survival rates ranging from 92% to 99%.[4] In contrast, DDLP

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evolve from well-differentiated liposarcomas and are characterized by a transformation within the tumor from an adipocyte-rich region to a non-lipogenic, spindle-cell-rich area. This transformation enhances the tumor's aggressiveness and malignant potential, increasing the likelihood of metastasis. Extensive surgical resection is typically required, and the probabilities of recurrence and metastasis are higher. Adjuvant treatments, such as radiotherapy or chemotherapy, are often necessary,[3] with 5-year overall survival rates falling between 70% and 84%.[4] Therefore, accurate differential diagnosis between DDLP and WDLP is crucial for selecting appropriate treatment strategies and predicting patient prognosis. The close histological similarity and frequent immunohistochemical expression of MDM2 and CDK4[5] amplifications add challenges to preoperative radiographic and biopsy-based pathological diagnoses.

Previous radiological studies have reported that imaging techniques possess high sensitivity and specificity for the diagnosis of liposarcomas.[6,7] However, differentiating between WDLP and DDLP can sometimes be challenging. Tumors that have recently undergone dedifferentiation from WDLP may still predominantly display fat signals on imaging, potentially leading to oversight. During a biopsy, the dedifferentiated regions might be missed, resulting in misdiagnosis or diagnostic omission. Therefore, identifying distinctive imaging features that clearly differentiate between WDLP and DDLP, and supporting these findings with targeted biopsy, is clinically significant. This approach helps accurately diagnose tumors, including those in the early stages of dedifferentiation.

This study aims to assess and compare the notable disparities in MRI imaging performance between WDLP and DDLP, to pinpoint imaging characteristics that can enhance preoperative imaging diagnosis and differentiation between WDLP and DDLP, and to guide biopsy or minimize unnecessary or inaccurate biopsies. This will provide more precise evidence to inform diagnosis and treatment.

Method

Patient

This study was approved by the ethical review committee of the Cancer Hospital of Guangxi Medical University in accordance with the principles of the Helsinki Declaration. Because it was a retrospective study, the requirement for informed consent was waived. Patients diagnosed with confirmed primary DDLP and WDLP by organized pathology from December 2013 to December 2023 were identified in our electronic medical record system (Table 1).

This included 14 patients with primary DDLP (6 males and 8 females; age range: 24–72 years; average age 60 years) and 16 patients with primary WDLP (6 males and 10 females; age range: 33–83 years; average age 50 years).

The pathological assessment is based on the 2020 World Health Organization classification of soft tissue and bone tumors. Immunohistochemical staining reveals that both WDLP and DDLP test positive for MDM2.

Table 1 Patient characteristics

		DD(n=14)	WD(n=16)
Age		24~72	33~83
Sex	Male	6	6
	Female	8	10
Location	Lower extremity	9	12
	Trunk	4	3
	Upper extremity	0	1
	Head and neck	0	0
MDM2		14	16

Magnetic Resonance Imaging (MRI)

The collected MRI images are either 1.5T or >1.5T. All patients receive T2-weighted, T1-weighted, contrast-enhanced T1-weighted, and fat-suppressed T2-weighted images in transverse, sagittal, and coronal planes. All MRI images were obtained at a section thickness of 5–8 mm with 1–2 mm intersection gap and a 20 × 20–45 × 45-cm field of view.

Image Assessment

Two radiologists, one with 5 and the other with 10 years of experience in musculoskeletal imaging, independently reviewed all images. Cases with discrepancies or disputes between the reviewers were directly excluded from the study. The reviewers were blinded to clinical information and pathological diagnosis. Upon reviewing the MRI data (Figures 1–3), we have identified the following imaging features for MRI assessment: tumor size, fat content, non-fat content, homogeneity of non-fat area MRI signal, strength of enhancement signal in non-fat area MRI, clarity of tumor margins, tumor vascularity, peritumoral edema, and necrosis.

