ORIGINAL ARTICLE MSK Imaging

T2-based MRI radiomic features for discriminating tumour grading in soft tissues sarcomas

Georgios C. Manikis[1, 2], Katerina Nikiforaki[1, 2], Eleni Lagoudaki[3], Eelco de Bree[4], Thomas G. Maris[1, 2], Kostas Marias[1, 5], Apostolos H. Karantanas[1, 2, 6]

[1]*Computational BioMedicine Laboratory, Institute of Computer Science, Foundation for Research and Technology-Hellas (FORTH), Heraklion, Greece*

[2]*Department of Radiology, University of Crete, Heraklion, Greece*

[3]*Department of Pathology, University Hospital of Crete, Heraklion, Greece*

[4]*Department of Surgical Oncology, University of Crete, Heraklion, Greece*

[5]*Technological Educational Institute of Crete, Department of Informatics Engineering, Heraklion, Greece*

[6]*Department of Medical Imaging, Heraklion University Hospital, Heraklion, Greece*

SUBMISSION: 23/6/2019 | ACCEPTANCE: 15/9/2019

ABSTRACT

Purpose: The proposed study aims to develop an MRI-based radiomics analysis framework and investigate the feasibility of the calculated quantitative imaging features for differentiating low from high grade soft tissue sarcomas (STSs).

Material and Methods: A total of 22 patients (9 low grade and 13 high grade) who were pathologically diagnosed with soft tissue sarcomas were recruited for the analysis and corresponding T2-weighted MR images were acquired for further post-processing. Tumour delineations were manually traced slice by slice concluding to whole tumour annotated volumes from all enrolled patients. A total of 1165 high-throughput patient-specific quantitative imaging features were exported from each volume using radiomics and evaluated using random forest machine learning classifiers. The overall analysis framework was coupled with feature selection and oversampling techniques to address high-dimensionality dataset issues and the unbalanced ratio between the two examined groups. Validation was performed using repeated nested cross-validation to eliminate overfitting problems and assess the stability of the classification performance.

CORRESPONDING AUTHOR, GUARANTOR

Corresponding author: Georgios C. Manikis, Foundation for Research and Technology - Hellas (FORTH), Institute of Computer Science, N. Plastira 100, Vassilika Vouton, GR-700 13 Heraklion, Greece, Email: gmanikis@ics.forth.gr.
Guarantor: Apostolos H. Karantanas, Department of Radiology, Medical School-University of Crete, Voutes Campus, GR-71003, Heraklion, Greece, Email: akarantanas@gmail.com.

Results: The classifier, using the three most important radiomic features selected though training, yielded an accuracy of 0.781 ± 0.15, an area under the receiver operating characteristic curve (AUROC) equal to 0.814 ± 0.186, F1-score of 0.704 ± 0.198, 0.762 ± 0.267 and 0.725 ± 0.283 for precision and recall respectively using multiple independent test sets.
Conclusions: Radiomic features from routine MR imaging protocols can provide a strong discriminatory performance between low and high grade soft tissue sarcomas.

KEY WORDS
Radiomics; Soft tissue sarcomas; Machine learning; Imaging biomarkers; Quantitative MRI

Introduction

Soft tissue sarcomas (STSs) are neoplasms arising from the mesoderm derived tissues such as muscle, fat and connective tissue, thus constituting a broad and heterogeneous category of space occupying lesions. More than 50 different STSs subtypes have been defined by the World Health Organisation (WHO), which are often associated with having distinct radiological phenotype, different tumour biology and clinical outcome [1]. WHO divides tumours into benign, low grade (locally aggressive), intermediate grade (rarely metastasising) and malignant. Histopathologic type, grade and tumour size and depth are determinant factors for soft tumour staging and therefore provide significant prognostic information. Grading is based on the analysis of the degree of cell differentiation, histopathologic subtype, mitotic activity and presence of necrosis. The most widely used systems for grading are the three tiered ones suggested by the French Federation of Cancer Centers Sarcoma Group (FNCLCC) [2] and the one proposed by the National Institutes of Health (NIH) whereas the first system proposed by the American Joint Committee on Cancer (AJCC) was a 4-degree (grade 1-4) system. Staging in practice though has functioned through a two stage system, classifying tumours as low or high grade [3]. Core needle biopsy has been established for preoperative tumour grading in an attempt to classify tumours as high or low grade, in order to contribute to the most appropriate therapeutic scheme. Although histopathologic assessment of biopsy samples is the gold standard method for accurate tumour characterisation and grading, it might often be subject to sampling errors underestimating thus tumour grade and misguiding therapeutic approach [4]. Moreover, biopsy is an invasive procedure that can provoke several undesirable effects such as bleeding, pain, wound infection or breakdown and spillage of tumour cells. Noninvasive tumour characterisation at the early stage of imaging is therefore of utmost importance to ensure the choice of the most appropriate therapeutic plan and minimise patient discomfort.

