ORIGINAL RESEARCH

Role of time intensity curve in magnetic resonance imaging evaluation of soft tissue tumors

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ABSTRACT

Background: Soft tissue tumors are commonly encountered in the oncologic practice and cause major concern to the patients as well as treating clinicians regarding its nature whether it is benign or malignant.

Dynamic contrast enhanced MRI is physiologic imaging method which can monitor tumor enhancement *in vivo* and give information regarding tumor vasculature and interstitial space volume. Time intensity curve is one of the parameter in Dynamic contrast enhanced MRI which can predict tumor nature*in vivo*.

Aims and Objectives

- Toidentify the role ofTime intensity curve inMRimaging ofsofttissuetumorsindifferentiating benign and malignant tumors.
- To evaluate itsadditional role in management of soft tissue tumors in differentiatingbenign and malignant tumors.
- Toevaluate its additional role in management of soft tissue tumors like treatment follows up.

Results andConclusion

Time intensity curves when combined with routine MRI can improve the diagnostic performance in the prediction of malignancy.

TypeIII,IV&V curves are predictorsofmalignancyand type IVis more specific.

DynamiccontrastenhancedMRIhas apotential roleinevaluatingthe response to chemotherapy and guiding the biopsy.

Key words: Time intensity curves, MRI, malignant &diagnostic accuracy F1

INTRODUCTION

Soft tissue tumors are commonly encountered in the oncologic practice and cause major concern to the patients as well as treating clinicians regarding its nature whether it is benign or malignant.

There is growing need to stage the tumor precisely before starting the treatment because staging is essential to compare the efficacy of various treatment strategies as well as to assess the response to treatment like chemotherapy.

Among various imaging modalities available MRI is considered to be the modality of choice for imaging of soft tissue tumors because of its inherent soft tissue contrast and multiplanar imaging capability.

Conventional MR imaging has increased sensitivity for tumor detection and allows for local staging. But conventional MR imaging is limited with regard to better characterization and distinguishing benign and malignant tumors. Though histo pathological examination remains gold standard there are few advanced MRI techniques which are able to better characterize these tumors and thereby distinguishing benign and malignant tumors. These techniques include Dynamic contrast enhanced MRI, in phase-opposed phased imaging, MR spectroscopy and

Diffusion weighted imaging. These methods together with conventional MR can improve diagnostic accuracy.

Dynamic contrast enhanced MRI is physiologic imaging method which can monitor tumor enhancement *in vivo* and give information regarding tumor vasculature and interstitial space volume. Time intensity curve is one of the parameter in Dynamic contrast enhanced MRI which can predict tumor nature*in vivo*. In this study comprised of 32 patients the role of time intensity curve in soft tissue tumor imaging is studied.

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MATERIAL AND METHODS

1. MATERIAL&METHODS

STUDYDESIGN: Prospective study.

STUDY DURATION:2 years.

The study population consisted of32consecutive patients having soft tissue mass, referred for Magnetic resonance imaging to Barnard Institute of Radiology, Rajiv Gandhi Government General Hospital. The study period includes two years from June2010 to May 2012.The study group consisted of 21 male and 11 female patients, between the age of 12 to 72years(mean age 39 years; Median age, 40 years).

The indications for MRI in these patients include assessment of local extent and characterization of the soft tissue mass. Obvious benign lesions like subcutaneous lipoma were excluded. Patients with benign lesions but atypical features and indeterminate lesions have undergone MRI with dynamic contrast. Two patients with giant cell tumor were also included in the study who were operated previously for giant cell tumor of the lower end of radius and later presented with soft tissue mass near the wrist.

Standard of reference was Histopathological results of the operated specimen.Histopathologicalconfirmationswere obtained for31patients.

Aspiration cytopathology for1patient. Subjects were followed up for a period of 6 months.

The study wasapproved by the institutionalethical committee.