Tumor size was determined by measuring the maximum diameter of the entire lesion. Unclear tumor margins were defined as the difficulty in distinguishing the boundary of the tumor from surrounding tissues. Fat content was defined as high signal on T1-weighted images (T1-WI) and low signal when fat suppression techniques such as fat saturation (FS) or inversion recovery (eg STIR [short tau inversion recovery]) were applied (Figure 1A and C). Non-fat content was defined as areas with signal intensity similar to that of skeletal muscle on T1-weighted images (Figure 1B). Peritumoral edema was evaluated using fat-suppressed T2-weighted images (Figure 1A). Subsequently, the percentage of non-fat content was calculated. In all MRI images with visible lesions, the entire tumor and fat content areas were measured by manually outlining their contours. The non-fat content percentage was defined as the ratio of non-fat content to the entire tumor. It was then categorized as follows: 1 to 5, where 1 for < 5%, 2 for 6% - 25%, 3 for 25% - 50%, 4 for 50% - 75%, and 5 for > 75% of the non-fat area. Enhancement of non-fat content on MRI was defined as a significant increase in

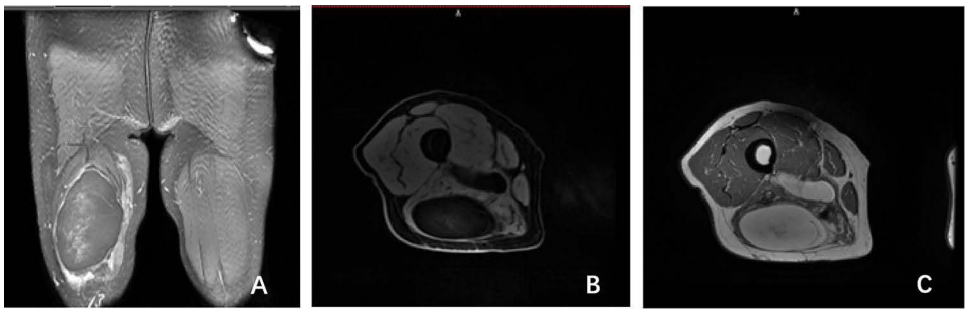

Figure 1 A 62-year-old male patient with a well-differentiated liposarcoma in his right thigh. (**A**). Fat-suppressed T2-weighted image reveals a well-defined, low-signal soft tissue mass in the right thigh, surrounded by high-signal edema. (**B**) T1-weighted image shows a mass with a fatty signal and a small amount of flocculent low-signal non-fatty area in the center. (**C**) Fat-suppressed T1-weighted contrast-enhanced image reveals only mild enhancement in the non-fatty area.

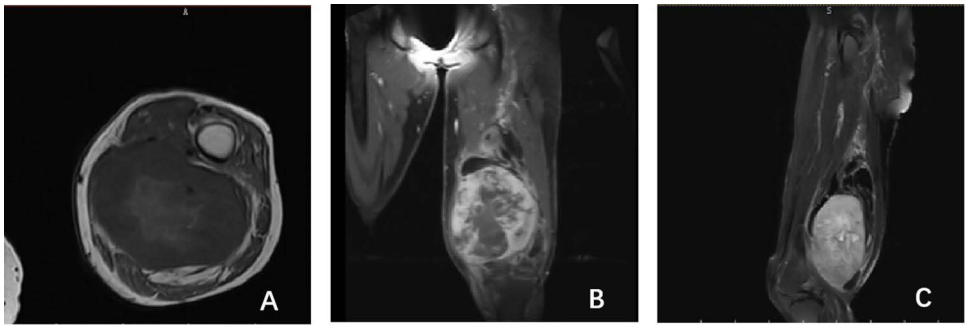

Figure 2 A 72-year-old female patient with a dedifferentiated liposarcoma in her left popliteal fossa. (**A**) T1-weighted image shows an indistinct soft tissue mass in the left popliteal fossa, predominantly consisting of low-signal non-fat areas and displaying heterogeneous signal. Additionally, there is an irregular area of moderate signal at the center. Irregular fat signal is visible at the edge of the mass; (**B**) Fat-suppressed T1-weighted image; (**C**) Fat-suppressed T2-weighted image shows suppressed low signal fat areas and high signal non-fat areas, as well as thick septations within the fat areas.

