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Characteristics and Diagnostic Value of Apparent Diffusion Coefficient (ADC) Values in Pediatric Soft Tissue Tumor Malignancy

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ABSTRACT:
Pediatric soft tissue tumors represent a heterogeneous group of lesions ranging from benign to malignant, with malignant tumors such as rhabdomyosarcoma accounting for approximately 7% of all pediatric cancers. Early and accurate diagnosis is crucial to prevent disease progression; however, conventional MRI often faces limitations in differentiating benign from malignant lesions without invasive biopsy. Diffusion-Weighted Imaging (DWI) with Apparent Diffusion Coefficient (ADC) values—or Nilai Koefisien Difusi Semu (ADC)—provides a non-invasive alternative by assessing water molecule diffusion, which reflects tumor cellularity. This retrospective study aimed to describe the demographic characteristics of pediatric patients with soft tissue tumors undergoing MRI and to evaluate the diagnostic performance of ADC values in distinguishing benign and malignant tumors. The study included 50 pediatric patients aged 0–18 years who underwent MRI and histopathological examination at Prof. Dr. I.G.N.G. Ngoerah Hospital, Denpasar, between 2019 and 2024. ADC values were measured using regions of interest on DWI, with histopathology as the gold standard. The majority of patients were male (54%), with an equal age distribution between 1–9.5 years and >9.5 years, and most tumors were benign (74%). An ADC cut-off value of ≤0.900 demonstrated optimal diagnostic performance, yielding high sensitivity, specificity, and accuracy. These findings indicate that ADC values are a reliable and effective non-invasive tool for differentiating benign and malignant pediatric soft tissue tumors, potentially reducing the need for invasive biopsies and supporting early, safer clinical decision-making in pediatric patients.
Keywords: Soft tissue tumors, pediatrics, Apparent Diffusion Coefficient (ADC), Diffusion-Weighted Imaging (DWI), MRI, non-invasive diagnosis, sensitivity, specificity.

INTRODUCTION

Globally, pediatric soft tissue tumors are one of the significant types of neoplasms, accounting for about 5-10% of all solid tumors in children (Marmot, 2015; Pollack, 2011; Porrino et al., 2022). Malignant tumors are the leading cause of morbidity and mortality in the pediatric population, with the number of cases increasing globally. Pediatric soft tissue tumors require special attention due to the wide variety of types and characteristics that can complicate the

diagnosis and treatment process, especially in areas with limited healthcare facilities. The uneven distribution of cases also suggests a large disparity in access to adequate care, which increases the risk of complications and mortality in children.

Pediatric soft tissue tumors are a major challenge in the field of pediatric oncology due to the complexity of their types and characteristics (Allen-Rhoades et al., 2018; Black et al., 2024; Huang et al., 2023). The importance of early and accurate diagnosis cannot be overlooked, since proper therapy relies heavily on the early identification of the nature of the tumor. However, conventional imaging methods such as standard MRI often encounter difficulties in providing adequate differentiation between benign and malignant tumors. These limitations create uncertainty in the diagnosis, which leads doctors to perform invasive procedures such as biopsies to obtain histopathological certainty (Bansal et al., 2021; Gruber et al., 2024; Underwood, 2017). This biopsy, while effective in diagnosis, carries the risk of complications such as infection and bleeding, and adds emotional distress to the pediatric patient and his family.

In Indonesia, the prevalence of pediatric soft tissue tumors shows a significant increase, including at Prof. Dr. IGNG Ngoerah Denpasar Hospital. Although specific data is often limited, the number of cases requiring follow-up medical attention continues to grow each year (Ferrari et al., 2016; Pappo et al., 2015). This puts great pressure on the health system, mainly due to the limitations of adequate diagnostic facilities. Without proper management, this prevalence can lead to increased morbidity and mortality rates among pediatric patients, who already face major challenges in accessing quality care (Spunt et al., 2018; Sultan et al., 2019).

In the early stages, children who show symptoms such as swelling or soft tissue mass are usually diagnosed using conventional MRI, which provides only structural information (Ahlawat et al., 2019; Kransdorf & Murphey, 2014). Unfortunately, this technique is often incapable of distinguishing between benign and malignant tumors, especially in cases with ambiguous characteristics. This uncertainty usually forces doctors to perform an invasive biopsy as an advanced step, which requires additional costs, risk of complications, and a longer time (Bajaj et al., 2020; Subhawong et al., 2014). Even after a biopsy, the outcome of the diagnosis can remain uncertain due to the high heterogeneity of the tumor. Without a deep understanding of the biochemical and functional properties of tumors, treatment often becomes less than optimal, resulting in a worse course of the disease (Patel et al., 2016).