Magnetic resonance imaging (MRI) has emerged as the imaging modality of choice for identification, staging, and monitoring of the response to therapy [5]. However, conventional MRI sequences have not equal power to biopsy in differentiating high from low soft tissue neoplasms as they exhibit a significant number of overlapping radiological features [6]. Quantitative MRI (qMRI) biomarkers derived from multiple or dynamic series such as volume transfer constant (Ktrans), perfusion fraction (f), and transverse magnetisation relaxation constant (T2 value) contribute to better description of pathology microenvironment. Nevertheless, MR quantification comes at the expense of prolonged acquisition time, comprised spatial resolution, sensitivity to artefacts and patient motion, and/or may require administration of contrast medium. To overcome the aforementioned challenges, the exploitation of conventional (T2) high resolution MRI, acquired in short acquisition time using a post-processing radiomic analysis framework, can potentially yield to complete coverage of soft tissue tumours in high resolution and multiple planes, improved robustness to artefacts, low requirements in hardware and less patient discomfort.

The emerging field of radiomics has recently been introduced to oncology involving the massive ex-

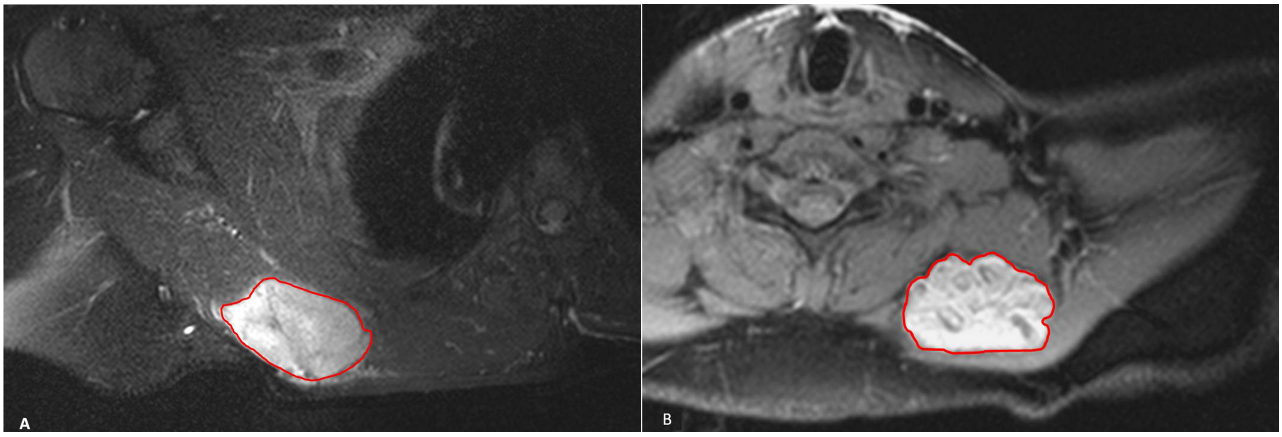

Fig. 1. *Axial fat suppressed T2w (TE=80 ms) TSE MR images in two different patients:* ***A.*** *low grade myxoid tumour from a 26-year-old male patient, and* ***B.*** *high grade soft tissue tumour (alveolar soft tissue sarcoma) from a 28-year-old female patient. Both are located in the shoulder girdle area.*