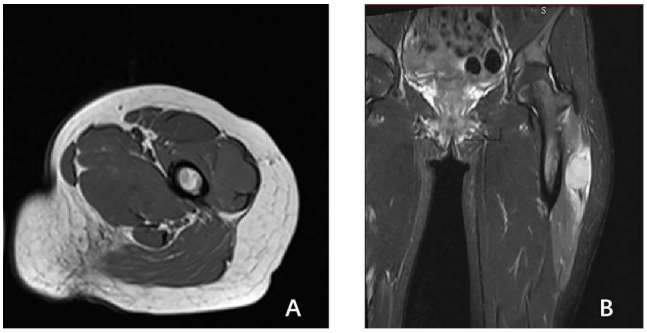

Figure 3 A 24-year-old female patient with a differentiated soft tissue sarcoma in her left thigh. (**A**) T1-weighted image shows a non-fat signal soft tissue mass with a relatively distinct boundary on the outer side of the left thigh, predominantly displaying homogeneous low signal intensity. (**B**) The fat-suppressed T2-weighted image shows predominantly homogeneous high signal non-fat areas, with the tumor infiltrating along muscle fascicles and exhibiting irregular edges.

signal on enhanced T1-weighted images. Homogeneity of non-fat content was primarily observed on T2-weighted images, with signal intensity categorized as low (similar to muscle signal), moderate, or high (similar to water signal). If an area displayed at least two different signal intensities among low, moderate, and high signals, it was considered heterogeneous. Vessels were defined as high-signal vessels on T1-weighted images. Necrosis was defined as unenhanced areas on enhanced T1-weighted images.

Statistical Analysis

The Mann–Whitney *U*-test is used to compare the quantitative results between DDLP and WDLP. Fisher's exact test is utilized to compare the qualitative results between DDLP and WDLP. A $p < 0.05$ is considered significant. All statistical analyses were conducted using the SPSS system.

Results

Table 2 summarizes the findings of DDLP and WDLP in MRI images. The median tumor size for 16 cases of WDLP was 11.3 cm, while for 14 cases of DDLP, it was 19.1 cm. The WDLP group was smaller than the DDLP group (p=0.259), but the difference was not statistically significant. All cases of WDLP showed areas of fat, whereas in the DDLP group, 10

Table 2 The Clinical and imaging results of DDLP and WDLP

MRI Characteristics		WDLP(n=16, %)	DDLP(n=14, %)	P
Medium tumor size(range)		11.3(2.3-32.8)	19.1(1.5-40.2)	
Unclear		2(12.5%)	10(57.14%)	0.002
Visible fat signal		16	10	0.037
Non-fat area(>1cm)				
<5%	1	9	0	0.001
6%-25%	2	7	0	0.007
26%-50%	3	0	2	0.209
51%-75%	4	0	4	0.037
>75%	5	0	8	0.001

(*Continued*)

Table 2 (Continued).

MRI Characteristics	WDLP(n=16, %)	DDLP(n=14, %)	P
Non-fat area (>1cm)			
Even	14	2	
Uneven	2	12	0.000
Non-fat area (>1cm)			
Significant enhancement	7	14	0.001
Slight enhancement	9	0	
Necrotic area	0	3	0.09
Tumor edema	2	3	0.642
Multiple blood vessels	1	2	0.586

Notes: *Significant differences were observed between the two pathologies ($p < 0.05$).

cases exhibited areas of fat, and 4 cases did not show any fat signals (100% vs 62.5%, p=0.037). Non-fat areas in the WDLP typically consisted of small nodules or thick septa. In 16 cases, 9 cases (56.25% vs 0%, P=0.001) had a non-fat area occupancy rate of less than 5%, and 7 cases (43.75% vs 0%, P=0.007) had an occupancy rate of 6%-25%. None of them had an occupancy rate higher than 25%. In 14 cases of DDLP, none had an occupancy rate lower than 25%, 2 cases (14.29% vs 0%, P=0.209) had an occupancy rate of 26–50%, 4 cases (28.57% vs 0%, P=0.037) had an occupancy rate of 51%-75%, and 8 cases (57.14% vs 0%, P=0.001) had an occupancy rate greater than 75%. Except for the 26%-50% range, the non-fat area occupancy rates in the two groups were statistically different in the other four ranges. In terms of the uniformity of non-fat areas, 14 cases (87.5%) in the WDLP group exhibited more uniformity compared to only 2 cases (14.28%) in the DDLP group, with P<0.001, indicating a significant statistical difference. In terms of enhancement of non-fat tumor areas, 7 cases (43.75%) in the WDLP group showed significantly less enhancement compared to 14 cases (100%) in the DDLP group, with P=0.001, also showing a significant statistical difference. The incidence of necrotic areas (0% vs 21.42%, P=0.09), peritumoral edema (12.5% vs 21.42%, P=0.642), and multiple vessels (6.25% vs 14.28%, P=0.586) in WDLP patients was lower than in DDLP patients. However, the statistical analysis did not show a significant difference.

