Egyptian Journal of Radiology and Nuclear Medicine

RESEARCH

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Qualitative and quantitative parameters of dynamic contrast-enhanced (DCE) MRI as a diagnostic determinant of soft tissue tumor malignancy: a study from Indonesia

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Abstract

Background Soft tissue tumors encompass a large variety of benign and malignant lesions which are classified histologically based on the components. Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) is a non-invasive technique that is used in differentiating benign from malignant lesions by observing the differences in the enhancement rates, index of lesion vascularity and perfusion. Therefore, this research aimed to evaluate the diagnostic efficacy of qualitative and quantitative parameters of DCE-MRI in the malignancy of soft tissue tumors.

Methods The type of time-intensity curve (TIC), K_{trans}, $K_{ep,}$ and V_e values were obtained from 30 soft tissue tumor (17 malignant and 13 benign) from patients who performed the DCE-MRI examination. The obtained values were then statistically analyzed to get the cutoff point, sensitivity, and specificity in determining the malignancy of soft tissue tumors.

Results TIC, K_{trans}, and K_{ep} values were significantly differentiated into benign and malignant soft tissue tumors except for V_e. The TIC for benign soft tissue tumors was predominantly by type 2, while type 3, 4, and 5 were predominantly malignant. The AUC of the ROC curve demonstrated a diagnostic potential of K_{trans} (0.873) and K_{ep} (0.889). Furthermore, the cutoff point for K_{trans} and K_{ep} was 0.2905 and 0.3365 with a sensitivity of 88.2% and 94.1%, specificity of 84.6%, PPV of 88.2% and 88.9%, and NPV of 84.6%, and 91.7%.

Conclusions Qualitative and quantitative parameters of DCE-MRI helped diagnose soft tissue tumor malignancy with a cutoff point for K_{trans} 0.2905 and K_{ep} 0.3365.

Keywords DCE, Malignancy, MRI, Soft tissue tumor

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Background

Soft tissue originates from the mesenchyme and differentiates during development to become fat, skeletal muscle, peripheral nerves, blood vessels, and fibrous tissue. Furthermore, the soft tissue tumor (STT) was classified histologically based on the component that comprises the lesion. The benign tumors have an incidence of approximately 300/100,000 and asymptomatic patients suffering from this condition only require clinical observation or surgical excision [1]. However, malignancy incidence is about 1% or 5/10,000 per year and is primarily treated using surgical resection and chemotherapy [1, 2]. The prognosis of patients with soft-tissue tumors depends on early diagnosis which affects the therapy process due to the distinct clinical treatment involved [3].

Histopathology remains the gold standard of assessing the types and grades of tumors, but this examination requires a biopsy which is invasive to patients. Imaging plays a fundamental role in the initial assessment of soft tissue tumors. For example, magnetic resonance imaging (MRI) is considered a modality of choice due to its high tissue contrast and multi planarity [1, 4]. Furthermore, Dynamic contrast-enhanced MRI (DCE-MRI) is a promising non-invasive method that provides not only morphological information about soft-tissue tumors but also enables monitoring of dynamic changes in the enhanced characteristics of a lesion. This technique can be used to provide important information about the function, perfusion, vasculature, capillary permeability, and interstitial space volume of a tissue [3, 5].

Dynamic contrast-enhanced MRI analysis may be based on a qualitative, and quantitative approach. It has been used in cases of breast and prostate cancer, glioma, and musculoskeletal cases. However, there are limited studies about the value of DCE-MRI in the differential diagnosis of soft-tissue tumors, especially in Indonesia. These few reports mostly focused on qualitative and semiquantitative, rather than quantitative analysis of DCE-MRI [3]. Previous studies also used semiquantitative parameters, namely Emax/1, Emax/2, Emax, and steepest slope. It was found that the combination of these parameters had a 95.5% of overall accuracy in classifying benign and malignant lesions [5]. Another study also stated that wash-in rates were the most specific parameter, with a cut-off value of 15.4 1/s. sensitivity of 87.9% and specificity of 90.9% [4]. Furthermore, another research evaluated the time-signal intensity curve and discovered the sensitivity, specificity, and overall accuracy of DCE images for the differentiation of benign and malignant lesions was 94%, 75%, and 86%, respectively [6]. Quantitative parameters were used in previous study and obtained that diffusion-weighted imaging (DWI) with Apparent diffusion coefficient (ADC) mapping and DCE parameters (Ktrans, Kep, Ve, and iAUC, and TCC plots) significantly differentiated benign and malignant lesions (except Ve) [7]. Therefore, this study aimed to evaluate the diagnostic efficacy of qualitative and quantitative parameters of DCE-MRI in the malignancy of soft tissue tumors.

Methods

This study was approved by the Health Research Ethics Committee, Faculty of Medicine, Diponegoro University and the Ethics Council of Dr. Kariadi Hospital Semarang with registration number 847/EC/KEPK-RSDK/2021, and written informed consent was obtained from a total of 30 patients/guardian.

Patients This retrospective study was conducted at Dr. Kariadi Hospital Semarang, Indonesia using a cross-sectional method. Patients with soft tissue tumors recognized on physical examination or other imaging modalities sent to Radiology Installation for MRI—including DCE, between April 2020 and September 2021 were included. The exclusion criteria were previous history of chemotherapy or radiotherapy and patients with intermediate/borderline group of soft tissue tumors. The tumors were diagnosed pathologically and classified according to World Health Organization (WHO) 2013 [8, 9]. Additionally, a total of 30 patients with soft tissue tumors—17 malignant and 13 benign lesions—were enrolled.

Magnetic resonance imaging The MRI examination was conducted using 1.5 T MRI Scanner [General Electric (GE) Signa Voyager]. The body or surface coil was used depending on the location and size of the lesion. Furthermore, conventional MRI series were initially conducted to locate lesions (axial, sagittal, and coronal spin-echo T1-weighted imaging [T1WI] {[time to repetition (TR)/time to echo (TE)]; 642/16.3 slice thickness 4.0 mm}, T2-weighted imaging [T2WI] (TR 1000/TE 90; slice thickness 4 mm), and fat-suppressed T2WI) [3, 5, 7, 10].

A pre-contrast T1WI fast spoiled gradient echo (FSPGR) (5.6/2.6–12; flip angle 12°; slice thickness 4.0 mm) for DCE-MRI was carried out before contrast injection. DCE-MRI was performed in the axial, sagittal, or coronal plane depending on the lesion, with administering intravenous bolus injection of 0.1 mmol/kg gadolinium. Furthermore, the T1WI FSPGR sequence was made into 11 phases, and added about 4.5 min to the total MRI examination [10].