traction of quantitative imaging features aiming to capture non-intuitive information hidden in the images that can be linked to tumour characterisation and prognosis [7]. Although radiomics has been extensively studied in many anatomical areas including head and neck, breast, liver and lung cancer, few studies examined the role of radiomics in STSs to the best of our knowledge [8, 9]. Corino et al. presented a radiomics analysis based on the apparent diffusion coefficient (ADC) generated maps from diffusion-weighted MRI to distinguish intermediate from high grade STSs [10]. The performed analysis derived 64 imaging features and, when applied to 19 patients, achieved an area under the receiver operating characteristic curve (AUROC) of 0.85 ± 0.16 and 0.87 ± 0.34 using the validation and test set respectively. Another study explored the association between STS patients' overall survival (OS) and T1-weighted (T1w) contrast-enhanced MRI and found that the extracted radiomic features can be promising predictors of OS [11]. The proposed radiomics model was trained using 165 patients and performance was assessed using external validation (independent cohort comprising of 61 patients). Crombe and co-workers investigated the role of T2-based MRI delta-radiomics in predicting response of high-grade STS patients to neoadjuvant chemotherapy [12]. A limited number of radiomic features was calculated (33 features) and best predictive performance was achieved from 3 top-ranked features (accuracy of 74.6%). In a similar to the presented study, a radiomics analysis framework performed on fat-suppressed T2-weighted (T2w) MRI on a 3.0 T scanner from 35 pathologically diagnosed STS patients identified 5 radiomic features that best discriminate low from high-histopathological grades. The provided model obtained an AUROC of 0.92 ± 0.07 using a 5-fold cross-validation where final performance was calculated from the average accuracy of the 5 folds [13].

The purpose of the present study is to propose a radiomics analysis framework for the identification of a set of quantitative imaging features that can potentially differentiate low from high grade STSs.

Material and Methods

Study Population

Twenty six patients with soft tissue tumours of variable degree of malignancy underwent MRI examination from July 2015 to February 2019. Exclusion criteria included patients who underwent therapy prior to imaging or between imaging and surgical excision and patients with tumours completely suppressed by fat saturation. Patients with compromised co-operation were not included in the study. Hence, a total of 22 patients were eligible for this study and corresponding images were anonymised and transferred to a local database for further post processing. The examination protocol was submitted and approved by the local ethics committee and moreover all patients signed an informed consent for the use of their data for research purposes. All data were anonymised at the hospital premises. Within a short time inter-

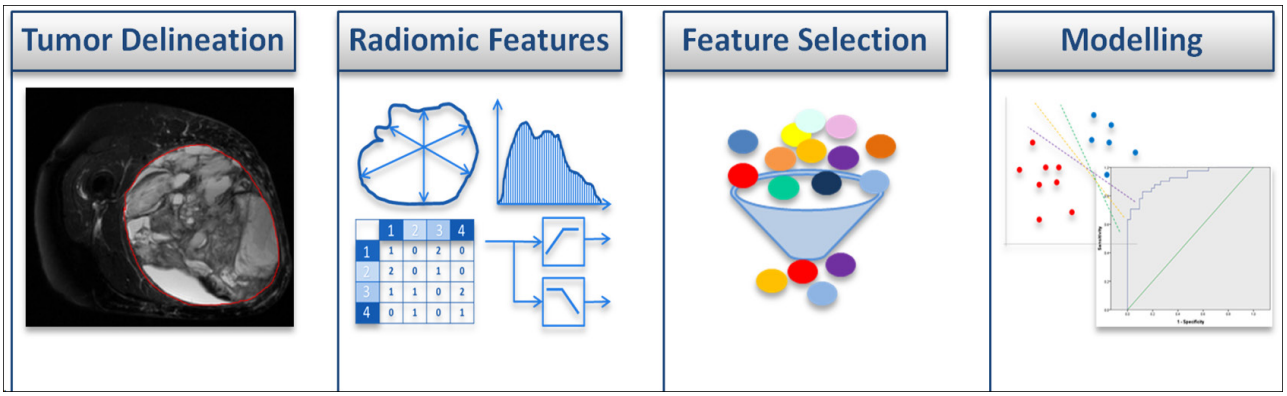

Fig. 2. *Conceptual overview of the proposed radiomics analysis framework comprising of the four major steps of tumour segmentation, feature extraction, feature selection and model development.*

val from radiological examination, surgical excision took place and the specimen was transferred to the pathology department for histopathologic analysis to conclude on tissue type and grading. Grading was based on the FNCLCC system (grades 1-3). Group A tumours of grade 1 (low grade) comprised 9 patients with histopathologically proven well differentiated liposarcomas, myxoid liposarcomas and desmoid tumour. Group B (high grading tumours of grade 2 and 3) was composed of 13 patients with poorly differentiated liposarcoma, pleomorphic liposarcomas, Ewing sarcoma, leiomyosarcoma and alveolar soft tissue sarcoma. Indicative MR images depicting low and high grade STSs are shown in **Fig. 1**.