Discussion

Current research indicates that both WDLP and DDLP exhibited fat-based masses with non-fat components on imaging.[8] In our study, we observed this presentation and conducted a more detailed observation of the fat and non-fat components, as well as other imaging characteristics of these two types of tumors. We correlated these imaging features with their specific histological components, which assists in guiding our biopsy and treatment planning.

Our research shows that there is no difference in the MRI signal presentation of the two subtypes of fat components. However, a higher proportion of fat components can be observed in WDLP compared to DDLP, and some DDLP may not contain any fat tissue signal. The core biopsies of the fat areas in both cases consist of atypical fat cells and adipocytes,[5] making it difficult to distinguish them initially. If only the DDLP sample is obtained from this area, it may be mistakenly identified as a well-differentiated liposarcoma or benign lipoma, leading to potential oversight. However, it can be preliminarily diagnosed as tissue of fat origin.[9]

Reviewing the literature, the non-fat area has consistently been a primary focus in the study of liposarcoma. In DDLP, the non-fat component is significantly higher compared to the fat component, as opposed to WDLP Our research

indicates that the non-fat area in WDLP generally accounts for less than 25%, appearing as uniformly low-signal thick septa or small nodular areas in T1 and T2, with minimal enhancement. In contrast, the non-fat area in DDLP typically accounts for more than 50%, presenting as non-uniform low to moderate signals. These non-fat areas generally manifest as relatively large nodular areas or irregular fluffy, streaky areas, showing significant enhancement. This is related to the histological differences between the two. The non-fat area in WDLP usually represents collagen matrix or inflammatory components,[10] often with uniform signals. While in DDLP, the non-fat area consists of dedifferentiated components with a wider range and more complex histological composition, rosarcomatous, or vascular sarcomatous, typically with non-uniform signals, possibly resembling highly malignant fibrosarcoma or malignant fibrous histiocytoma components.[11] It may also include dense mixed inflammatory infiltration or even components of heterologous differentiation such as myogenic, osteochond Performing a biopsy in this area can help obtain a more accurate pathological diagnosis and is also crucial for distinguishing between WDLP and DDLP.

Our research also shows that DDLP is more likely to have ambiguous boundaries, which may be associated with its highly aggressive behavior and invasive spread to surrounding tissues, as well as its poor prognosis and high grade.[12] However, features such as abundant blood vessels, peritumoral edema, and necrosis did not exhibit statistically significant differences in the study.

Based on the above analysis, a preliminary differential diagnosis of WDLP and DDLP can be achieved through the assessment of imaging features. This is significant for preoperative diagnosis and the selection of surgical strategies. WDLP is prone to local recurrence, which is associated with the tumor's inherent local invasiveness. However, a good prognosis can still be achieved through secondary local excision. On the other hand, DD not only has a higher tendency for recurrence but also for metastasis. The prognosis of DDLP is largely determined by the extent of resection, making extensive surgical excision crucial for initial treatment.[13] Therefore, a preoperative diagnosis is important based on these prognostic characteristics.

According to our research results, for the soft tissue masses with a large proportion of fat (less than 25% non-fat area), homogeneous signal, mild enhancement, and well-defined tumor borders are highly likely to be indicative of WDLP. In cases with such typical imaging features of WDLP, it is feasible to reduce unnecessary preoperative biopsy procedures and, based on clinical evaluation, opt directly for surgical intervention. However, in cases with a lower proportion of fat (more than 50% non-fat area), non-uniform signal in the non-fat area, significant enhancement, and unclear borders, WDLP may not be considered, and there may be a greater tendency towards DDLP or other subtypes of liposarcoma. In such instances, further needle biopsy is required to ascertain the nature of the tumor. Once a definitive diagnosis is established, treatment modalities can be selected based on clinical assessment.