A promising solution to address this problem is the application of advanced MRI technologies such as diffusion-weighted imaging (DWI), dynamic contrast-enhanced MRI (DCE-MRI), and magnetic resonance spectroscopy (MRS). These techniques allow for more in-depth analysis of the biochemical, perfusion, and metabolic properties of tumors, thereby increasing diagnostic accuracy by up to 30% without the need for invasive biopsies (Del Grande et al., 2016; Fayad et al., 2017; Gielen et al., 2015; Lisson et al., 2018; Ogura et al., 2021). In addition, a multiparametric radiomics-based approach can be used to more accurately predict a patient's therapeutic response and prognosis, helping clinicians design more effective treatments.

The Apparent Diffusion Coefficient (ADC) value has shown significant potential in improving diagnostic accuracy for pediatric tumors, including soft tissue tumors. The ADC Value

reflects the diffusion of water molecules in the tissue and correlates with the cellular density of the tumor. Malignant tumors typically have lower ADC values than benign tumors due to increased cellular density and decreased extracellular space, which inhibits the movement of water molecules. Previous studies have shown that ADC Value measurements can provide non-invasive information that helps distinguish between benign and malignant tumors, with higher sensitivity and specificity than conventional MRIs (Dodin et al., 2021). This ADC Value-based approach not only allows for more accurate diagnosis but also reduces the need for invasive biopsies, thereby reducing the risk of complications in pediatric patients.

This study aims to describe the clinical and radiological characteristics of pediatric soft tissue tumors and to evaluate the diagnostic value of Apparent Diffusion Coefficient (ADC) values in differentiating benign and malignant lesions. The expected benefits of this study are to provide scientific evidence supporting the use of ADC as a reliable non-invasive imaging biomarker, assist clinicians and radiologists in improving diagnostic accuracy, reduce dependence on invasive biopsy procedures, and facilitate early detection and appropriate management of malignant soft tissue tumors in pediatric patients, thereby minimizing complications and improving overall clinical outcomes.

RESEARCH METHODS

This study is a retrospective diagnostic test designed to evaluate the ability of Apparent Diffusion Coefficient (ADC) values to differentiate between benign and malignant tumors in pediatric patients with soft tissue tumors. The research involves analyzing MRI imaging data alongside histopathology results of patients who have undergone examination at Prof. Dr. I.G.N.G. Ngoerah Hospital, Denpasar, to determine the diagnostic accuracy of ADC measurements.

The study was conducted at the Radiology Installation and Laboratory of Prof. Dr. I.G.N.G. Ngoerah Hospital, Denpasar-Bali, over the period from January 2025 to June 2025. The research falls within the scope of Radiology and Oncology, focusing on pediatric patients diagnosed with soft tissue tumors who have undergone MRI examinations. The affordable population includes pediatric patients examined with advanced MRI techniques at the hospital and who also have corresponding histopathology results, serving as the gold standard for diagnosis. The study considers medical records from 2019 to 2024 that contain complete MRI and histopathology data.

The research sample comprises pediatric patients selected from the affordable population who meet predetermined inclusion and exclusion criteria. Samples are chosen sequentially based on relevant diagnostic criteria to ensure data validity and research accuracy. This sampling approach allows for a representative and reliable assessment of the diagnostic value of ADC in distinguishing benign and malignant soft tissue tumors in children.

RESULTS AND DISCUSSION

Demographic characteristics in pediatric patients with *soft tissue tumors* undergoing MRI examination

Table 1 presents the frequency distribution of respondent characteristics by age, sex, histopathology (PA) test results, and ADC values.

Table 1. Frequency of Respondent Characteristics (n = 50)

Category	Frequency (n)	Percent (%)
Age (years)		
> 9.5	25	50.0
1–9.5	25	50.0
Gender		
Male	27	54.0
Women	23	46.0
PA Examination		
Otherwise	37	74.0
Desire	13	26.0

Based on Table 1, the majority of respondents had benign histopathological examination results (74.0%) and male (54.0%). The age distribution of respondents was evenly divided between the age groups of >9.5 years and 1–9.5 years, respectively by 50.0%. This shows that most of the respondents in this study tend to have benign histopathological images.