MR acquisition protocol

Imaging protocol performed at a 1.5 T scanner (Vision/Sonata hybrid System, Siemens, Erlangen, Germany, Gradient Strength: 45mTm^{-1}, Slew Rate: 200mTm^{-1}s^{-1}) included dual PD to T2w echo (TE1/TE2/TR: 13/80/3250 ms, NEX: 1) sequence in axial and coronal planes with slice thickness 4 mm (20% interslice gap) to ensure complete lesion coverage as well as pre and post contrast T1w TSE (TE/TR: 13/498 ms) sequences. The number of slices differed between patients depending on lesion size. Given the variable locations of the lesions, the coil selection differed between acquisitions to ensure complete lesion coverage at highest possible SNR. The field of view depended on the lesion size and location and was set to 200x200mm (frequency phase matrix: 320x289) or 400x400 mm (384x320). Spectral fat suppression was used to create fluid sensitive images with increased lesion conspicuity. Acquisition time was 12 min 49 s, regardless the variance in the number of slices.

MRI post-processing

The overall framework within this study was developed to address four major steps of radiomics analysis including tumour segmentation, calculation of high-dimensional quantitative imaging features, feature selection, and development of predictive models relying on machine learning techniques **(Fig. 2)**. A thorough review concerning radiomics analysis workflow is given in [14]. Initially, tumour delineations were manually traced slice by slice on T2w images by an MR physicist with 12 years of experience in the clinical environment of an MRI suite. Regions of Interest (ROIs) were reexamined and confirmed or modified by a senior radiologist with 34 years of experience in musculoskeletal MRI. Tumour delineations were performed using a modified version of our in-house developed software written in Matlab 2013a, concluding to 22 whole tumour volumes from all enrolled patients [15]. High-throughput patient-specific quantitative imaging features were calculated from all tumour volumes using image analysis techniques to derive a comprehensive spatial and functional view of the examined tissue areas based on intensity, shape and textural characteristics. Specifically, histogram analysis describing the spatial relationships between pixels was applied to each volume resulting to quantitative metrics including mean signal intensity (SI), standard devia-