Image Processing The DCE-MRI data were transferred to postprocessing workstation and analyzed using a software by two radiologists with more than five years of experience, and were unaware of the clinical and histopathological findings of the patients.

Optimal slices were selected on conventional map, then the volume of interests (VOI) was applied to contain the

mass. On the color map of the VOI, there are several color patterns. Red represents the greatest presumed hyper-perfusion, and other colors, such as yellow or blue, have relatively low perfusion. Based on the color pattern within each given VOI, 3 round ROIs were applied to regions of greatest presumed hyper-perfusion (red). Total pixel areas of ROIs and VOIs were dependent on tumor sizes and the sizes of regions of greatest presumed hyper-perfusion. After applying VOI and ROIs, time intensity curve (TIC) as qualitative parameter was evaluated, and the type of TIC was determined. TIC was classified based on Van Rijswijk et al. [11, 12] into 5 types: type I curve shows no enhancement, resulting in a horizontal curve; type II shows gradual increase of enhancement; type III shows rapid early enhancement followed by plateau phase; type IV shows rapid early enhancement followed by washout; V shows rapid initial enhancement followed by sustained late enhancement.

The quantitative parameters obtained were K_{trans}, K_{ep} and V_e. K_{trans} represents the influx volume transfer constant of a contrast agent from vascular to the interstitial compartment (min^{-1}). K_{ep} is the rate constant between extravascular-extracellular space (EES) and plasma or reflux rate ($K_{trans}/V_{e,}$ min^{-1}), and V_e is the EES fractional volume per unit volume tumor [13, 14].

Data Analysis: The DCE-MRI data were statistically analyzed using SPSS. The collected data were processed, statistically analyzed, and underwent diagnostic test. The values were expressed as mean ± standard deviation, median, and minimal-maximal for numeric (ratio/interval) and frequency-distribution for categoric data (nominal/ordinal). In addition, TIC, K_{trans}, K_{ep} and V_e were analyzed using 2 × 2 table and Receiver Operating Characteristic (ROC) curve to determine cut-off point, sensitivity, specificity, positive and negative predictive values. The area under curve (AUC) value, which represents the mean accuracy, was obtained based on the ROC analysis. Additionally, the cut-off value of TIC, K_{trans}, K_{ep} and V_e was obtained from the highest sensitivity and specificity among all the ROIs.

Results

Based on inclusion criteria, total samples in this study were 30; 57% of the patients were male, and 43% were female. Moreover, the median age of the patients was 37.5 years old (Table 1).

Patients with soft tissue tumors were classified histopathologically into benign (n = 13 patients) and malignant (n = 17 patients). The most common types of malignant tumor were fibroblastic/myofibroblastic tumors (n = 6) and adypotic tumors (n = 4). Meanwhile, the most common types of benign tumor were peripheral nerve sheath (n = 4), adypotic, vascular and fibroblastic/myofibroblastic tumors (respectively n = 2). The anatomic locations of benign lesions were upper thigh (n = 5), lower thigh (n = 2), cervicothoracic region (n = 2), shoulder (n = 1), forearm (n = 1), flank (n = 1) and vulva (n = 1) (Table 2).

Table 1 Subject's characteristics and the location of soft tissue tumors

	Malignant (n = 17)	Benign (n = 13)	Total
Gender			
Male	9 (52.9%)	8 (61.5%)	17
Female	8 (47.1%)	5 (39.5%)	13
Age			
Median, year	38.5 (7–70)	29 (6–52)	37.5 (6–70)
Location			
Femur	9	5	14
Cruris	1	2	3
Antebrachii	2	1	3
Shoulder	1	1	2
Glutea	2	0	2
Genu	1	0	1
Pedis	1	0	1
Cervicothorakal	0	2	2
Flank	0	1	1
Vulva	0	1	1

Characteristics of the Types of TIC with soft tissue tumor grading: Out of the 17 malignant soft tissue tumors, the most common type of TIC was type 5 (41.2%), followed by type 3 (29.4%), type 4 (17.6%) and type 2 (11.8%) (Table 3). Type 2 TIC (92.3%) were predominant among the 13 benign soft tissue tumors, followed by type 1 (7.7%) (Table 3 and Figs. 1, 2, 3, 4). The statistical result showed a significant difference among the types of TIC in relation to the histopathologically proven benign and malignant groups of soft tissue tumors ($p < 0.01$).

Characteristic of K_{trans} Value against soft tissue tumor grading: The data analysis of K_{trans}, K_{ep} and V_e value of 3 ROIs were placed in regions of greatest presumed hyper-perfusion against the histopathology grade of soft tissue tumor.

The Mann–Whitney test result showed a statistically significant difference in Ktrans-1, Ktrans-2, and Ktrans-3 values in relation to the benign and malignant groups of soft tissue tumors ($p < 0.01$). In addition, it was found that the K_{trans} value in malignant soft tissue tumors was higher than the benign group (Table 3). The result of the ROC curve analysis on K_{trans} showed that the AUC value for all ROI of K_{trans} was more than 0.8 (Fig. 5). The highest AUC value was obtained in K_{trans}-3 (0.873) with a cutoff point of 0.2905, sensitivity of ± 88.2%, specificity

Table 2 Characteristic of types of soft tissue tumors

Tumor type	Malignant	Total (n = 17)	Benign	Total (n = 13)
Adypotic tumors	Pleiomorphic liposarcoma	1 (5.9%)	Lipoma	2 (15.4%)
	Myxoid liposarcoma	1 (5.9%)		
	Dedifferentiated liposarcoma	2 (11.7%)		
Fibroblastic/Myo-fibroblastic tumors	Dermatofibrosarcoma protuberans	2 (11.7%)	Myositis ossificans	2 (15.4%)
	Myxofibrosarcoma	1 (5.9%)		
	Fibrosarcoma	2 (11.7%)		
	Low-grade fibromyxoid sarcoma	1 (5.9%)		
So-called fibro-histiocytotic tumors	Malignant fibrous histiocytoma	1 (5.9%)		
Peripheral nerve sheath tumor	Malignant peripheral nerve sheath tumor	1 (5.9%)	Schwannoma	2 (15.4%)
			Neurofibroma	2 (15.4%)
Vascular tumors			Intramuscular hemangioma	1 (7.7%)
			Lymphangitic malformation	1 (7.7%)
Chondro-osseous tumors	Chondrosarcoma	1 (5.9%)		
Undifferentiated/unclassified sarcoma	Malignant round cell tumor	1 (5.9%)		
Others	Metastasis	1 (5.9%)	Hidradenoma	1 (7.7%)
	Lymphoma	1 (5.9%)	Seroma	1 (7.7%)
	Melanoma malignant	1 (5.9%)	Hematoma	1 (7.7%)

Table 3 Quantitative and qualitative parameters in malignant and benign soft tissue tumors