INCLUSIONCRITERIA

1. All patients with soft tissue mass.
2. Age between 7to70years.

EXCLUSIONCRITERIA

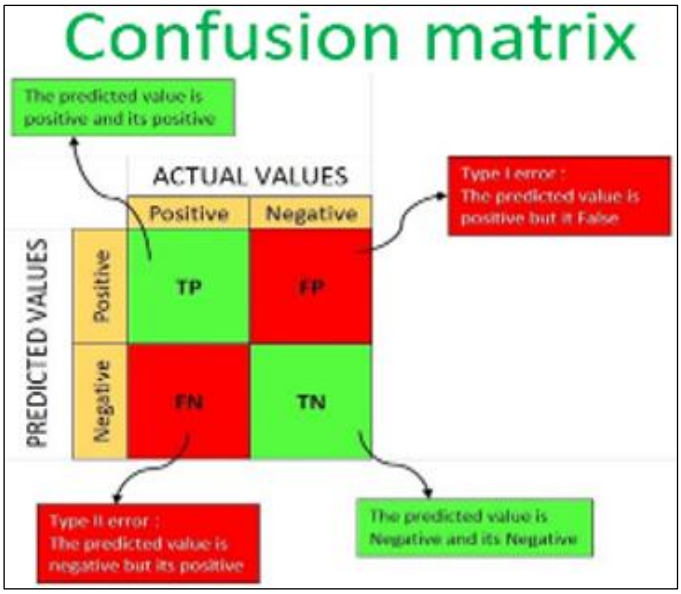
1. Mass near a moving structures like diaphragm.
2. Patients with contraindicationforMRIlikepatientshavingpacemaker, cochlear implants etc.
3. Claustrophobic patients.
4. Patients who underwent any chemotherapy or radiotherapy.

RESULTS & STATISTICAL ANALYSIS

1. RESULTSANDSTATISTICALANALYSIS

The frequency distribution of the above-mentioned MR parameters (Tumor Margin, Signal homogeneity & Time intensity curve type) in thehisto pathologicallyproven benign group was compared with that of themalignant tumor group by using X^2test and P value was calculated. The P value of <0.05 is considered as significant difference between two groups.

Sensitivity, specificity, Positive Predictive value & Negative Predictive value,Accuracy, Precision, Recall & F1of each parameter were analyzed and compared.



MATHEWCORRELATIONCOEFFICIENT

The Matthews correlation coefficient is used inmachine learning as a measure of the quality of binary and multiclass classifications. It takes into account true and false positives and negatives and is generally regarded as a balanced measure which can be used even if the classes are of very different sizes. The MCC is in essence a correlation coefficient value between -1 and +1. A coefficient of +1 represents a perfect prediction, 0 an average random prediction and -1 an inverse prediction. The statistic is also known as the phi coefficient.

MCC = (TP*TN-FP*FN)/√(TP+FP)(TP+FN)(TN+FP)(TN+FN)

The value for MCC ranges from -1 to 1 where:

- **-1** indicates total disagreement between predicted classes and actual classes.
- **0** is synonymous with completely random guessing.
- **1** indicates total agreement between predicted classes and actual classes.

COMPARISON WITH OTHERACCURACY MEASURES

To evaluate binary classifications and their confusion matrices, scientific researchers can employ several statistical rates, accordingly to the goal of the experiment they are investigating.

Despite being a crucial issue in machine learning, no widespread consensus has been reached on a unified elective chosen measure yet. Accuracy and F1 score computed on confusion matrices have been (and still are) among the most popular adopted metrics in binary classification tasks. However, these statistical measures can dangerously show overoptimistic inflated results, especially on imbalanced datasets.

The Matthews correlation coefficient (MCC), instead, is a more reliable statistical rate which produces a high score only if the prediction obtained good results in all of the four confusion matrix categories (true positives, false negatives, true negatives, and false positives), proportionally both to the size of positive elements and the size of negative elements in the dataset.

MCC produces a more informative and truthful score in evaluating binary classifications than accuracy and F1 score, by first explaining the mathematical properties, and then the asset of MCC in six synthetic use cases and in a real genomics scenario. We believe that the Matthews correlation coefficient should be preferred to accuracy and F1 score in evaluating binary classification tasks by all scientific communities.(11) David chicco *et al*.)