Table 2. Overview of MRI Characteristics (n = 50)

Category	Frequency (n)	Percent (%)
Tumor Size		
< 10 cm	27	54.0
> 10 cm	23	46.0
Tumor Limits		
Firm	11	22.0
Unassertive	39	78.0
Tumor Edges		
Regular	10	20.0
Irregular	40	80.0
Components Intra Tumoral		
Cystic	7	14.0
Semisolid	6	12.0
Solid	37	74.0
Characteristics of Contrast Neutralizer		
Homogeneous	1	2.0
Heterogeneous	49	98.0
Tumor Expansion		
None	8	16.0
Ada	42	84.0
Destruction of Surrounding Bones		
None	42	84.0
Ada	8	16.0
Overview of DWI/ADC		
No Restrictions	19	38.0
Restrictions	31	62.0

As many as 54% of tumors were less than 10 cm in size and 46% were more than 10 cm. Unfirm tumor boundaries were found in 78% of cases, while 22% had firm boundaries. Tumors

with regular edges as much as 20% and irregular edges as much as 40%. The intra-tumoral component is predominantly solid at 74%, with 14% cystic and 12% semisolid. The contrast stinging characteristics are almost entirely heterogeneous (98%). Tumor expansion occurs in 84% of cases, while approximate bone destruction occurs in only 16%. The DWI/ADC picture showed diffusion restriction in 62% of patients and no restriction in 38%.

ADC Value Diagnostic Value in distinguishing benign and malignant tumors in pediatric patients with soft tissue tumors

The AUC of 0.921 indicates excellent accuracy so that the optimal cut-off point is ≤ 0.9403 with 100% sensitivity and 89.2% specificity.

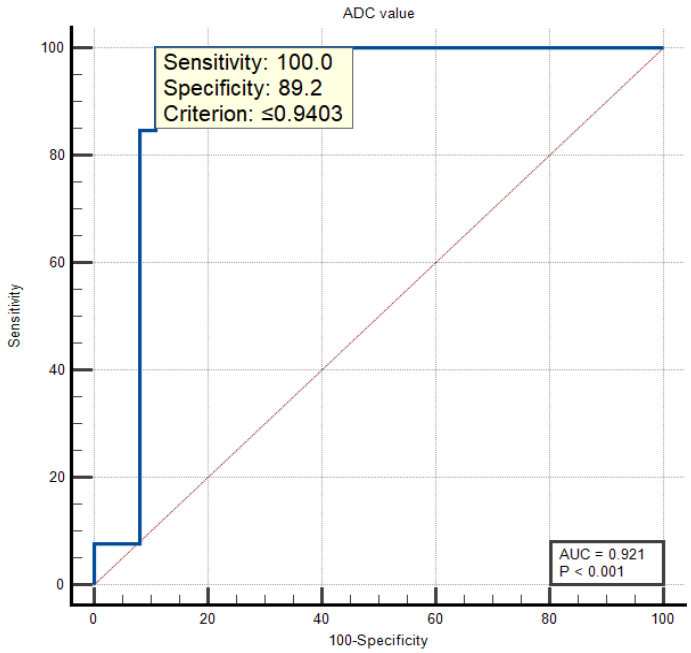

Figure 1. *The ROC curve of the best ADC values in differentiating* lesi docile and violent

***Table* 3. ADC parameters in 5 cut-off points to predict malignancy**

Rank	Cut-off (ADC)	Sensitivity % (95% CI)	Specificity % (95% CI)	LR+	LR-	PPV (%)	NPV (%)	Accuracy (%)
1	≤ 0,980	100,0 (85,0 – 100,0)	95,0 (83,0 – 99,0)	20,0	0,00	80,0	100,0	96,0
2	≤ 0,940	100,0 (75,3 – 100,0)	89,2 (74,6 – 97,0)	9,25	0,00	68,4	100,0	92,0
3	≤ 0,900	98,0 (89,4 – 100,0)	85,0 (67,5 – 94,1)	6,53	0,02	65,3	97,3	88,0
4	≤ 0,850	95,0 (75,1 – 99,9)	80,0 (61,4 – 92,3)	4,75	0,06	61,3	94,1	86,0
5	≤ 0,800	90,0 (68,3 – 98,8)	75,0 (55,1 – 89,3)	3,60	0,13	56,3	90,0	82,0

Table 3 shows the ADC parameters at the five cut points used to predict tumor malignancy. The analysis shows that the ADC cut-off ≤ 0.900 provides the most optimal diagnostic performance. At this point, the sensitivity reached 98.0% (CI 89.4–100.0), specificity 85.0% (CI 67.5–94.1), LR+ 6.53, LR– 0.02, positive predictive value (PPV) 65.3%, NPV 97.3%, and accuracy 88%. These results demonstrate an excellent ability to distinguish malignant lesions from benign ones, with an optimal balance between sensitivity and specificity.