	Tumor type		*p*	AUC of ROC
	Malignant (n = 17)	Benign (n = 13)		
*Time intensity curve (TIC)**				
Type 1	0 (0%)	1 (7.7%)	0.001	
Type 2	2 (11.8%)	12 (92.3%)	0.001	
Type 3	5 (29.4%)	0 (0%)	0.001	
Type 4	3 (17.6%)	0 (0%)	0.001	
Type 5	7 (41.2%)	0 (0%)	0.001	
K_{trans} **				
K_{trans}-1 (min^{-1})	0.663 (0.350–4.634)	0.117 (0.070–1.296)	0.003	0.819
K_{trans}-2 (min^{-1})	0.486 (0.160–4.546)	0.188 (0.780–1.338)	0.001	0.846
K_{trans}-3 (min^{-1})	0.680 (0.215–3.470)	0.156 (0.061–1.917)	0.001	0.873
K^{ep}**				
K_{ep}-1 (min^{-1})	0.872 (0.227–5.032)	0.270 (0.109–1.302)	0.000	0.889
K_{ep}-2 (min^{-1})	0.583 (0.161–20.970)	0.234 (0.106–1.340)	0.003	0.824
K_{ep}-3 (min^{-1})	0.704 (0.212–4.903)	0.239 (0.075–2.361)	0.001	0.873
V_e**				
V_e-1	0.972 (0.366–1.000)	0.929 (0.252–1.000)	0.340	
V_e-2	0.991 (0.278–1.000)	0.947 (0.390–1.000)	0.506	
V_e-3	0.996 (0.331–1.000)	0.962 (0.328–1.000)	0.550	

*Chi-square test, ** median (minimum–maximum), Mann Whitney test

of ± 84.6%, positive predictive value (PPV) of ± 88.2% and negative predictive value (NPV) of ± 84.6% (Table 4).

Characteristic of K_{ep} Value with soft tissue tumor grading: The Mann–Whitney test result showed a significant difference of K_{ep}-1, K_{ep}-2 and K_{ep}-3 values between the benign and malignant group of soft tissue tumors ($p < 0.01$). The K_{ep} value in the malignant group was higher than the benign ones. Furthermore, the result of the ROC curve analysis on K_{ep} showed that the AUC value for all ROI of K_{trans} was more than 0.8 (Fig. 6). The highest AUC value was found at K_{ep}-1 (0.889) with cutoff point of 0.3365, sensitivity

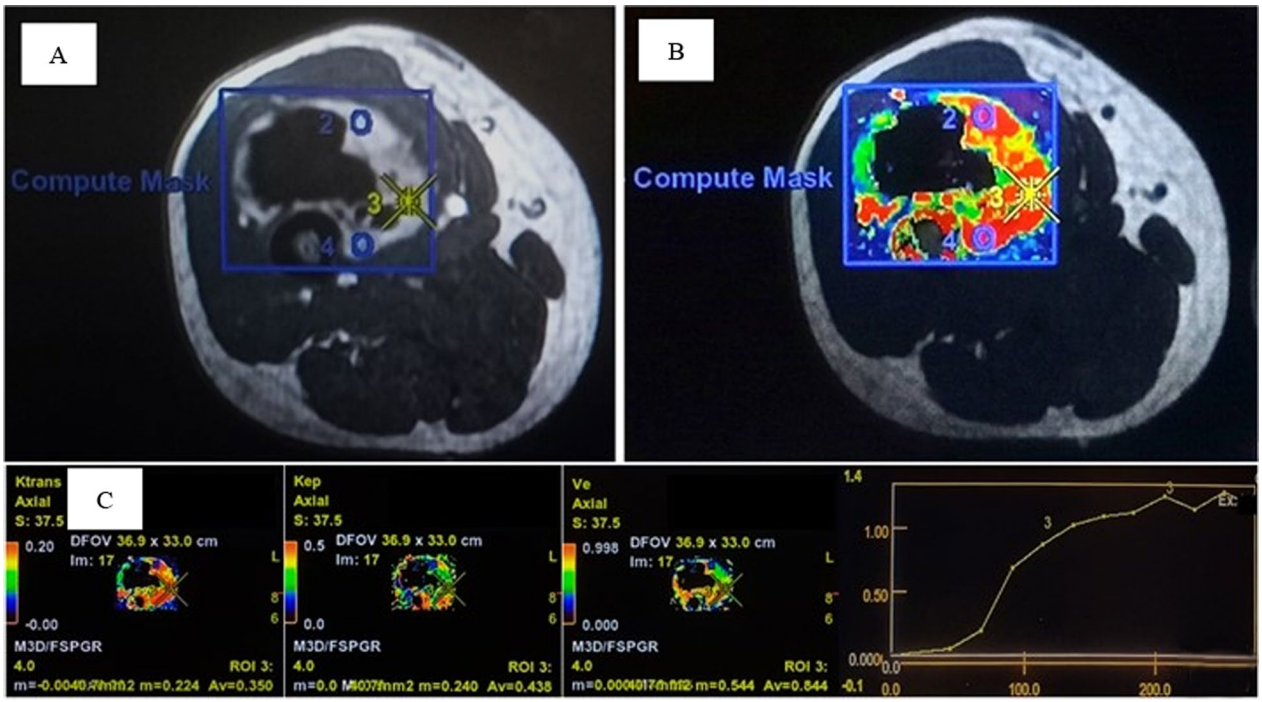

Fig. 1 A 47-year-old man with histopathologically confirmed dedifferentiated chondrosarcoma in thigh showed a well-encapsulated mass with irregular peripheral enhancement. By DCE imaging, several ROIs drawn in the most enhanced and hyperperfused region in axial post-contrast T1WI (**A)** and color map (**B**) showed parameters as follows, K_{trans} 0.350 min^{-1}, K_{ep} 0.438 min^{-1}, V_e 0.844 and TIC type 5 (**C**). DCE, dynamic contrast-enhanced; K_{ep}, microvascular permeability reflux constant; K_{trans}, volume transfer constant; ROI, region of interest; TIC, time intensity curve V_e, volume extravascular-extracellular space per unit tissue volume

of ± 94.1%, specificity of ± 84.6%, PPV of ± 88.9%, and NPV of ± 91.7% (Table 5).

Characteristic of Ve Value with soft tissue tumor grading: The Mann–Whitney test result showed no significant difference of V_e-1, V_e-2 and V_e-3 value between malignant and benign histopathological group ($p > 0.01$), as shown in Table 3.