1. ACCURACY

To calculate accuracy from confusion matrix, use the formula below:

accuracy = (TP + TN)/(TP + FN + FP + TN)

2. PRECISION

The precision can be calculated using the formula below:

precision = TP/(TP + FP)

3. RECALL

Find the recall using the formula below:

recall = TP/(TP + FN)

4. F1 SCORE

To estimate F1 score, use the following formula:

F1 score = (2 * precision * recall)/(precision + recall)

5. TRUE POSITIVE RATE(SENSITIVITY)

The true positive rate TPR (also called sensitivity) can be calculated using the formula below:

TPR = TP/(TP + FN)

6. FALSE NEGATIVE RATE

We express the false negative rate FNR in a similar way:

FNR = FN/(TP + FN)

7. FALSE POSITIVE RATE
The false positive rate FPR is as follows:
FPR = FP/(FP + TN)

8. TRUE NEGATIVE RATE(SPECIFICITY)
The true negative rate TNR (also called specificity) is:
TNR = TN/(TN + FP)

9. FALSE DISCOVERY RATE
We can calculate the false discovery rate as follows:
FDR = FP/(TP + FP)

10.MATTHEWSCORRELATIONCOEFFICIENT
Finally, we can calculate the Matthews correlation coefficient using the formula below:
MCC = (TP * TN - FP * FN)/√((TP + FP) * (TN + FN) * (FP + TN) * (TP + FN))

RESULTS
Nineteen malignant lesions and 13 benign lesions made the basis ofstudy. All malignant and 12 of the benign lesions were confirmed histopathologically and fine needle aspiration cytology for one benign lesion. The confirmed cases were 18 different pathological types of tumor/lesions and includes 11 types of malignant and 7 types of benign tumors. Table:1&2.

Table1: Different types of malignant tumorsfound in the study

MalignantTumors	No. of cases
Dermato fibrosarcoma	2
Dermato fibrosarcoma protuberans	1
Fibrosarcoma	1
Liposarcoma	2
Malignant fibrous histiocytoma	1
Malignant Peripheral nerves heath tumor	1
Malignant Pleomorphic sarcoma	2
Malignant roundcell tumor	1
Malignant spindle cell tumor	4
Recurrent Giant cell tumor	2
Synovial sarcoma	2

Table2: Different types of benign tumors found in the study

BenignTumors	No. ofCases
Angiomyxoma	1
GCT of Tendon sheath	1
Granulo matous lesion	1
Hemangioma/AVM	1
Lipoma	7
Myxoma	1
Neurofibroma	1

LOCATION
With regards to location 22 lesions were located in the lower extremity, 8 in the upper extremity and 2 in the lower extremity. Thus in this study lower extremity is the most common site followed in frequency are upper extremity and trunk. Fig:1.

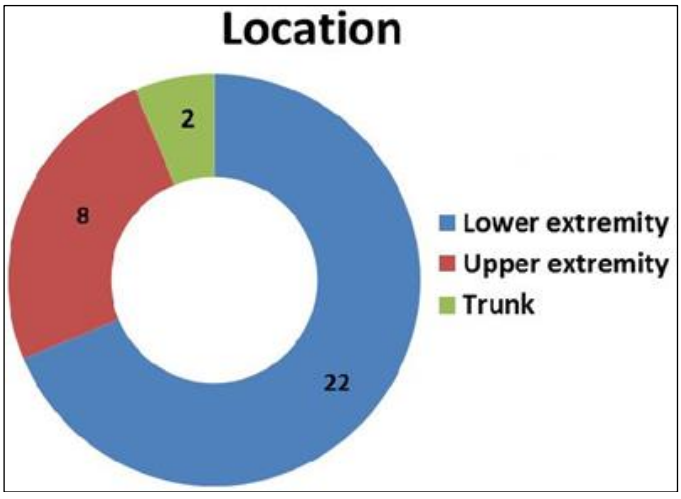


Fig1: Shows distributionofcasesinvariouslocations.Numberindicates number of cases in each group

AGE&SEXDISTRIBUTIONOFCASES

Among the 32 cases 21 were males and 11 were females.Fig2.When the age distribution of the cases was considered maximum cases were seen inthe age group of 41 to 50 years. Above 60 years only two cases were seen. Fig:2