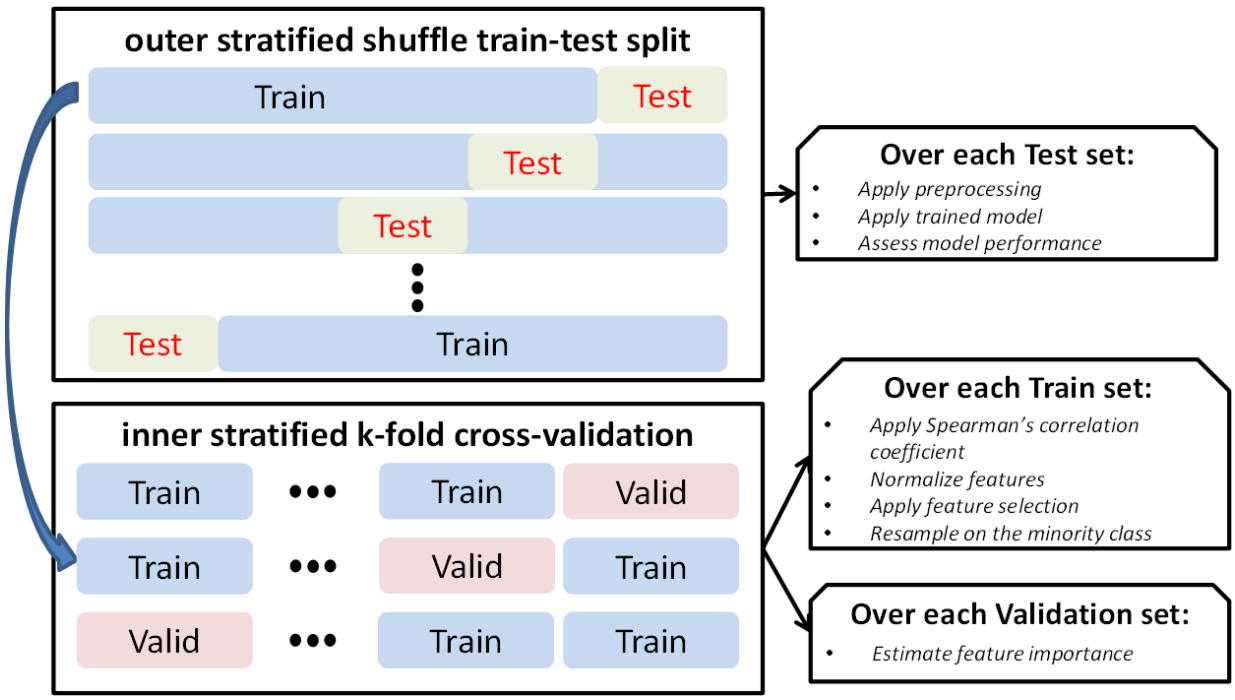

Fig. 3. *The proposed nested cross-validation schema to assess the generalisation performance of the radiomics framework and to select candidate radiomic features for discriminating low from high grade STSs.*

tion, median, skewness, kurtosis, variance, 10% and 90% percentiles, etc. Volumetric and shape-based features that capture the shape characteristics of the tumour were also calculated (e.g. volume, surface area, sphericity, spherical disproportion, maximum 3D diameter, etc.). Second-order statistics based on grey-level co-occurrence matrices (GLCM), Gray Level Run Length Matrix (GLRLM) and Gray Level Size Zone Matrix (GLSZM) were applied to all delineated tumour volumes providing relevant information about the inter-pixel relationships within each examined region. All the aforementioned techniques were extended to a multiresolution image scaling using wavelet decompositions of level 1 and 2 and the extracted radiomic features were exported across different scales and frequency directions. A total of 1165 imaging features were calculated using Python software and the Pyradiomics library [16].

Prior to predictive modelling, preprocessing of the extracted radiomic features was employed including feature selection, feature scaling and oversampling. To reduce high-dimensionality of the provided radiomic imaging signature, a univariate feature selection was initially performed and Spearman's rank correlation coefficient (rho) was calculated for each feature with respect to tumour grading. A correlation above 0.4 was considered as significant and the remaining, indicated by Spearman's correlation coefficient, features were normalised using RobustScaler using scikit-learn Python library [17]. RobustScaler was used instead of other widely used techniques (e.g. StandardScaler from scikit-learn) as it is robust to outliers and can operate on features that are not normally distributed. In this study all radiomic features were tested for normality using Shapiro-Wilk test and most of them failed to achieve a p-value higher than 5% indicating a non-normal distribution. A multivariate feature selection and ranking was then performed using minimum redundancy maximal relevance (mRMR) [18]. Feature selection and ranking was performed sequentially using a tradeoff for relevance and redundancy by calculating the mutual information (MI) between the radiomic features and the features with the correspond-

Table 1. The ten most important radiomic features according to their proportion of the number of times they appear in the classification process during the repeated nested cross-validation.

Radiomic Features	*Proportion (%)*
wavelet2-LLL_glrlm_LongRunLowGrayLevelEmphasis	80.25
wavelet2-LLL_glrlm_LowGrayLevelRunEmphasis	79.75
wavelet2-LLL_glrlm_ShortRunLowGrayLevelEmphasis	75.75
wavelet2-LLL_glszm_LowGrayLevelZoneEmphasis	71.75
wavelet2-LLH_firstorder_Skewness	65.5
wavelet-LLH_firstorder_Skewness	62.75
original_glrlm_LongRunLowGrayLevelEmphasis	62.5
wavelet2-LLL_glszm_SmallAreaLowGrayLevelEmphasis	61.25
original_glrlm_LowGrayLevelRunEmphasis	61
original_glrlm_ShortRunLowGrayLevelEmphasis	58.5

ing outcome. The 100 most highly ranked radiomic features selected from mRMR were then forwarded as input to the predictive modelling phase. In the current study, an unbalanced ratio was evident between the two classes (9/22 patients with low grade tumour). To tackle this issue, a synthetic minority oversampling (SMOTE) technique was conducted to increase the size of the minority class by introducing synthetic patients from the corresponding radiomic features [19]. The predictive modelling phase was based on ensemble techniques using Random Forest classifier from scikit-learn Python library. Random Forest (RF) classifier was chosen to discriminate low from high grade STSs as it is less prone to overfitting and generally performs well when applied to high-dimensional low sample size datasets [20].