Based on the characteristic imaging features and the correlation between imaging and pathological tissues, more accurate preoperative pathology can be obtained through needle biopsy guided by imaging data. Especially for DDLP, when there is a strong suspicion of a lesion being a DDLP based on imaging, biopsies should be taken from both the fatty and non-fatty areas of the lesion. Moreover, when the non-fatty area is large, biopsies should be obtained from the areas with inconsistent signals within the non-fatty region to acquire a more representative tissue composition and attain a more precise preoperative pathology result.

Based on these discussions, we have developed a procedural flow for preoperative puncture biopsy (Figure 4). First, when the non-fat area of the mass is less than 25%, we consider the tumor to be WDLP, and we also need to distinguish it from a benign lipoma. In this instance, we can opt for direct surgery without the necessity of a puncture biopsy. When the non-fat area of the mass exceeds 25%, the possibility of the mass being a DDLP or another subtype of liposarcoma is higher. In this scenario, we should routinely use puncture biopsy to obtain accurate pathology. The areas targeted for puncture include the fat area and the non-fat area (low, medium, and high signal areas). Puncture examination methods include core needle biopsy and incisional biopsy of the mass. The puncture route is based on the standard surgical approach for limb-sparing surgery and should align with the incision line of the final surgical design. If necessary, a multi-point puncture method can be used to obtain a wide variety of pathological components.[14] All of these procedures can be more effectively performed under imaging guidance.[15]

This study has several limitations. First, it was conducted at a single institution, resulting in a relatively small sample size. Future studies will aim to collaborate with multiple centers to collect a broader dataset for statistical analysis,