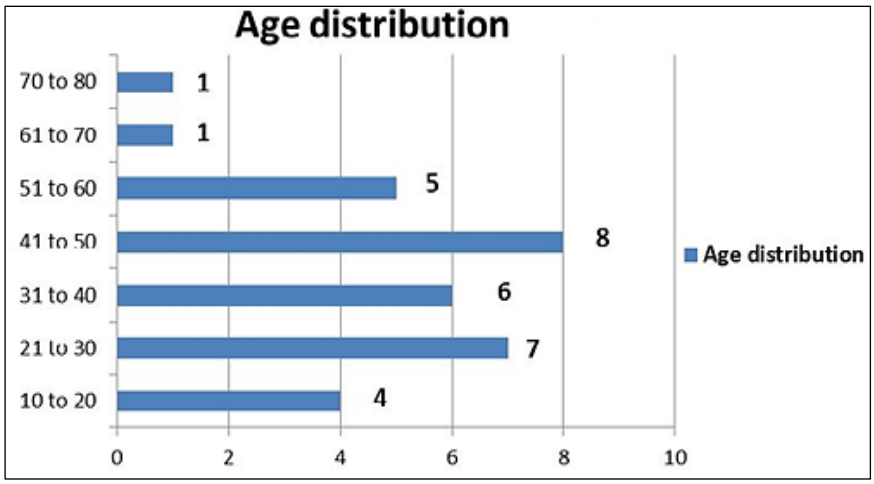


Fig2: Shows distribution of cases among various age groups. Number denotes number of cases in each age group

Among32cases21weremalesand11werefemales.Thisis dueto common occurrence of soft tissue sarcomas among males.

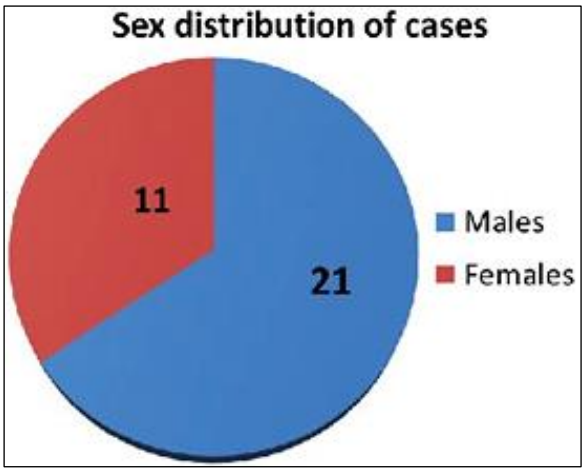


Fig3:shows distribution ofcases among males and females

DISTRIBUTION OF BENIGN ANDMALIGNANT CASES

Among 32 cases 19 were malignant and 13 were benign.(Fig:6.3) When location was considered 11of the23lesions inlower limb and6of the7 lesions in the upper limb were malignant.

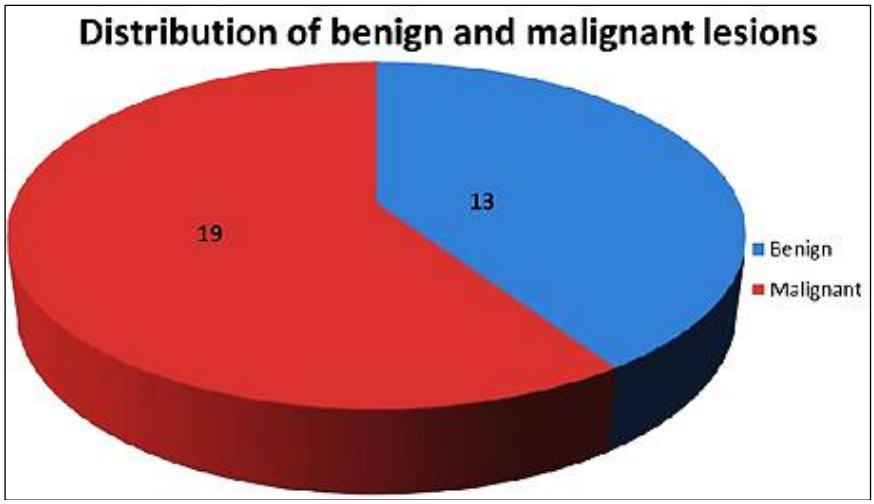


Fig4: Shows distribution ofbenign andmalignant lesions

DISTRIBUTION OF NON-ENHANCED MRIPARAMETERS

Table:3 shows the frequency distribution of tumor margin & signal heterogeneity and their correlation with final diagnosis (malignant or benign). Among 18 lesions with well-defined margin 11(61%) were benign and 7 (39%) were malignant. In the ill-definedmargin group 12 (86%) were malignant and 2 (14%) were benign. The sensitivity and specificity for predicting themalignancyusingtumormargin were84%and 63%respectively.(Table:6.4 & Fig: 6.6) Thus it has low specificity and positive predictive value.