Discussion

The visualization of tumors on contrast-enhanced imaging was performed in order to assess the structural abnormalities of new tumor vessels along with pathophysiological changes. In addition, functional imaging measures the effects of angiogenesis produce on tumor perfusion and permeability [15]. Currently, DCE-MRI is an imaging tool for evaluating the microvascular environment of a tumor, and it shows promising potential for clinical applications such as identification, characterization, and treatment response assessment. The results indicated that qualitative and quantitative parameters from DCE-MRI provides the ability to differentiate between benign and malignant soft-tissue tumors [3].

This study aimed to evaluate the diagnostic efficacy of qualitative and quantitative parameters of DCE-MRI in the malignancy of soft tissue tumors. In this study, patients with soft tissue tumor were slightly higher in males (57%) with median age between 37.5 and 70 years. Furthermore, the median age for malignant and benign soft tissue tumors was 38.5 and 29 years. These results were in accordance with the data of Cancer Research United Kingdom and National Cancer Institute which states that the incidence of soft tissue cancer was slightly higher in males [16, 17]. The frequency of malignant soft tissue tumors and those that come to seek treatment in hospitals was higher than the benign group. However, this was contradictory to WHO data which states that benign soft tissue tumors were 10× more common than malignant ones [18–20]. This is because patients suffering from this condition mostly do not feel the urgent of going to the hospital since their lesion is not growing, painless and does not affect their daily activities. Also, this study was conducted at type A hospital with advanced cases referred from primary and secondary health facilities.

The type of soft tissue tumor in this study were classified based on WHO 2013 [8, 9]. The most common types of malignant tumor were fibroblastic/myofibroblastic tumors and adypotic tumors. Meanwhile, the most common types of benign tumor were peripheral nerve sheath, adypotic, vascular and fibroblastic/myofibroblastic tumors. This is in line with previous studies,

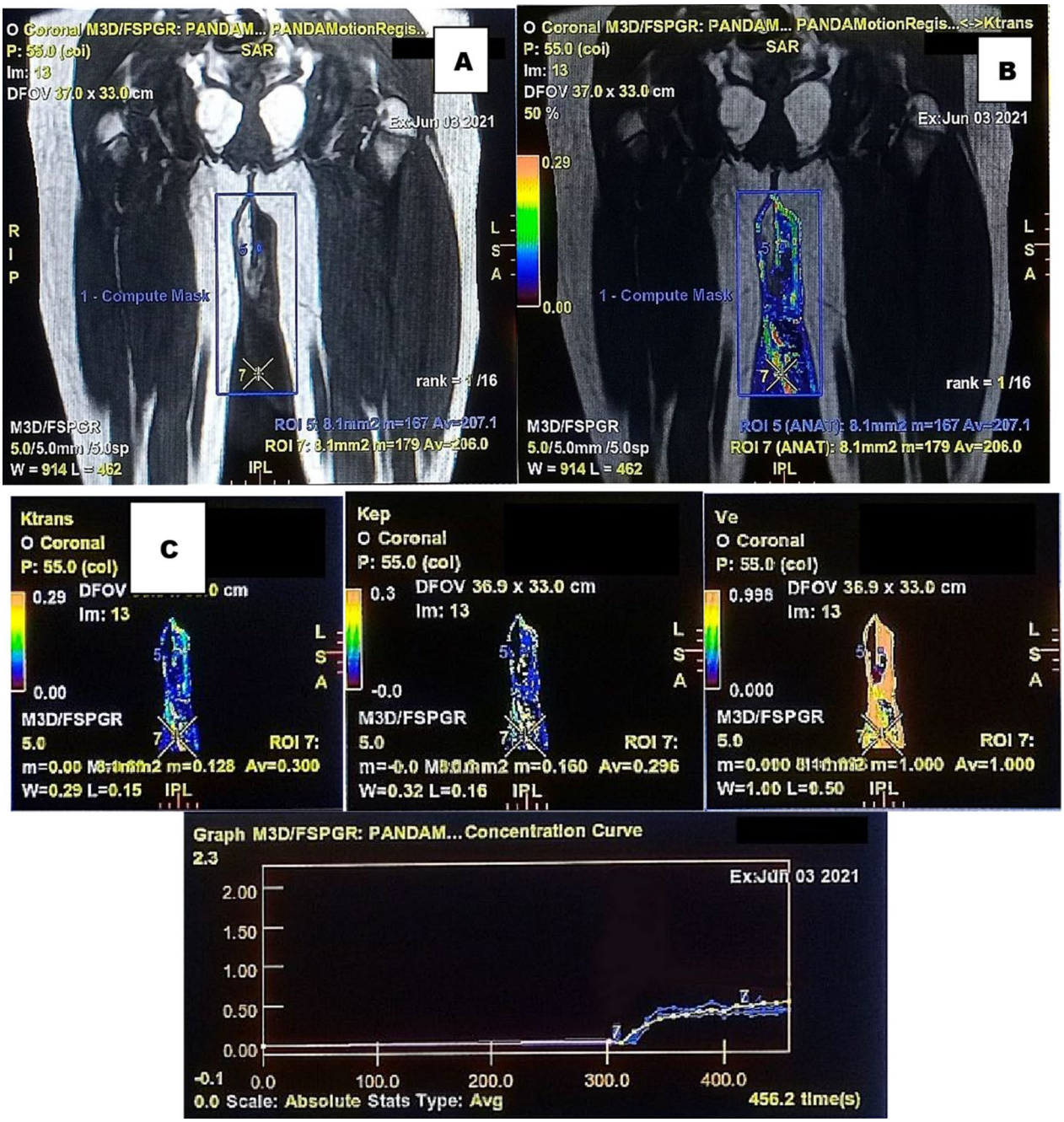

Fig. 2 A 13-year-old girl with histopathologically confirmed fibroma in the vulvar region, with DCE imaging, several ROIs drawn in the most enhanced and hyperperfused region in axial post-contrast T1WI (**A**) and the color map (**B**) showed K_{trans} 0.300 min^{-1}, K_{ep} 0.296 min^{-1}, V_e 1.000 and TIC type 2 (**C**). DCE, dynamic contrast-enhanced; K_{ep}, microvascular permeability reflux constant; K_{trans}, volume transfer constant; ROI, region of interest; TIC, time intensity curve V_e, volume extravascular-extracellular space per unit tissue volume

which revealed that the most common types of malignant soft tissue tumors are liposarcoma (subgroup of adypotic tumor), fibrosarcoma, malignant peripheral nerve sheath, angiosarcoma, synovial sarcoma and malignant fibrous histiocytoma. Furthermore, the most common types of benign soft tissue tumors are lipoma, vascular, neural, fibrous, smooth muscle and fibrous histiocytic [21].