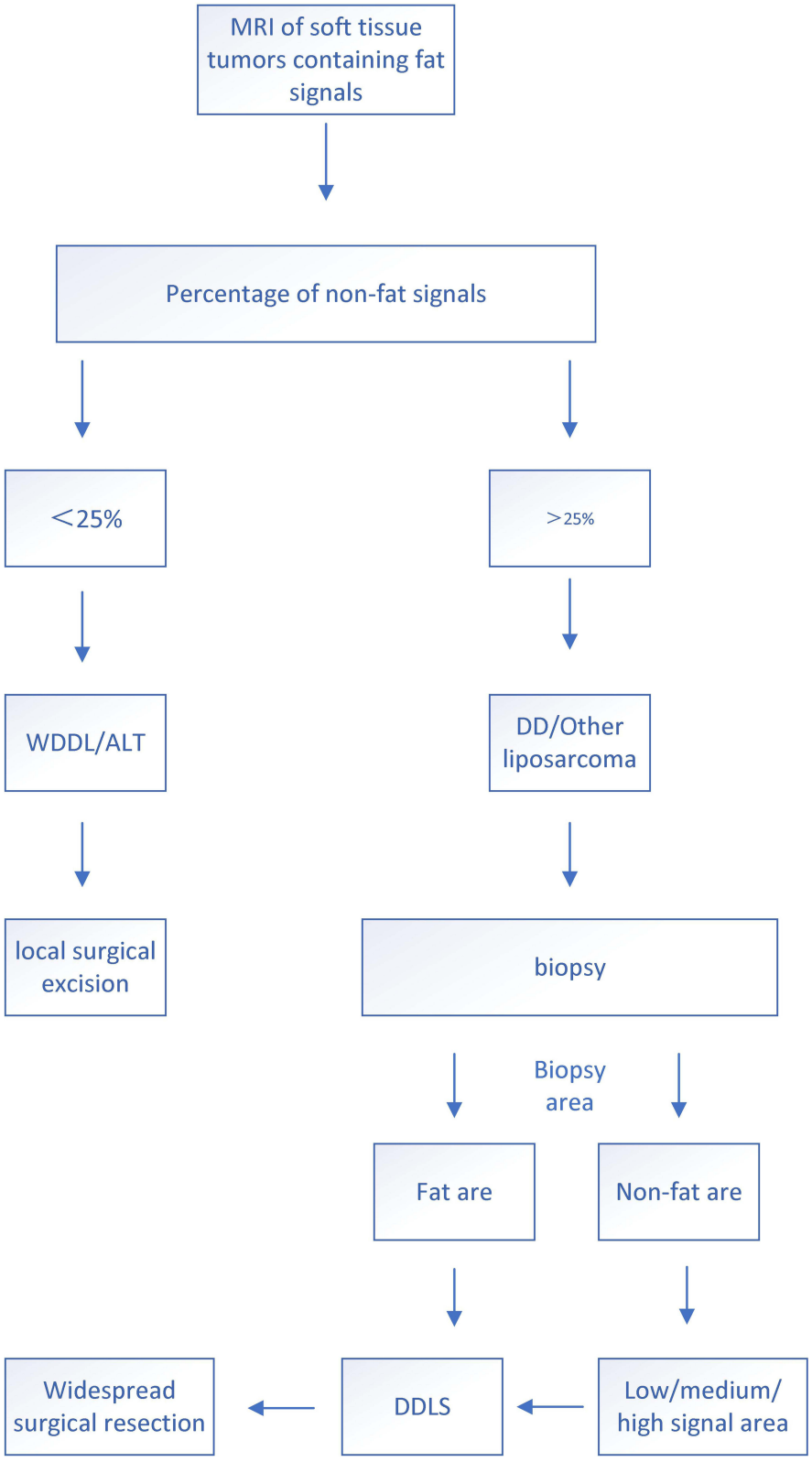

Figure 4 In soft tissue tumors containing fat signals, when the non-fatty area is less than 25%, WDLP is diagnosed in combination with the features in the text, and direct local surgical resection is performed. Whereas, when the nonfat area is greater than 25%, we can initially consider DDLP or other subtypes of liposarcoma, and obtain a wider range of tissue components by image-guided puncture of the fat area, the nonfat area (low, intermediate, and high signal areas) to obtain a wider range of tissue components, and after confirming the diagnosis of DDLP, extensive surgical resection is performed.

thereby increasing the sample size. Second, due to the retrospective nature of the study, the initial MRI scans varied in resolution, which could affect the consistency of the data. Prospective studies are planned to verify the accuracy of the conclusions further. Additionally, the identification and measurement of imaging features might be prone to human error or limited by the experience of the researchers and the resolution of MRI. The integration of artificial intelligence, such as radiomics, is anticipated to mitigate these limitations progressively. Finally, this study focused exclusively on musculoskeletal lesions, and the findings may not be applicable to retroperitoneal liposarcomas.

Conclusion

Due to the similarities between WDLP and DDLP, as well as their differences in clinical behavior, it is crucial to differentiate between the two preoperatively. We analyzed the imaging features that can distinguish between the two conditions, and based on this analysis, we discussed the feasibility of image-guided biopsy. DDLP exhibits a lower proportion of fatty areas and a larger proportion of non-fatty areas, with more complex and heterogeneous signals. It typically shows significant enhancement and unclear tumor margins. In contrast, WDLP exhibits a higher proportion of fatty areas and a smaller proportion of non-fatty areas, with more uniform signals. The enhancement of non-fatty areas may be mild or significant, with clear and regular tumor margins. Tumor size, vascularity, necrosis, and peritumoral edema are not distinctive features for differentiation. After conducting a preliminary differentiation by MRI, we use a non-fatty area that is less than 25% as the threshold for biopsy. In cases of soft tissue tumors exhibiting fat signals, when the non-fatty area less than 25% of the tumor, the likelihood of a WDLP is high. Considering these imaging characteristics alongside clinical assessments, direct surgical intervention may be chosen without the necessity for a biopsy. When the non-fatty area exceeds 25%, we can preliminarily consider DDLP or other subtypes of liposarcoma. Biopsy of both fatty and non-fatty areas (low, medium, high signal areas) guided by imaging can provide a more comprehensive assessment of tissue composition and obtain the most accurate preoperative pathological results to inform subsequent clinical treatment steps. WDLP can be effectively treated with local excision, while DDLP requires a more extensive surgical resection to ensure a favorable prognosis for the patient.

Ethics Approval and Consent to Participate

This study was approved by the ethical review committee of the Cancer Hospital of Guangxi Medical University in accordance with the principles of the Helsinki Declaration. In this retrospective study, all data remained anonymous, and the requirement for written informed consent from patients was waived. Written informed consent from participants was not required in accordance with local/national guidelines.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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