Table3:DistributionofTumor margin and itscorrelationwith Final diagnosis

	Benign	**Malignant**	
Well defined margin	11	7	18
Ill-defined margin	2	12	14
	13	19	

Table4: Diagnosticaccuracyoftumormarginas apredictorof malignancy

Sensitivity	63.16%
Specificity	84.62%
PositivePredictiveValue	85.71%
NegativePredictiveValue	61.11%
Accuracy	71.88%
Precision	85.71%
Recall	63.16%
F1(Harmonic mean of Precision& Recall)	72.73%
Mathew correlation coefficient	47.3%

Table5: Distribution of Tumor signal heterogeneity&its correlation with Final diagnosis

	Benign	**Malignant**	
Homogeneity	9	4	13
Heterogeneity	4	15	19
	13	19	

Table6

Sensitivity	78.95%
Specificity	69.23%
PositivePredictiveValue	78.95%
NegativePredictiveValue	69.23%
Accuracy	75.00%
Precision	78.95%
Recall	78.95%
F1(Harmonic mean of Precision& Recall)	78.95%
Mathew correlation coefficient	48.18%

Among 13 lesions with homogenous signal intensity 9 of them were benign (69%) and 4 were malignant (31%). Whereas 15 of the 19 lesions with heterogeneous signal intensity were malignant (79%). 21% of lesions (4) with heterogeneous signal intensity in the T1 or T2 were benign.

Among 13 benign tumors, 11 showed either type 2 or 1 curve and only 2 lesions showed type 3/4/5 curve. Among 19 malignant lesions 17 showed either of the three curve types 3,4/5 and 2 of them showed type 2 curve. Based on these type I & II curves were designated as benign type and type III, IV& V curves were designated as malignant types. Frequency distribution of differenttypes of curves were tabulated and the diagnostic accuracy of time intensity curves in characterizing the lesion was identified and the results were shown in the table 7.The diagnostic value of non-enhanced MR parameters & Time intensity curves were shown in table 6.8and also in the Figs.

Table7: Distribution ofTICsamongbenignandmalignantlesions

	Benign	**Malignant**	
TIC1&2	11	2	13
TIC3,4,5	2	17	19
	13	19	

Table8: Diagnostic accuracy ofTICs as a predictor ofmalignancy

Sensitivity	89.47%
Specificity	84.62%
PositivePredictiveValue	89.47%
NegativePredictiveValue	84.62%
Accuracy	87.55%
Precision	89.47%
Recall	89.47%
F1(Harmonic mean of Precision& Recall)	89.47%
Mathew correlation coefficient	74.09%

Thus when the type I and II curves were taken as benign types and type III, IV & V curves were taken as malignant types the sensitivity and specificity approached 89.47% and 84.62% respectively.

There were two cases inbenignand two casesin malignant group showed a false positive and false negative for malignancy.

DISCUSSION

Non contrast MRI parameters taken in our study were tumor margin and signal heterogeneity of the lesion. When irregular margin of the tumor is usedas criteria for malignant tumor it showed a sensitivity of 85% and specificity of 63% with P value 0.02.

Signal heterogeneity could be due to various causes like tumor hemorrhage, liquefaction, necrosis and indicate the lesion as malignant. When signal heterogeneity of the lesion is considered as a criteria the sensitivity is 69% and specificity is 79% with P value of 0.01.The low sensitivity could be due to the fact that malignant lesions show necrosis, hemorrhage only after they attained a large size.

Both of these parameters were useful because their P values are< 0.05. These results are consistent with the study done by van Rijswijk *et al*.They studied 67 benign and 73 malignant soft tissue tumor and found that various MRI parameters are useful for predicting malignant lesions and tumor margin& signal heterogeneity are among them.