Angiogenesis is regarded as one of the main hallmarks of cancer involved in tumorigenesis. Furthermore, tumoral angiogenesis is the chronic overproduction of angiogenic factors, which induces the uncontrollable

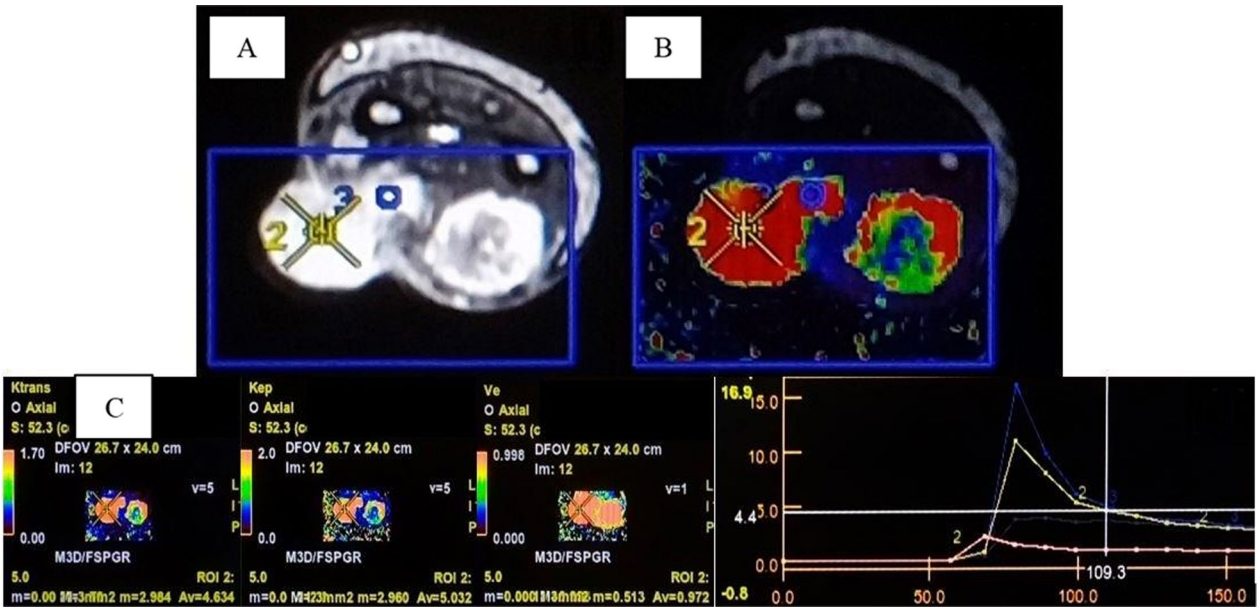

Fig. 3 A 19-year-old female patient with histopathologically confirmed fibrosarcoma in the lower arm, by DCE imaging, several ROIs drawn in the most enhanced and hyperperfused region in axial post-contrast T1WI (**A**) and the color map (**B**) showed parameters as follows, K_{trans} 4.634 min^{-1}, K_{ep} 5.032 min^{-1}, V_e 0.972 and TIC type 4 (**C**). DCE, dynamic contrast-enhanced; K_{ep}, microvascular permeability reflux constant; K_{trans}, volume transfer constant; ROI, region of interest; TIC, time intensity curve V_e, volume extravascular-extracellular space per unit tissue volume

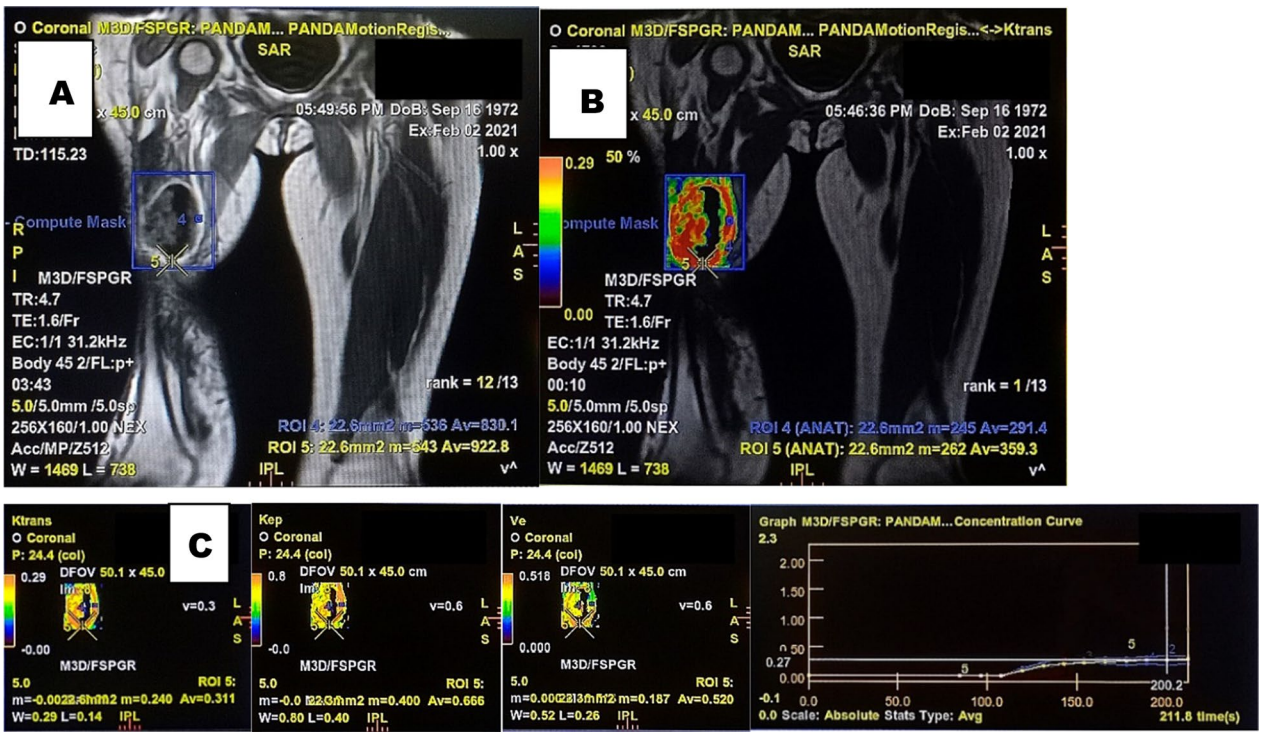

Fig. 4 A 47-year-old female patient with dedifferentiated liposarcoma in the thigh. In DCE imaging, several ROIs drawn in the most enhanced and hyperperfused region in axial post-contrast T1WI (**A**) and the color map (**B**) showed parameters which were more likely found in benign tumors. The values were as follows, K_{trans} 0.311 min^{-1}, K_{ep} 0.666 min^{-1}, V_e 0.520 and TIC type 2 (**C**). DCE, dynamic contrast-enhanced; K_{ep}, microvascular permeability reflux constant; K_{trans}, volume transfer constant; ROI, region of interest; TIC, time intensity curve V_e, volume extravascular-extracellular space per unit tissue volume