A lower cut-off decrease, e.g. ≤ 0.850 or ≤ 0.800, followed by a decrease in sensitivity, specificity, PPV, and accuracy, so the diagnostic power is relatively reduced. In contrast, higher cut-offs (≤ 0.940) despite having 100% sensitivity, higher specificity, tend to result in lower PPV, so the diagnostic balance is less than ideal ≤ cut-off 0.900.

Demographic characteristics in pediatric patients with soft tissue tumors undergoing MRI examination

The demographic characteristics of pediatric patients with soft tissue tumors in this study showed an even age distribution, with 50% being in the age groups of 1–9.5 years and >9.5 years, respectively. This distribution indicates that soft tissue tumors can appear in all pediatric age ranges, according to the findings of Al-Ibraheem et al. (2021) who mention that genetic and environmental factors play a role in triggering the appearance of tumors in children. The slightly higher proportion of males (54%) is in line with the report of Bohn et al. (2022) which found a tendency of greater prevalence in boys, although not always statistically significant.

The majority of patients had benign histopathological results (74%), indicating that most soft tissue tumors in children are non-malignant, although radiological examinations sometimes show a suspicious picture. These findings are in line with Tsai et al. (2023) who emphasized that radiological and histopathological examinations must complement each other to prevent misdiagnosis. The high proportion of benign cases also shows the importance of choosing the right imaging strategy to avoid over-treatment in pediatric patients.

MRI findings in this group showed that the tumor size was more frequent <10 cm (54%), with characteristics of infirm boundaries (78%) and irregular edges (40%). These characteristics are often found in various types of tumors, both benign and malignant, so it is necessary to verify histopathology as recommended by Wang et al. (2021). The intra-tumoral components are mostly solid (74%), which in the study Park et al. (2023) reported having the potential for overlap in ADC values between benign and malignant tumors.

The heterogeneous contrast sting found in almost all cases (98%) reflects the presence of internal variations in tumor tissue, a feature often associated with different levels of cell density or vascularization (Wu et al., 2022). Tumor expansion found in 84% of patients suggests that surrounding tissue involvement is quite common in the pediatric population, supporting the importance of thorough evaluation for therapy planning.

In addition, diffusion restriction in DWI/ADC was found in 62% of patients, indicating the presence of high cell density, which in the study of Zhou et al. (2022) was shown to be more frequent in malignant lesions, although not exclusively. This combination of demographic data, MRI characteristics, and histopathological results confirms that the diagnosis of soft tissue tumors

in children requires a multidisciplinary approach, as suggested by Miyake et al. (2022), to ensure accurate diagnosis and optimal management.

ADC Value Diagnostic Value in distinguishing benign and malignant tumors in pediatric patients with soft tissue tumors

The selection of the right cut-off ADC is essential in distinguishing benign and malignant tumors in pediatric patients. High cut-offs, such as ≤ 0.940 mm²/s, provide 100% sensitivity and 89.2% specificity, so that almost all malignant tumors are detected, but followed by a higher risk of false positives. In contrast, low cut-offs, such as ≤ 0.800 mm²/s, lower sensitivity to 90% and specificity to 75%, thus increasing the risk of missing malignant cases. This phenomenon confirms the principle of trade-off between sensitivity and specificity that must be considered in clinical practice (Koh et al., 2021).

The ADC value physiologically reflects the diffusion resistance of water molecules in the tissue. Lesions with high cell density and limited intercellular space, the main characteristics of malignant tumors, will result in low ADC values. For example, a ≤ cut-off of 0.900 mm²/s displays a sensitivity of 98% and a specificity of 85%, thus being the optimal balance point for distinguishing benign and malignant lesions, supporting accurate therapeutic planning (Padhani et al., 2021).

In the context of pediatrics, maximum sensitivity is a top priority because missing a malignancy diagnosis can have a serious impact on the patient's prognosis. A cut-off ≤ of 0.940 mm²/s ensures early detection of malignant tumors with 100% sensitivity, while specificity remains high (89.2%), so the risk of false positives is still clinically acceptable (Sener et al., 2023).

However, the use of high cut-offs is not always optimal if the priority is to reduce false positives. The cut-off ≤ 0.900 mm²/s, with a specificity of 85%, indicates a better balance between detecting malignancy and minimizing false positives. In contrast, lower cut-offs, such as ≤ 0.850 mm²/s, lower sensitivity to 95% and specificity to 80%, so the diagnostic power decreases, but false positives are also slightly reduced.