While using Time intensity curves the sensitivity and specificity were 85% and 89% respectively. Thus when dynamic contrast enhanced MRI is added to routine MRI it improved the diagnostic accuracy.

But few benign lesions like vascular lesions may show high contrast enhancement and mimic malignant lesions. Likewise few malignant lesions like necrotic mass may show lesser contrast enhancement thus necessitating other methods to better characterize the lesion.

In our study malignant tumors (17/19)showed type III and IV curves more commonly. Type V curve wasseen in only2 patients. Two lesions whichshowed type III curve were finally proven to be benign lesions. One lesion was angiomyxoma and the other one was granulomatous lesion. The probable explanation for this fast enhancement is relatively increased vascularity in some inflammatory lesions. No benign lesions showed type IV or V curve. Thus when only type IV & type V were considered the test becomes more specific but the sensitivity will be considerably low. But type V curve occurs only in 2 patients. So, type IV curve could be considered more specific for malignant lesions. This is consistent with the result of the study on breast tumor by Katharina *et al*. In their study they concluded that Type III curve of the breast tumors is the strong indicator of malignancy.This curve having fast initial enhancement and washout phase is similar to the type IV curve of our study.

Two lesions which showed type II curve were finally turned out to be malignant. Both were histologically proven spindle cell tumor. Few malignant tumors

show relatively low vascularity in the early stage due to biological variations. This could be the reason for slow enhancement of the lesion with benign type of curve.

CONCLUSION

Time intensity curves when combined with routine MRI can improve the diagnostic performance in the prediction of malignancy. In ourresultsType III,IV & V Accuracy is 87.55,F1 score is 81.47 and Matthews correlation coefficient (MCC) is 74.09.Among the threeaccuracy measuresMatthews correlation coefficient should be preferred to accuracy and F1 score in evaluating binary classification tasks by all scientific communities.

Type III,IV&V curves are predictors ofmalignancy.

Dynamic contrast enhancedMRIhas a potential role in evaluating the response to chemotherapy and guiding the biopsy.

REFERENCES

1. AndersonMW,H.ThomasTemple,PhoebeA.Kaplan,Robert.
2. Dussault,.CompartmentalAnatomy:Relevance to Staging and Biopsy of Musculoskeletal Tumors.AJR:173, December 1999.
3. RobbinsandCotranPathologicBasisofDisease,8thEd.Philadelphia: Saunders Elsevier;2010.
4. EricA.Walker,MichaelE.Fenton,*etal*.Magneticresonanceimagingof benign soft tissue neoplasmsin adults.
5. Eric A. Walker, Joel S. Salesky, Michael E. Fenton, *et al*.Magnetic ResonanceImagingofMalignantSoftTissueNeoplasmsintheAdult. RadiolClin N Am 49 (2011) 1219-1234.
6. MurpheyMD.WorldHealthOrganizationclassificationofboneandsoft tissue tumors: modifications and implications for radiologists. Semin Musculoskelet Radiol 2007;11(3):201-14.
7. CadmanNL,SouleEH,KellyPJ.Synovialsarcoma;ananalysisof34 tumors. Cancer 1965;18:613-27.
8. DucatmanBS,ScheithauerBW,PiepgrasDG,*etal*.Malignantperipheral nerve sheath tumors. A clinicopathologic study of 120 cases. Cancer 1986;57(10): 2006-21.
9. Brenton GE, JohnsonDE, EadyJL. Leiomyosarcoma of the hand and wrist.Reportoftwocases.JBoneJointSurgAm. 1986;68(1):139-42.
10. De Beuckeleer LH. *et al*. MR imaging of clear cell sarcoma (malignant melanoma of the soft parts): a multicenter correlative MRI-pathology studyof21casesandliteraturereview.SkeletalRadiol. 2000;29(4):187-95.
11. David Chicco *et al*. Theadvantages of the Matthews CorrelationCoefficient(MCC)overF1score andaccuracy in binary classification evaluation. Chicco and Jurman BMC Genomics (2020) 21:6 https://doi.org/10.1186/s12864-019-6413-7