To assess the generalisation performance of the proposed radiomics analysis framework and eliminate any bias occurred during training, validation and testing of the technique, a repeated nested cross-validation (CV) schema was followed as outlined in **Fig. 3**. Although hyperparameter optimisation was out of scope of this study, since the provided classifier was launched using its default parameters, a nested CV comprising of an inner stratified 3-fold CV and an outer stratified shuffle split (20% for testing and 80% for training) was used for selecting the optimal subset of radiomic features and avoid any overfitting issues. The overall preprocessing of the radiomic features was nested using the inner CV level and the chosen subset of features were finally used to calculate the predictive performance of the model at the outer shuffle split level. In more detail, at the outer level, the overall dataset was divided into training (80% of the overall patients) and testing set (20%) using stratified random sampling. Subsequently, the training set from the outer level was further divided into 3 inner folds to define and evaluate the preprocessing phase. Each fold was acted as a validation set within the inner CV to evaluate the performance generalisability of the classifier when trained using the remaining inner folds. The whole nested schema was repeated 100 times to iterate through all possible combination of train, validation and test sets.

Results

A high-dimensional dataset comprising of 1165 radiomic features was calculated from 22 patients (9 of

Table 2. The ten most important radiomic features according to Gini impurity criterion using a RF classifier.

Radiomic Features	*Gini Impurity*
original_shape_Elongation	0.036
wavelet2-LLL_glrlm_LongRunLowGrayLevelEmphasis	0.033
original_firstorder_Kurtosis	0.031
wavelet2-LLL_glrlm_LowGrayLevelRunEmphasis	0.029
wavelet2-LLL_glrlm_ShortRunLowGrayLevelEmphasis	0.028
wavelet2-LLL_glszm_LowGrayLevelZoneEmphasis	0.018
wavelet2-LLH_firstorder_Skewness	0.016
wavelet-LLH_firstorder_Skewness	0.016
original_glrlm_LongRunLowGrayLevelEmphasis	0.016
wavelet2-LLL_glszm_SmallAreaLowGrayLevelEmphasis	0.013

low grade STS) and further analysed using the proposed repeated nested cross-validation (CV) schema. A total of 300 independent training/validation iterations (3 inner folds x 100 outer iterations) were performed to assess the importance of each radiomic feature in discriminating low from high grade STSs and 957 out of 1165 features were reported from the mRMR method as candidate features for modelling. During the inner part of the repeated nested CV, feature importance was quantified using: a) the proportion of the number of times each of the 957 features was selected as input to the classifier out of the maximum number of iterations (300), and b) the feature importance as it is calculated from the RF using Gini impurity as a criterion. Indicative results from the 10 most important radiomic features in terms of a) and b) are presented in **Tables 1 and 2** respectively. Concerning criterion a), a subset of radiomic features with proportion values above the 95% percentile of the proportions related histogram was selected as candidate biomarkers. Accordingly, all features having an importance based on Gini impurity above a specific threshold (above 95% percentile) were also determined. To account both in radiomic feature stability as it is quantified using criterion a) and feature's classification importance as determined by the RF (criterion b), an intersection of the two distinct aforementioned subsets was generated. Given the fact that a ratio of 1/10 (number of selected features with respect to the examined patients) is recommended in the classification process, the three most highly ranked radiomic features from the intersection were selected as the optimal set (see **Table 3**).

RF performance was evaluated comprehensively across the 100 outer stratified shuffle split iterations using accuracy, AUROC, F1-score, precision and recall. The selected radiomic "signature" from the inner part of the proposed CV schema comprising of three imaging features was examined in terms of its predictive performance using the unseen 100 testing sets. All metrics are reported as mean ± std where "std" stands for standard deviation. The classifier achieved an accuracy of 0.781 ± 0.15, an AUROC equal to 0.814 ± 0.186, F1-score of 0.704 ± 0.198, 0.762 ± 0.267 and 0.725 ± 0.283 for precision and recall when tested from multiple independent test sets from the outer loop respectively. Classification performance was also calculated from the inner part of the repeated

Table 3. The three most significant radiomic features based on both criteria as outlined from the proportion of the number of times they appear in the classification process and their feature importance level according to Gini impurity criterion from the RF classifier during the repeated nested cross-validation.