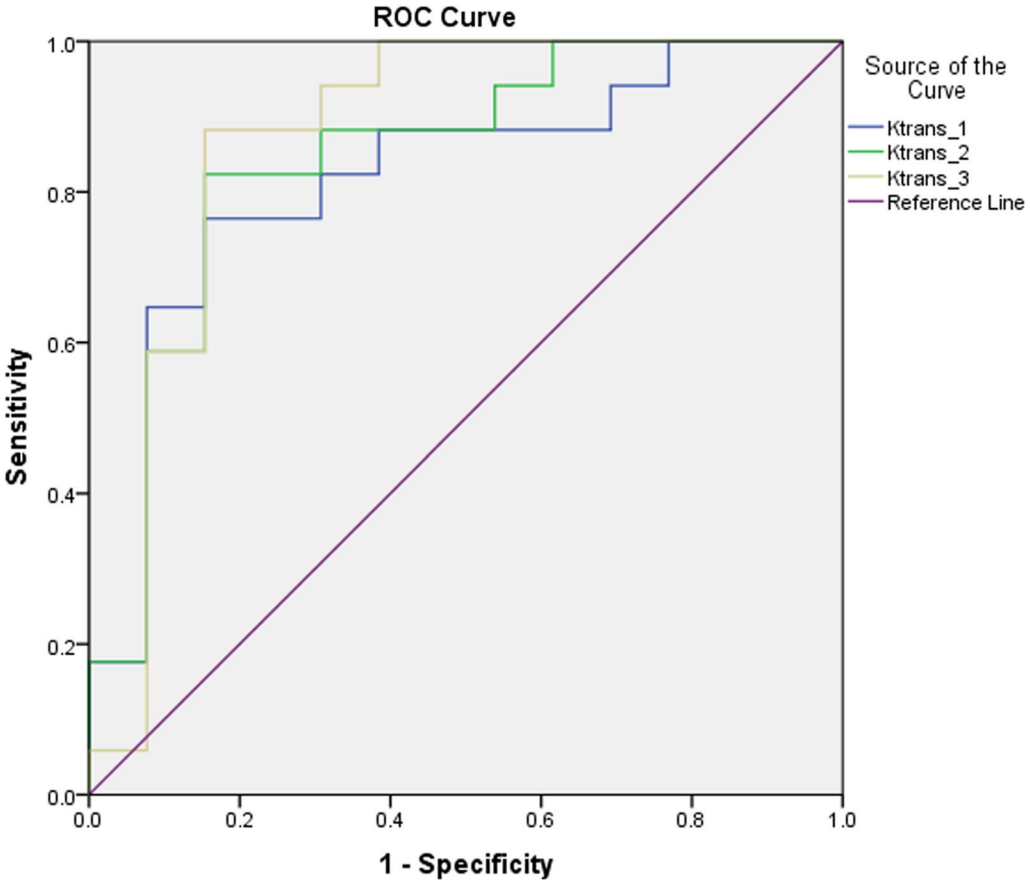

Fig. 5 ROC Curve Analysis of K_{trans} value with malignant soft tissue tumor

Table 4 Diagnostic test of K_{trans}-3 Value

K_{trans}-3 value	Histopathology		Total
	Malignant	Benign	
Malignant (≥ 0.2905)	15 (88.2%)	2 (11.8%)	17
Benign (< 0.2905)	2 (15.4%)	11 (84.6%)	13
Total	17	13	30

Sensitivity of ± 88.2%, specificity of ± 84.6%, positive predictive value (PPV) of ± 88.2% and negative predictive value (NPV) of ± 84.6%

development of new tumor vessels. Stimulation from the microenvironment of soft tissue tumor, such as hypoxia and weak acid, could increase the level of angiogenic factors such as vascular endothelial growth factor (VEGF). With VEGF stimulation, a soft-tissue tumor tends to generate a large number of tumor vessels from the nearest capillary, and is also protected from apoptosis. The tumor vascular structure is morphologically incomplete and lacks intact muscular and basal layers. Therefore, microcirculation in the newly formed tumor is disorganized, and the fragile vessels are highly permeable. The kinetics of the contrast agent transit depends heavily on tissue perfusion, vessel permeability, and volume of the EES [3, 15]

In this study, malignant soft tissue tumors were predominantly (88.2%) showed in TIC type 5 (41.2%), type 3 (29.4%), and type 4 (17.6%) which were not present in the benign soft tissue tumors. Almost all benign soft tissue tumors (92.3%) showed TIC type 2 which indicates a gradual increase of enhancement, and few showed type 1 (7.6%). This result is similar with previous studies, which also discovered rapid initial enhancement in malignant soft tissue tumors [4–7]. The majority of malignant tumors showed rapid and high contrast enhancement because they are highly vascularized and had narrow interstitial space; thus, wash-in occur rapidly after contrast injection. Whereas benign lesions, due to their slower perfusion characteristic and wider interstitial space, almost always showed late contrast enhancement [3, 7]. A study conducted by Choi et al., found that the majority of malignant lesions showed early washout (type 4) [7]. Early washout (type 4) in our study was found only in 17.6% of malignant tumors. The majority of malignant