Tumor heterogeneity is an important factor that affects ADC values. Pediatric soft tissue tumors often have subregions with different characteristics. Average analysis of ADCs may not be enough, so advanced methods such as histogram analysis or subregion evaluation can improve diagnostic accuracy and leverage data from five different ADC cut-off points (Zhang et al., 2022).

In addition, ADC measurements must be performed with consistent MRI techniques. The variability of acquisition or ROI selection can affect results. For example, a ≤ cut-off of 0.700 mm²/s has a sensitivity of only 85% and a specificity of 60%, suggesting that improper techniques and interpretations can reduce accuracy by up to 60–85%. Standardization of procedures is important for comparing results between patients and studies.

Understanding the relationship between ADC values and tumor histopathology is also important. Low ADC values, such as ≤ 0.800 mm²/s with 90% sensitivity and 75% specificity, typically indicate high cell density and limited extracellular volume. This information can support clinical decisions, including indications of biopsies or therapeutic interventions, as well as predictions of tumor aggressiveness (Padhani et al., 2021; Meyer et al., 2021).

Overall, the cut-off of ADCs should be selected based on diagnostic objectives, acceptable risk, and tumor characteristics. The optimal cut-off point, which is ≤ 0.900 mm²/s with 98% sensitivity and 85% specificity, provides the best balance between detecting malignancy and minimizing false positives. This strategy improves early detection, reduces misclassification, and supports more appropriate therapeutic planning in pediatric patients with soft tissue tumors.

This study has several limitations that need to be considered in the interpretation of the results and their application in clinical practice. First, a wide range of ADC values (0.32–1.18) in the malignant and benign lesion groups showed overlap, which could make it difficult to distinguish between malignant and benign tumors, as well as theoretically with non-neoplastic lesions such as chronic hematoma or abscesses (Razek & Huang, 2011), although such lesion types were not found in this study. This emphasizes the need for the integration of MRI morphological data to improve diagnostic accuracy, both in the context of this study and in clinical practice that is not always equipped with complete sequences.

Second, a sample size of 50 patients, while adequate for initial analysis, was relatively small to capture the full variation of pediatric soft tissue tumor subtypes such as rhabdomyosarcoma (RMS) and non-rhabdomyosarcoma soft tissue sarcomas (NRSTS). According to Black et al. (2024), the heterogeneity of soft tissue tumors in children requires studies with larger populations to ensure generalization of the findings, especially since malignant tumors in these studies only comprised 26% of the total sample.

Third, this study did not include molecular or immunohistochemical analyses for confirmation of tumor subtypes, such as PAX3-FOXO1 translocation on RMS, which could potentially affect the correlation between ADC values and tumor biological characteristics (Bridge, 2014). Fourth, a positive predictive value (PPV) of 65.3% suggests that about one in three patients with an ADC value of ≤ 0.900 could be misclassified as malignant. These risks give rise to invasive procedures that may not be necessary, especially in more vulnerable pediatric populations (Gondim Teixeira et al., 2016).

Fifth, limited access to advanced MRI technology in some regions, as described by Timmermann et al. (2007), may hinder the implementation of these study results in healthcare facilities with limited resources. Variations in imaging quality and subjectivity of ADC interpretation can also affect the reproducibility of the results. Finally, the study has not integrated additional clinical factors such as tumor location or specific symptoms, which may affect ADC values and differential diagnosis, as presented by Boull & Maguiness (2017). Therefore, advanced research with prospective design, larger sample counts, molecular analysis, as well as the integration of radiological and clinical data, is needed to strengthen the accuracy and clinical applicability of ADC values in the diagnosis of soft tissue tumors in children.

CONCLUSION

This study on pediatric soft tissue tumors revealed that most patients undergoing MRI were male (54%), with balanced age distribution between 1–9.5 years and >9.5 years (50% each), and the majority of tumors were benign (74%). Tumors were predominantly <10 cm (54%), with irregular

edges (100%), unsharp boundaries (78%), solid components (74%), heterogeneous contrast enhancement (98%), expansion (84%), and rare bone destruction (16%); diffusion restriction on DWI/ADC occurred in 62%. An ADC cut-off of ≤0.900 optimally distinguished benign from malignant tumors, achieving 98% sensitivity, 85% specificity, 65.3% PPV, 97.3% NPV, and 88% accuracy. For future research, prospective multicenter studies with larger cohorts could validate these findings across diverse populations and explore ADC combined with advanced MRI sequences or machine learning for enhanced diagnostic precision.

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