Radiomic Features	*Proportion (%)*	*Gini Impurity*
wavelet2-LLL_glrlm_LongRunLowGrayLevelEmphasis	80.25	0.033
wavelet2-LLL_glrlm_LowGrayLevelRunEmphasis	79.75	0.029
wavelet2-LLL_glrlm_ShortRunLowGrayLevelEmphasis	75.75	0.028

nested CV using the aforementioned metrics, yielding training accuracy equal to 0.802 ± 0.196, AUROC of 0.831 ± 0.206, F1-score of 0.711 ± 0.166, 0.759 ± 0.187 of precision and 0.731 ± 0.124 for recall and no statistical difference according to Mann-Whitney test when compared to the results obtained using the unseen test sets.

Discussion

Our results suggest that the emerging field of radiomics offer a massive amount of quantitative imaging features from T2w MR images from which significant biomarkers for differentiating low from high grade soft tissue sarcomas can be identified after proper analysis. In the current study a total of three radiomic features were selected as the most significant imaging features that contribute to the best predictive performance when Random Forest classifier was used for classification. Features Long Run Low Gray Level Emphasis (LRLGLE), Low Gray Level Run Emphasis (LGLRE) and Short Run Low Gray Level Emphasis (SRLGLE) were derived from the Gray Level Run Length Matrix (GLRLM) of the image after a two level wavelet decomposition. The proposed classifier achieved an AUROC of 0.814 ± 0.186 using a repeated nested cross-validation schema comprising of 100 independent testing sets to assess its generalisation performance. A comprehensive preprocessing phase including feature selection, feature scaling and oversampling was applied through the training phase to each independent training set and a subset of radiomic features was defined each time to serve as candidate biomarkers for differentiating low from high grade STSs. Two distinct criteria were followed to select the most important set of radiomic features that concluded to the best predictive performance. The radiomic analysis framework reported in the introduction achieved an AUROC of 0.92 ± 0.07 in discriminating low from high-histopathological grades, whereas the performance from the proposed methodology in terms of AUROC was equal to 0.814 ± 0.186 [13]. However, one may notice that performance might be influenced by the increased signal to noise ratio (SNR) and the spatial resolution of the acquired MR images when a 3.0 T scanner is used instead of a 1.5 T (our study). Additionally, different techniques were implemented to train and validate each radiomics analysis workflow. According to the flowchart illustrated in [13], feature selection was first applied to the overall dataset and a 5-fold cross-validation then divided the dataset for training and testing. In this study, to eliminate overfitting and proper assess the generalisation performance, a repeated nested CV schema was used for training, validation and classification testing, as well as to find the optimal subset of radiomic features.

A limitation of our study is related to the rather limited size of patients recruited for the analysis. The increased standard deviation in the performance metrics imply that the limited sample size affected the stability of the classifier, thus rendering our study as an initial one calling for further, more extensive studies on this field of research. Limited sample sizes of high-dimensional imaging features are a general concern when performing radiomics analysis and overfitting problems might easily occur when data is not handled carefully during model training and testing. Additionally, RF classifier and mRMR

were chosen by default as the most suitable methods for classification and feature selection respectively. A large parameter grid, consisting of several classifiers and feature selection techniques which runs in parallel under a generalised repeated cross-validation framework, might potentially yield to a better predictive performance. Lastly, advanced MRI acquisition protocols such as the Diffusion Weighted MRI, when further analysed using radiomics, can provide additional information to the corresponding anatomical information retrieved from the T2w images about the functional and morphological environment of the STSs.

In summary, radiomic analysis has the potential to present a novel emerging field for the quest of imaging biomarkers in oncology and in soft tissue tumours specifically, since it is minimally invasive and can be easily repeated enabling the extraction of valuable information for preoperative histopathology grading prediction, early treatment response assessment and personalised clinical diagnosis.

Conclusion

Taken together, advanced post-processing using radiomics can provide a complementary perspective for quantifying conventional T2w MRI sequences into high-dimensional imaging features, contributing to the efficient differentiation of histopathology grading in soft tissue sarcomas. **R**

Conflict of interest

The authors declared no conflicts of interest.