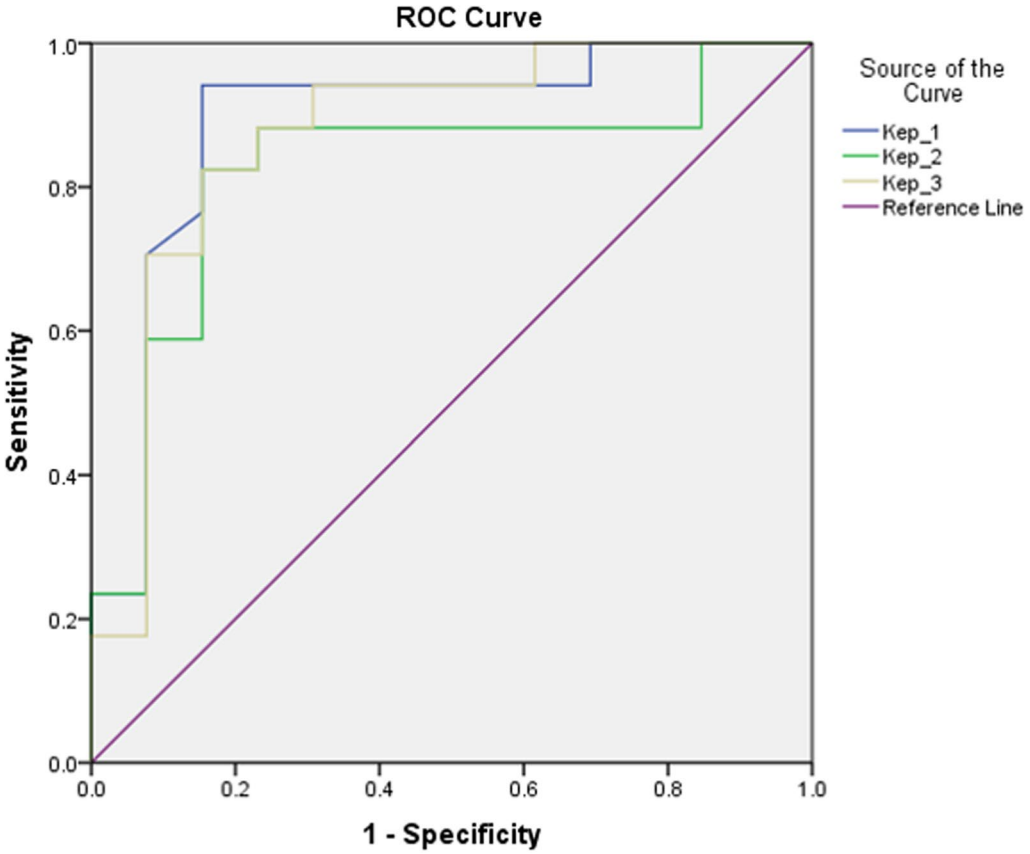

Fig. 6 ROC Curve Analysis of K_{ep} value with malignant soft tissue tumor

Table 5 Diagnostic test of K_{ep}-1 value

K_{ep}-1 value	Histopathology		Total
	Malignant	Benign	
Malignant (≥ 0.3365)	16 (88.9%)	2 (11.1%)	18
Benign (< 0.3365)	1 (8.3%)	11 (91.7%)	12
Total	17	13	30

Sensitivity of ± 94.1%, specificity of ± 84.6%, PPV of ± 88.9%, and NPV of ± 91.7%

soft tissue tumors in our study showed a plateau after early rapid enhancement (type 5), which might be due to the presence of a necrotic or fibrotic component in the tumor. Consequently, the elimination of the contrast medium from the tumor occurs slowly and produces a persistently delayed enhancement [7, 8].

K_{trans} value reflects the transendothelial transportation and diffusion of contrast media through the vascular wall (depends on capillary permeability) and interstitial space. In a malignant tumor, vascular permeability was higher than blood inflow [8]. Therefore, with the increasing malignancy of soft tissue tumors, the ability of tumor vessel generation became stronger. A tumor vessel has a high level of permeability, which results in a higher level of perfusion and permeability in microcirculation, K_{trans} and K_{ep} values [3]. In this study, the K_{trans} value from 3 ROIs that were placed in regions of greatest presumed hyperperfusion showed higher value in malignant soft tissue tumor than in the benign group. Statistical analysis also showed that K_{trans} value significantly correlates with grading histopathology. Therefore, the higher the value of $K_{trans,}$ the more likely the soft tissue tumor is malignant, and vice versa. The result was consistent with previous studies that found a K_{trans} value of 0.35 (0.048–1.822) ± 0.303 and 0.188 (0.008–0.566) ± 0.109 in malignant and benign soft tissue tumors. Another study also revealed K_{trans} value of 0.192 ± 0.122 and 0.071 ± 0.036 in benign and malignant groups of soft tissue tumors [3, 7].

K_{ep} value were affected by tumor vascular permeability and interstitial space. K_{ep} value reflect the transfer of contrast agent from EES to intravascular space or the washout rates. Therefore, when the vascular permeability increases and the interstitial space is narrows, the higher the K_{ep} value. Malignant tumors have high vascular permeability and narrow interstitial

space, that is why the reflux of contrast media into the blood vessel occurs rapidly. Meanwhile, in benign tumors contrast media passes slowly back into vascular compartement [8]. The K_{ep} value of 3 ROIs that were placed in regions of greatest presumed hyperperfusion showed higher K_{ep} value in malignant soft tissue tumors than benign ones. Statistical analysis also showed that the Kep value significantly correlated with grading histopathology of soft tissue tumor. Therefore, the higher the Kep value, the most likely the lesion is malignant, and vise-versa. These results were consistent with previous studies that found higher Kep value of 0.458 ± 0.300 and 0.161 ± 0.076 for malignant and benign tumors [3]. Another study also revealed Kep value of 0.918 (0.061–3.261) ± 0.599 and 0.378 (0.032–1.381) ± 0.261 for benign and malignant groups of soft tissue tumors [7].

The V_e value from 3 ROIs showed no significant difference between malignant and benign soft tissue tumor. It was slightly higher in malignant soft tissue tumors, but there was no statistically significant difference, and this result was similar to Zhang et al. study. Furthermore, V_e value reflects EES volume per unit volume tumor, which is restricted by vessel walls and cell plasma membranes. Some studies have demonstrated that Ve values can increase or decrease as the malignancy of the tumor increases, and it is unstable, probably because of edema around the lesions [3].

Vascular tumors usually show early rapid and uniform enhancement after contrast injection, while the washout characteristic varies. Moreover, vascular tumors have numerous blood vessel components, promoting faster and stronger contrast enhancement. This type of enhancement makes overlap between benign vascular lesions and other malignant soft tissue tumors [22, 23]. This study identified two vascular tumors: lymphangitic malformation and intramuscular hemangioma. Both tumors showed a gradual enhancement pattern of TIC (type 2). However, their K_{trans} and K_{ep} value were higher than other type of benign tumors. Despite the contradictory results, the number of vascular tumors was too small to represent the overall entity.

Several limitations of this study were, soft tissue tumor encompass a large variety that was used as criteria for sampling with various composing components and not with the types of tissue involved. In addition, vascular tumors have many blood vessel components, affecting the perfusion and permeability rates in microcirculation, and influencing in parameters' value. That is why it is still yet unclear when it is proper to include vascular tumors into the benign groups.

Conclusions

In conclusion, $K_{trans,}$ K_{ep} value, and time-intensity curve (TIC) can be used as diagnostic determinants with high accuracy. The cutoff point of K_{trans} and K_{ep} was ± 0.2905 and ± 0.3365 with a sensitivity of 88.2% and 94.1%, specificity of 84.6% and 84.6%, PPV of 88.2% and 88.9%, and NPV of 84.6% and 91.7%. The quantitative DCE-MRI parameters, Ktrans and Kep, and qualitative parameter, TIC, are independent predictors of soft tissue tumors malignancy.