References

1. WHO Classification of Soft Tissue Tumours. 2006; 139: 35–39.
2. Guillou L, Coindre JM, Bonichon F, et al. Comparative study of the National Cancer Institute and French Federation of Cancer Centers Sarcoma Group grading systems in a population of 410 adult patients with soft tissue sarcoma. *J Clin Oncol* 1997; 15(1): 350-362.
3. Edge SB, Byrd DR, Compton CC, et al. *AJCC cancer staging manual*, 7th edition. France: Springer 2010.
4. Leithner A, Maurer-Ertl W, Windhager R. Biopsy of bone and soft tissue tumours: Hints and hazards. In: Tunn P-U, ed. *Treatment of bone and soft tissue sarcomas*. Berlin, Heidelberg: Springer Berlin Heidelberg, 2009; pp. 3-10.
5. De La Hoz Polo M, Dick E, et al. Surgical considerations when reporting MRI studies of soft tissue sarcoma of the limbs. *Skeletal Radiol* 2017; 46(12): 1667-1678.
6. Papp DF, Khanna AJ, McCarthy EF, et al. Magnetic resonance imaging of soft-tissue tumours: determinate and indeterminate lesions. *J Bone Joint Surg Am* 2007; 89 Suppl 3: 103-115.
7. Lambin P, Leijenaar RTH, Deist TM, et al. Radiomics: the bridge between medical imaging and personalized medicine. *Nat Rev Clin Oncol* 2017; 14(12): 749-762.
8. Liu Z, Wang S, Dong D, et al. The applications of radiomics in precision diagnosis and treatment of oncology: Opportunities and challenges. *Theranostics* 2019; 9(5): 1303-1322.
9. Sanduleanu S, Woodruff HC, de Jong EEC, et al. Tracking tumour biology with radiomics: A systematic review utilizing a radiomics quality score. *Radiother Oncol* 2018; 127(3): 349-360.
10. Corino VDA, Montin E, Messina A, et al. Radiomic analysis of soft tissues sarcomas can distinguish intermediate from high-grade lesions. *J Magn Reson Imaging* 2018; 47(3): 829-840.
11. Spraker MB, Wootton LS, Hippe DS, et al. MRI radiomic features are independently associated with overall survival in soft tissue sarcoma. *Adv Radiation Oncol* 2019; 4(2): 413-421.
12. Crombé A, Périer C, Kind M, et al. T2-based MRI Delta-radiomics improve response prediction in soft-tissue sarcomas treated by neoadjuvant chemotherapy. *J Magn Reson Imaging* 2019; 50(2): 497-510.
13. Zhang Y, Zhu Y, Shi X, et al. Soft Tissue Sarcomas: Pre-

operative predictive histopathological grading based on radiomics of MRI. *Acad Radiol* 2019; 26(9): 1262-1268.
14. Papanikolaou N, Santinha J. An introduction to radiomics: Capturing tumour biology in space and time. *Hell J Radiol* 2018; 3(1): 61-71.
15. Manikis GC, Nikiforaki K, Papanikolaou N, et al. Diffusion modelling tool (DMT) for the analysis of diffusion weighted imaging (DWI) magnetic resonance imaging (MRI) data. *CGI* 2016; 97-100.
16. Griethuysen JJ M, Fedorov A, Parmar C, et al. Computational radiomics system to decode the radiographic phenotype. *Cancer Res* 2017; 77(21): e104-e107.
17. Pedregosa F, Varoquaux, G, Gramfort A, et al. Scikit-learn: Machine learning in Python. *J Machine Learn Res* 2011; 12: 2825-2830.
18. Ding C, Peng H. Minimum redundancy feature selection from microarray gene expression data. *J Bioinforma Comput Biol* 2005; 03(02): 185-205.
19. Chawla NV, Bowyer KW, Hall LO, et al. SMOTE: Synthetic minority over-sampling technique. *J Artif Intell Res* 2002; 16: 321-357.
20. Dutta S, Ghosh AK. On some transformations of high dimension, low sample size data for nearest neighbor classification. *Machine Learning* 2016; 102(1): 57-83.

READY - MADE CITATION

Manikis GC, Nikiforaki K, Lagoudaki E, de Bree E, Maris TG, Marias K, Karantanas AH. T2-based MRI radiomic features for discriminating tumour grading in soft tissues sarcomas. Hell J Radiol 2019; 4(3): 22-31.