Abbreviations

AUC	Area under curve
DCE	Dynamic contrast-enhanced
EES	Extravascular-extracellular space
FSPGR	Fast spoiled gradient echo
GE	General electric
MRI	Magnetic resonance imaging
PPV	Positive predictive value
ROC	Receiver operating characteristic
ROI	Region of interest
STT	Soft tissue tumor
TIC	Time intensity curve
VEGF	Vascular endothelial growth factor
VOI	Volume of interest
WI	Weighted imaging

Acknowledgements

Not applicable

Author contributions

YRR: conception, design and analysis, interpretation of data, drafting the article and revising, final approval of the version to be published. HS: conception, design and analysis, interpretation of data, drafting the article and revising, final approval of the version to be published. SI: interpretation of MRI examination. YWP: conception, interpretation and expert in oncology science. US: conception, interpretation in the anatomic and pathology science. All authors have read and approved the manuscript.

Funding

All authors declare that they did not receive any financial support.

Availability of data and materials

The dataset used and analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Health Research Ethics Committee, Faculty of Medicine, Diponegoro University and the Ethics Council of Dr. Kariadi Hospital Semarang with registration number was 847/EC/KEPK-RSDK/2021, and written informed consent were obtained from all patients/guardian.

Consent for publication

All patients included in this research gave written informed consent to publish the data contained within this study.

Competing interests

The author(s) declared no potential competing interests.

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Received: 17 July 2022 Accepted: 4 July 2023
Published online: 07 July 2023

References

1. Bruno F, Arrigoni F, Mariani S et al (2019) Advanced magnetic resonance imaging (MRI) of soft tissue tumors: techniques and applications. Radiologia Medica 124:243–252
2. El Maadawy MM, Elsorougy LG, Abdel Razek AA et al (2013) Perfusion CT: a biomarker for soft tissue tumors of extremities. Egypt J Radiol Nucl Med 44:805–815. https://doi.org/10.1016/j.ejrnm.2013.05.010
3. Zhang Y, Yue B, Zhao X et al (2020) Benign or malignant characterization of soft-tissue tumors by using semiquantitative and quantitative parameters of dynamic contrast-enhanced magnetic resonance imaging. Can Assoc Radiol J 71:92–99. https://doi.org/10.1177/0846537119888409
4. El Backry M, Shady M, Mousa AE, Zaky MM (2015) Role of dynamic contrast enhanced MR perfusion in differentiation between benign and malignant tumors. Egypt J Radiol Nucl Med 46:715–726. https://doi.org/10.1016/j.ejrnm.2015.01.001
5. Tuncbilek N, Karakas HM, Okten OO (2005) Dynamic contrast enhanced MRI in the differential diagnosis of soft tissue tumors. Eur J Radiol 53:500–505. https://doi.org/10.1016/j.ejrad.2004.04.012
6. Yıldırım A, Doğan S, Okur A et al (2016) The role of dynamic contrast enhanced magnetic resonance imaging in differentiation of soft tissue masses. Eur J Gener Med 13:37–44
7. Choi YJ, Lee IS, Song YS et al (2019) Diagnostic performance of diffusion-weighted (DWI) and dynamic contrast-enhanced (DCE) MRI for the differentiation of benign from malignant soft-tissue tumors. J Magn Reson Imaging 50:798–809. https://doi.org/10.1002/jmri.26607
8. Verstraete KL, Dutoit JC, Drapé JL, Bloem JL (2017) Magnetic resonance imaging: advanced imaging techniques. In: Imaging of soft tissue tumors. Springer International Publishing, pp 85–113
9. Jo VY, Fletcher CDM (2014) WHO classification of soft tissue tumours: an update based on the 2013 (4th) edition. Pathology 46:95–104. https://doi.org/10.1097/PAT.0000000000000050
10. Voyager S (2020) SIGNA voyager operator manual. Accessed 17 Apr 2023 from https://dmec.moh.gov.vn/documents/10182/32560981/upload_00005762_1657680127209.pdf?version=1.0&fileId=32565131
11. Van Rijswijk CSP, Geirnaerdt MJA, Hogendoorn PCW et al (2004) Soft-tissue tumors: Value of static and dynamic gadopentetate dimeglumine-enhanced MR imaging in prediction of malignancy. Radiology 233:493–502. https://doi.org/10.1148/radiol.2332031110
12. Costa FM, Martins PH, Canella C, Lopes FPPL (2018) Multiparametric MR imaging of soft tissue tumors and pseudotumors. Magn Reson Imaging Clin N Am 26:543–558
13. Jahng GH, Li KL, Ostergaard L, Calamante F (2014) Perfusion magnetic resonance imaging: a comprehensive update on principles and techniques. Korean J Radiol 15:554–577
14. Vilanova JC, Baleato-Gonzalez S, Romero MJ et al (2016) Assessment of musculoskeletal malignancies with functional MR Imaging. Magn Reson Imaging Clin N Am 24:239–259
15. García-Figueiras R, Padhani AR, Beer AJ et al (2015) Imaging of tumor angiogenesis for radiologists-part 1: biological and technical basis. Curr Probl Diagn Radiol 44:407–424
16. Cancer Research (2017) Soft tissue sarcoma incidence statistics. Cancer Research, United Kingdom. Accessed 3 Feb 2020 from https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/soft-tissue-sarcoma#:~:text=Soft%20tissue%20sarcoma%20incidence,84%20(1996%2D2010)
17. National Cancer Institute (2020) Cancer stat facts: soft tissue including heart cancer. National Cancer Institute, United States. Accessed 3 Feb 2023 from https://seer.cancer.gov/statfacts/html/soft.html
18. Fletcher CDM, Unni KK, Mertens F (2002) World Health Organization classification of tumours: pathology and genetics of tumours of soft tissue and bone. International Agency for Research on Cancer, France
19. Gruber L, Loizides A, Luger AK et al (2017) Soft-tissue tumor contrast enhancement patterns: diagnostic value and comparison between ultrasound and MRI. Am J Roentgenol 208:393–401. https://doi.org/10.2214/AJR.16.16859
20. Shidham VB (2018) Benign and malignant soft-tissue tumors. Medscape, New York. Accessed 2 Mar 2020 from https://emedicine.medscape.com/article/1253816-overview#a9
21. Ann Ivan R (2015) Incidence of various soft tissue tumours among benign and malignant cases
22. Yang LH, Ma S, Li QC et al (2013) A suspicious breast lesion detected by dynamic contrast-enhanced MRI and pathologically confirmed as capillary hemangioma: a case report and literature review. Korean J Radiol 14:869–873. https://doi.org/10.3348/kjr.2013.14.6.869
23. Glazerbrook KN, Morton MJ, Reynolds C (2015) Vascular tumors of the breast: mammographic, sonographic, and MRI appearances. Am J Roentgenol 184:331–338

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